THE CUTTING EDGE

AMERICAN ASSOCIATION OF Pathologists' Assistants

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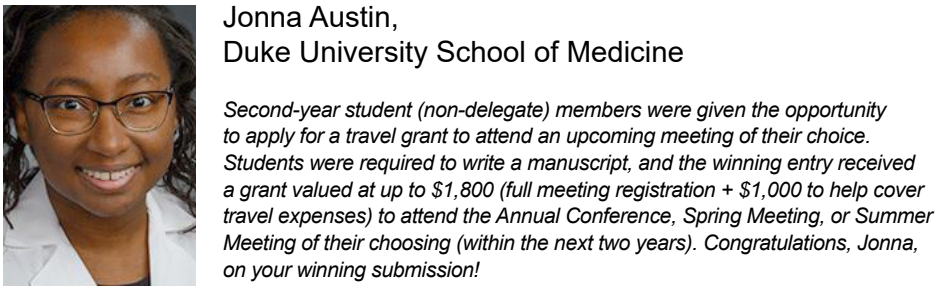

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Peer-Reviewed

ADVANCED PATHOLOGY

Epithelioid Angiosarcoma of the Maxillary Sinus: A Rare and Difficult Diagnosis

2024 AAPA Student Non-Delegate Conference Travel Grant Winner

Jonna Austin,
Duke University School of Medicine

Second-year student (non-delegate) members were given the opportunity to apply for a travel grant to attend an upcoming meeting of their choice. Students were required to write a manuscript, and the winning entry received a grant valued at up to $1,800 (full meeting registration + $1,000 to help cover travel expenses) to attend the Annual Conference, Spring Meeting, or Summer Meeting of their choosing (within the next two years). Congratulations, Jonna, on your winning submission!

Abstract
A 60-year-old female patient initially presented with right-sided facial droop and facial numbness, and a mass in her maxillary sinus was identified on imaging. Biopsies of the mass were taken, and after extensive review and expert consultation, the biopsies were signed out as intermediate to high grade sarcoma with vascular differentiation. The patient then underwent a right partial maxillectomy with en bloc orbital exenteration. Histology revealed epithelioid cells with areas of vascular differentiation, confirmed by positive immunohistochemical (IHC) vascular markers. The positive IHC stains along with the exclusion of other malignancies led to the final diagnosis of epithelioid angiosarcoma. Epithelioid angiosarcoma is an aggressive subtype of angiosarcoma characterized by epithelioid cells; it often requires IHC stains to differentiate it from other sarcomas and carcinomas. This case was notable due to the rarity of its location and the difficulty of the diagnosis.

Key Words: Angiosarcoma, epithelioid angiosarcoma, maxillectomy, head and neck cancer

Introduction

Angiosarcoma is an aggressive malignant tumor that arises from the endothelial cells of blood and lymphatic vessels.[1] It makes up 2-3% of adult soft tissue sarcomas, has a 5-year survival rate of around 30-40%, and has a local recurrence or metastasis rate of 20-40%.[1] The risk factors of angiosarcoma include radiation exposure, chronic lymphedema, environmental carcinogens (e.g., vinyl chloride, androgens, chronic arsenic ingestion, and colloidal thorium dioxide), certain genetic syndromes (e.g., neurofibromatosis type I, xeroderma pigmentosa, Ollier disease, Maffuci disease, and Klippel-Trenaunay syndrome), and arteriovenous fistulae.[1,2] While the pathogenesis is not understood, studies have shown that vascular-specific receptor tyrosine kinases are upregulated in angiosarcoma.[1]

Due to the ubiquitous nature of blood vessels and lymphatics, angiosarcoma can occur in any location in the body; therefore, the clinical presentations can vary.[3,1] That being said, it commonly presents as a cutaneous lesion (60% of total cases), appearing grossly as a hemorrhagic, spongy mass with indistinct borders.[1,3] The histological appearance of angiosarcoma also varies, so immunohistochemistry (IHC) is often required to confirm the diagnosis by positive staining of vascular and endothelial antigens.[1]

Epithelioid angiosarcoma is a subtype of angiosarcoma characterized by large, pleomorphic epithelioid cells with abundant cytoplasm and vesicular nuclei arranged in sheets and irregular vascular structures.[3] This is in contrast to the conventional appearance of angiosarcoma, which ranges from vascular

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JOURNAL SUBMISSIONS

The AAPA encourages any AAPA member or interested party to contribute articles, updates, photos or upcoming event announcements for the quarterly edition of *The Cutting Edge*. In particular, articles related to the field of pathology are welcomed. Articles and photos may be submitted electronically. (**Note: photo files must be a minimum of 300 dpi resolution.**)

Use the upload link on the AAPA website to send your contributions. All submitted material is edited for content and clarity. Research articles and case reports are subjected to a peer review process. Please see the AAPA website for complete submission details.

JOURNAL DEADLINES

Issue 1: January 2
Issue 2: April 1
Issue 3: July 1
Issue 4: October 30

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Pathologists' Assistants

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Vision:

The AAPA will be the premier professional association for pathologists' assistants, supporting the individual practitioners as they serve patients, pathologists, and the profession.

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Letter from the Editor

Beth Felicelli, PA(ASCP)CM
Editor-in-Chief

Beth Felicelli works at Western Michigan Pathology Associates in Holland, MI. She has been a member of the AAPA since 1997, and is Managing Editor of The Cutting Edge. *She serves as the Print Communication Subcommittee Chair for the MarComm Committee.*

As we wind down 2024, I hope all our members are enjoying the holiday season. Our cover manuscript is a fascinating, rare angiosarcoma of the maxillary sinus, and is an Advanced Pathology CE. This is the student non-delegate travel grant winner, Jonna Austin. Our second CE article is a General Pathology CE and the student general scholarship winner, Salem Sullivan, featuring a case study of an unexpected autopsy finding of Pott's puffy tumor. Lastly, our third peer-reviewed article is a journal submission by fellow member, Olivia Josephsen, PA(ASCP), with a case of primary tumors in both a kidney and contralateral adrenal gland.

This issue also features our annual fall conference recap. These conferences are a highlight of the year and Fort Lauderdale looked like a wonderful location! I'll be in Denver next fall and am already looking forward to it.

This is our first issue with our new management company, Kellen. I would like to extend a warm welcome to all of Kellen's staff, including our new AAPA executive director Christy Levine. Much gratitude to Michelle Sok and Association Development Services for their many years of hard work and support with the AAPA.

AAPA Core Values:

Quality Patient Care:
The AAPA ensures quality patient care is an integral component to the environment and endeavors of the Association.

Education:
The AAPA provides educational opportunities that support patient care and promote the advancement of professional competencies.

Advocacy:
The AAPA advocates for pathologists' assistants.

Collaboration:
The AAPA commits to active collaboration with outside organizations whose purposes are synergistic with the Association.

Epithelioid Angiosarcoma cont. from cover >

channels lined by well-differentiated, atypical endothelial cells to poorly differentiated spindle cells with poorly formed vascular spaces.[1,3] One study found that 16% of angiosarcoma cases were epithelioid while 44% were vasoformative, 21% were spindled, and 18% were mixed.[4] Epithelioid angiosarcoma is associated with a decreased disease-specific survival and a higher rate of local recurrence when compared to other types of angiosarcoma.[5] It shows early metastasis, particularly to soft tissues, skin, bone, and lung.[3] Like other types of angiosarcomas, epithelioid angiosarcoma arises in many locations and has diverse clinical presentations.[3] Adults in their sixties and seventies are most often affected, and there is a male predilection.3 The deep soft tissues of the extremities are the most common primary site, but it can also affect the thyroid gland, skin, adrenal glands, and bone.[2,3]

Epithelioid angiosarcoma can be difficult to differentiate from many other types of malignancies, including carcinoma, melanoma, anaplastic lymphoma, and epithelioid sarcoma because of its epithelioid appearance and potential lack of obvious vascular structures.[3] IHC plays a significant role in narrowing down the differential to the final diagnosis.[2] Common positive IHC markers include endothelial markers, such as CD31, ERG and FLI-1, mesenchymal markers, such as vimentin, and cytokeratins (PanCK), the latter being a potential diagnostic pitfall.[3] After determining the final diagnosis of epithelioid angiosarcoma, treatment generally involves surgical resection and neoadjuvant or postoperative radiation therapy or chemotherapy.[3]

The maxillary sinus is one of the rarest locations for angiosarcoma with less than 30 reported cases as of 2007.[6,7] Patients commonly present with headache, facial asymmetry, and/or diplopia.6 Epithelioid angiosarcoma of the maxillary sinus has been reported in only a few studies but appears to be extremely rare.[6,8,9] Based on the American Joint Committee on Cancer (AJCC) Cancer Staging Manual 8th edition, epithelioid angiosarcoma of the maxillary sinus is classified as a head and neck sarcoma and staged according to its size and invasion of other structures.[10]

Pertinent Patient History

A 60-year-old female patient initially presented to her primary care physician with right-sided facial droop and facial numbness with no significant past medical history or social history. The patient's family history was significant for a sibling with venous malformations. A magnetic resonance imaging (MRI) was performed which identified extensive mucosal thickening in the right maxillary sinus; this was initially interpreted as a sinus infection, and the patient was treated with multiple courses of oral antibiotics.

Several weeks later, the patient presented to a hospital with worsening symptoms, including blurred vision in the right eye, facial pain, and intense headaches. Another MRI and a computed tomography (CT) scan revealed a 4.5 x 4.1 x 3.4 cm, heterogeneous mass in the right maxillary sinus, that eroded the right orbital floor and extended into the right orbital cavity, superiorly displacing the inferior rectus muscle. It also extended posteriorly into the right masticator space, medially into the right nasal cavity, and anteriorly through the anterior wall. There was also possible involvement of the right pterygopalatine fossa, posterior right ethmoid air cell, and infraorbital nerve.

Fig. 1: Partial maxillectomy and segment of zygomatic bone with en bloc orbital exenteration.

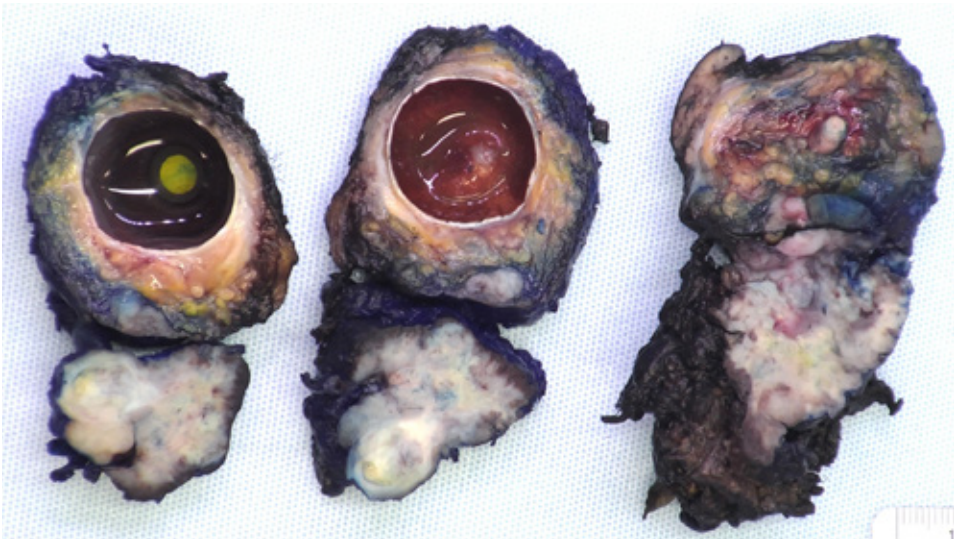

Fig. 2: Tumor posterior and inferior to the globe with invasion of the orbital adipose tissue.

Following imaging, the patient presented for a nasal endoscopy procedure and multiple biopsies were taken for pathology. The pathologist signed out the biopsies as high-grade malignancy with spindle cell and epithelioid areas, with the differential diagnosis including numerous types of sarcomas and carcinomas (e.g., epithelioid hemangioendothelioma, epithelioid sarcoma, sarcomatoid squamous cell carcinoma, and biphenotypic sinonasal sarcoma). Multiple IHC stains were performed on the biopsy, and after review at the intradepartmental consensus conference with the head and neck and soft tissue services, this case was sent out to another academic hospital for expert pathology consultation. After several weeks, the case was returned, with the expert consultation signing out the report as intermediate to high grade sarcoma with vascular differentiation. The patient's symptoms continued to worsen, and she ultimately elected for surgical treatment. She underwent a right partial maxillectomy with en bloc orbital exenteration.

Pathologic Findings

Due to the complex nature of this particular surgery, multiple tumor bed margins were submitted for frozen section to guide intraoperative resection. After negative margins were achieved surrounding the tumor, the main resection specimen was submitted to the pathology lab for permanent histologic processing.

The main excision was a 6.8 x 4.2 x 3.6 cm right partial maxillectomy and attached segment of zygomatic bone with en bloc orbital exenteration with a globe measuring 4.8 x 4.6 x 4.2 cm (**Fig. 1**). The specimen was differentially inked as follows: medial margin blue, lateral margin black, and posterior surface orange.

The optic nerve margin and the zygomatic bone margins were removed en face and then the specimen was sectioned from anterior to posterior. Sectioning demonstrated a 4.8 x 4.2 x 3.0 cm tan-gray, heterogeneous, solid tumor beneath the globe in the postero-inferior aspect of the specimen (**Fig. 2**). There was extension into the orbital soft tissue, but the globe and optic nerve margin were grossly spared from tumor involvement.

All margins, including the optic nerve, zygomatic bone margins, and orbital soft tissue margins were grossly negative for tumor, with the closest approach of 0.1 cm from the orbital soft tissue margins.

Multiple representative sections of tumor with relationships to orbital soft tissue and globe were submitted for microscopic examination. Multiple cross-sections of zygomatic bone were also submitted to make sure the tumor did not microscopically involve the bone.

Histology revealed spindle cell and epithelioid cell components with pleomorphism, abundant mitotic figures, necrosis, and areas of vascular formation (**Fig. 3**). The tumor extended to the medial and lateral soft tissue margins of the main resection specimen; however, the true (final) margins were called negative at the time of intraoperative frozen section.

As various carcinomas and sarcomas were included in the differential, multiple IHC stains for epithelial, mesenchymal, and vascular markers were ordered. S100, BAF47, and TLE1 were negative, ruling out melanoma, epithelioid sarcoma, and synovial sarcoma respectively.[11-13] Vascular markers suggesting angiosarcoma such as FLI-1 and ERG (**Fig. 4**) were positive.[14] Notably PanCK and CK8/18, which are usually carcinoma markers, were also positive; however, these stains can also be positive in other types of tumors, including angiosarcoma.15 EMA stain, another carcinoma marker, was negative.[16] The IHC stains are summarized in **Table 1**. The epithelioid components of the tumor identified histologically, along with the positive IHC vascular markers and the exclusion of other malignancies, ultimately led to the final diagnosis of epithelioid angiosarcoma.

Table 1: Summary of immunohistochemical stain

Positive	Negative
FLI-1	S100
ERG	BAF47
PanCK	TLE1
CK8/18	EMA

While working up the case, the tumor was also sent for molecular testing to help narrow down the differential; however, the molecular study found no diagnostically significant variants.

The tumor was staged according to the criteria for head and neck sarcomas from the AJCC Cancer Staging Manual 8th edition. Stages T1 (less than or equal to 2 cm), T2 (greater than 2 cm but less than or equal to 4 cm), and T3 (greater than 4 cm) are determined by size.[10] Stage T4a is determined by invasion of the orbit, skull base/dura, central compartment viscera, or pterygoid muscles or involvement of the facial skeleton.10 Stage T4b is determined by brain or prevertebral muscle invasion, carotid artery encasement, or central nervous system involvement due to perineural spread.[10] The N-stage is determined by the absence (N0) or presence of regional lymph node metastasis (N1), and the M-stage is determined by the presence of distant metastasis (M1).[10] This tumor was staged as pT4aN0 due to its orbital invasion and lack of regional lymph node or distant metastasis.

Discussion

This case report presents a patient with epithelioid angiosarcoma of the maxillary sinus who was treated with a right partial maxillectomy with en bloc orbital exenteration. Based on the AJCC Cancer Staging Manual 8th edition, the tumor was staged as pT4aN0 due to tumor invasion of the orbit.

The patient did not have a history of any risk factors of angiosarcoma. The patient presented with symptoms typical of a tumor in the maxillary sinus, but these symptoms were not specific for angiosarcoma. Grossly, the tumor did not have the typical hemorrhagic appearance of angiosarcoma. Histologically, the tumor showed epithelioid cells and vascular formation, along with positive IHC vascular markers; these findings are consistent with the diagnosis of epithelioid angiosarcoma.

After surgical resection, the patient underwent several weeks of radiation and chemotherapy. A few months later, the patient noticed right upper lip swelling, firmness, and pain. A positron emission tomography (PET) scan was completed which revealed a 2.5 x 1.4 cm right upper lip fluorodeoxyglucose (FDG)-avid lesion. A fine needle aspiration (FNA) biopsy was done on the lip lesion which ultimately revealed malignant cells, indicative of tumor recurrence. The patient was then restarted on chemotherapy. This is consistent with the high rate of local recurrence of epithelioid angiosarcoma.

This case was notable, not only because of the rarity of this particular type of malignancy and its location, but also because it was difficult to determine if the tumor was carcinoma or sarcoma based on the appearance of the initial biopsy. A diagnosis of carcinoma versus a diagnosis of sarcoma would have different staging protocols and subsequently different treatment plans for the patient. In the AJCC Cancer Staging Manual 8th edition, the tumor T-stage for carcinoma is determined by bone invasion for the maxillary sinus, while for sarcomas, the tumor T-stage would be determined by size for head and neck sarcomas.[10] Carcinomas would best be treated with surgery followed by chemotherapy; sarcomas would best be treated with neoadjuvant chemoradiation or radiation and then proceeding with surgery.[17, 18] Thus, the diagnosis of this case would have significant impacts on the patient's treatment plan and outlook.

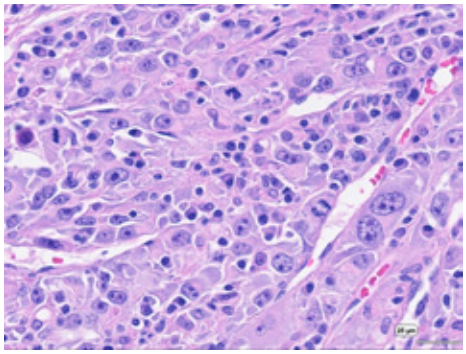

Fig. 3: Pleomorphic epithelioid cells with mitotic figures and vascular formation (40x magnification).

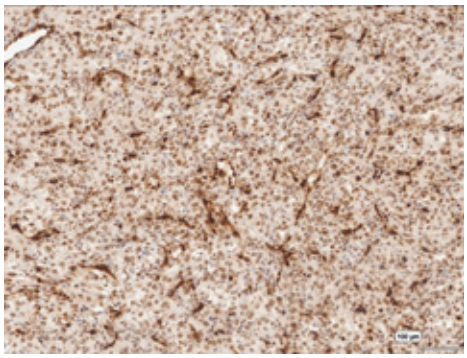

Fig. 4: Immunohistochemical stain for ERG, a vascular marker, is positive in the tumor cells (10x magnification).

At the time of gross examination, due to the complexity of the specimen, the head and neck pathologist on service was consulted before the specimen was grossed. Eye specimens are usually sectioned in the sagittal plane to show a cross section through the cornea; however, this specimen was sectioned in the coronal plane to best appreciate the tumor, as requested by the pathologist. As the tumor was a soft tissue tumor and not a primary tumor of the eye, a cross section of the cornea was not needed.

Tumor size and gross appearance, involvement of other structures, and distance to margins were important aspects to include in the gross description. Representative sections of the tumor and its relationship to other structures and the margins were important to sample and submit, to allow the pathologist to make the most accurate diagnosis and staging synoptic. Of particular importance was showing the tumor extension into the orbit, which upstaged the tumor to T4 for head and neck sarcomas.

The representative sections of the tumor played an essential role in the diagnosis as epithelioid angiosarcoma is diagnosed based on the presence of epithelioid cells, vascular formation, and vascular antigens. The section showing invasion of the orbit also allowed the tumor to be staged as T4. Thus, the pathologists' assistant had a significant impact on the diagnosis and staging of this case. This case highlights the importance of adequately submitting representative sections to allow for accurate diagnosis and staging. More importantly, whenever there is an unusual and complex specimen in the gross room, it is essential for the pathologists' assistant to consult

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Pott's Puffy Tumor: A Case of Infection and Cardiac Decompensation

Christina Jung Cho
Duke University School of Medicine

Student members were given the opportunity to apply for a $2,500 educational scholarship. Students were asked to choose a cancer and discuss its staging and the real-life impact on patient care, typing necessary sections and measurements to treatment and quality of life. Congratulations, Christina, on your winning submission!

Abstract
This case study examines a 61-year-old male who posed a diagnostic challenge after initially presenting with recurrent episodes of ventricular tachycardia and hypoxemic respiratory failure. Despite medical intervention, the patient's condition deteriorated until his passing. The subsequent autopsy revealed an unexpected finding: Pott's puffy tumor. Marked by osteomyelitis of the frontal bone and severe abscess formation, this rare complication of frontal sinusitis presents with forehead swelling, headache, fever, and rhinorrhea. The severe infection exacerbated the strain on the patient, leading to decompensated heart failure. This discovery underscores the importance of pathologists' assistants (PA) in elucidating disease mechanisms and enhancing patient outcomes through careful post-mortem examinations.

Key words
Pott's puffy tumor, osteomyelitis, frontal sinusitis, autopsy, postmortem examination

Introduction
In the post-antibiotic era, Pott's puffy tumor (PPT) is a rare complication of sinusitis. A comprehensive literature review highlights its rarity by compiling data on just 321 cases of PPT from 1950-2022.[1] Contrary to its name, coined by Percivall Pott in the 18th century, PPT is not a neoplastic condition; rather, the term "tumor" was historically used to describe swelling.[2] PPT arises from the spread of infection to the frontal bone, causing osteomyelitis and pyogenic abscess formation. Patients with PPT most often have a preceding viral or bacterial sinusitis, but may also have a history of head trauma, odontogenic injury, and substance use.[1] Approximately 30 million adults in the United States are diagnosed with sinusitis each year, with most cases (>80%) resolving without complications.[3,4] Frontal sinusitis, though relatively uncommon, poses unique risks due to its proximity to critical structures such as the orbit and the brain. The sequelae of unresolved PPT, including orbital involvement, meningitis, and brain abscesses, cannot be overlooked.[5]

Sinusitis arises from a series of events that predispose the upper airways to bacterial overgrowth. The upper airway spaces are interconnected by small passages, where the mucosa lining the airways can be either sterile or colonized with harmless bacteria. While most of these bacteria are commensal organisms, some can become pathogenic. Viral infections commonly trigger this transition, often seen as an upper respiratory infection (URI). The introduction of pathogens induces inflammation, congestion, and closure of small airway passages, and this obstruction creates an environment conducive to the overgrowth of previously harmless bacteria, resulting in infection.[6]

The spread of infection to bone can occur hematogenously, contiguously, or via direct implantation following trauma.[7] Bone and bone marrow tissue necrosis occur within the first 48 hours of the inflammatory response to bacteria. As the infection disseminates through the Haversian systems towards the periosteum, it initiates abscess formation. This subsequent abscess compromises blood supply to the affected area, resulting in tissue necrosis.[8] Should osteomyelitis persist longer than a week, the chronic inflammatory response engages in osteoclastic bone resorption, bone ingrowth, and deposition of new bone; this leads to the formation of a sequestrum, an area of dead bone, surrounded by a shell of new bone called an involucrum. Though variable, histological findings of chronic osteomyelitis usually include marrow fibrosis, sequestrum, and inflammatory infiltrates including lymphocytes and plasma cells.8 Severe frontal sinusitis poses the risk of bacterial infiltration of the frontal bone, causing frontal osteomyelitis.

An abscess within the membrane covering the outer surface of bones, known as the periosteum, is pathognomonic for diagnosing PPT. Persistent inflammation can erode the frontal bone, allowing the pyogenic debris to fill the subperiosteal space. The anterior periosteum is particularly susceptible to infection due to its rich venous plexus, which directly connects to the diploic veins of the frontal sinus cavity. These diploic veins drain the frontal sinus into dural venous complexes, enabling the infection to access the subperiosteal or subdural space.

The clinical presentation of PPT varies but typically presents with symptoms such as facial pain, headache, fever, and rhinorrhea. Patients may also occasionally exhibit focal neurological signs or changes in vision. Circumscribed swelling localized over the frontal sinus is commonly observed; however, it may also manifest as generalized edema extending to the periorbital area.[10,11]

Infections associated with PPT are classically polymicrobial, with an anaerobe-predominant microbiome. The sinus cavities are lined with specialized pseudostratified columnar epithelium that contains mucin-secreting goblet cells and cilia, which facilitate the movement of particles toward the ostia. Sinus ostial obstruction, especially in the presence of purulent secretions, leads to mucoid impaction, which decreases oxygen levels. This obstruction, along with persistent edema, swelling, and diminished blood supply creates a gradual low-oxygen environment that facilitates the growth of diverse microbial flora.[1,10]

While complications of sinusitis are rare, certain populations, such as adolescents, are more prone to developing PPT due to anatomical variation during development.[10] Continued pneumatization through late adolescence predisposes this group to bacterial infection on account of narrow sinus drainage tracts.[6] Increased vascularity of the diploic veins during development supports frontal sinus development, but also facilitates septic thrombi propagation at higher rates.[9] Additionally, the periosteum and cortex are loosely attached in development, increasing the risk to detach and subsequently form a subperiosteal abscess.[8]

The misuse of recreational substances, including cigarettes, marijuana, and cocaine, is a recognized risk factor for PPT. Both marijuana and cigarette smoking cause epithelial damage, decreased cell

viability, and increased chronic nasal symptoms.[12,13] Cocaine is notorious for its nasal complications which causes damage to epithelium, cartilage, and bone in the upper aerodigestive tract. Studies have shown that cocaine significantly reduces ciliary beat frequency over time, suggesting mechanical inhibition by cocaine crystals and impaired particle clearance.[14] Abnormal cilia function can lead to chronic inflammation due to the presence of pathogens or other environmental factors in stagnant mucus.[7,15]

Diagnosis of PPT requires a high level of suspicion as laboratory tests can sometimes help with narrowing the differential, but often do not make a definitive diagnosis of PPT. Lab values from PPT patients often detect signs of inflammation, such as elevated erythrocyte sedimentation rate (>22mm/hr in males, >29 mm/hr in females) and C-reactive protein levels (>8mg/L).[8,16] In addition to laboratory tests, imaging modalities, particularly computed tomography (CT) and magnetic resonance imaging (MRI), are crucial to visualize bone, sinus, and intracranial involvement in patients with suspected PPT infection. This not only helps guide treatment planning, but also helps rule out intracranial involvement.[1]

There are no established standard guidelines for optimal treatment of PPT yet. Typically, treatment involves a combination of antibiotic therapy and surgical intervention. Streptococcus (35.5%), Staphylococcus (21.2%), Fusobacterium (5.3%), and Pseudomonas (3.4%) make up the majority of causative organisms in PPT.[1] Due to the diverse range of microorganisms in PPT, broad-spectrum antibiotic coverage is necessary before confirming specific speciation. Endoscopic surgical drainage and bone debridement have shown success by decompressing the infected area and reducing the number of bacteria.[17,18] Antibiotic therapy alone is often insufficient to cure PPT, demonstrating the refractory nature of PPT to conventional rhinosinusitis management.

Patient History

A 61-year-old male presented to the Emergency Department (ED) with symptoms suggestive of a URI. His medical history was significant for an implantable cardioverter defibrillator (ICD), chronic hypertension, dilated cardiomyopathy, polysubstance use (tobacco, cocaine, marijuana), and class III obesity. He reported a 5-day history of congestion, productive cough, and fever. A positive respiratory syncytial virus (RSV) polymerase chain reaction test confirmed the diagnosis of a URI, and he was discharged with a cough suppressant. He returned ten days after the initial onset of symptoms with incessant ventricular tachycardia and hypoxemic respiratory failure, prompting intubation and sedation to alleviate discomfort. Notably, an initial exam reported a swollen area around the patient's left eye.

Due to the patient's incapacitation, the care team faced challenges in gathering extensive medical history. Treatment decisions were therefore based on limited information and minimally invasive tests. Given the patient's complex medical history, initial treatment primarily focused on the cardiovascular system. Chest imaging studies and cardiac catheterization revealed no significant development of disease. Despite the administration of anti-arrhythmic medications, the patient continued to experience episodes of ventricular tachycardia and cardiac arrest that were unresponsive to treatment. An evaluation of the patient's ICD was performed to ensure programming was functioning as intended. Comfort measures were put in place until the patient's passing. This overall treatment approach prioritized addressing the immediate life-threatening condition of cardiac arrhythmias while also considering the patient's comorbidities.

The lack of understanding surrounding the patient's death prompted an autopsy, revealing an unexpected finding at the conclusion of the autopsy: acute osteomyelitis of the frontal bone associated with abscess formation, also known as Pott's puffy tumor.

Results

The decedent was a well-developed male, 319 lb and 6 feet 0 inches, with a body mass index (BMI) of 43 kg/m². No evident external abnormalities or injuries were noted. Various signs of medical intervention were noted, including stellate ganglion nerve blocks, intravenous catheters, a central line, and a foley catheter.

Opening of the skull revealed purulent exudate extending throughout the frontal bone (**Fig. 1a & b**). Gross examination of the calvarial floor and skull cap showed no pathological defects in the dura. Macroscopic examination of the brain and leptomeninges showed no significant signs of pathology.

Samples of right frontal sinus contents were cultured, revealing mixed gram-positive and negative organisms, including Klebsiella pneumoniae and anaerobes, while fungal cultures were negative.

Microscopic analysis confirmed typical features of a suppurative abscess and acute osteomyelitis. Histological examination of the right frontal sinus contents revealed areas of eosinophilic fibrin mesh and basophilic leukocytes within granulation tissue (**Fig. 2**). Additionally, examination of decalcified bone near the abscess showed an acute inflammatory infiltrate of neutrophils surrounding sequestrum fragments without osteocytes in lacunae and peripheral resorption (**Fig. 3**).

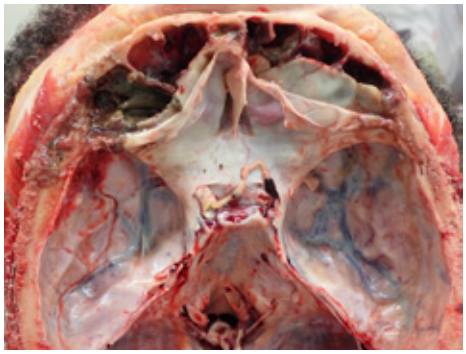

Fig. 1a: Superior view of calvarial floor.

Fig. 1b: Inferior view of skull cap. Purulant exudative material seen throughout the frontal bone.

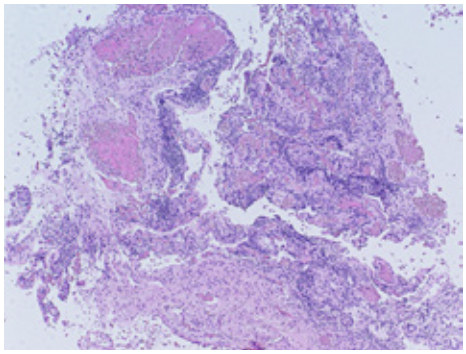

Fig. 2: Low power micrograph of sinus contents reveals areas of eosinophilic fibrin mesh and basophilic leukocytes within granulation tissue (H&E stain; 4x magnification).

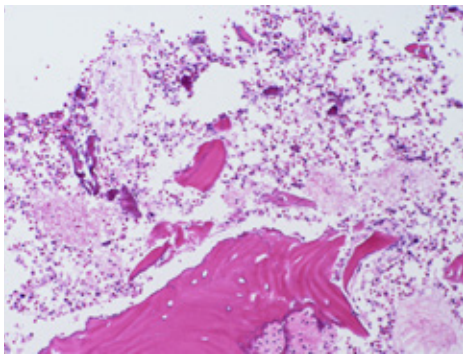

Fig. 3: Medium power micrograph of decalcified bone reveals acute inflammatory and fibrin exudate surrounding necrotic lamellar bone. Lacunae without osteocytes and irregular contours can be seen at the bottom (H&E stain; 10x magnification).

The heart was enlarged weighing 850 g, with a moderately dilated left ventricle. Thinning and scarring of the posterior left ventricular wall were present. This replacement fibrosis

Pott's Puffy Tumor cont. on page 8 >

Pott's Puffy Tumor cont. from page 7 >

was confirmed by trichrome stain; Congo Red stain was negative for amyloid deposition. Additionally, a 2 cm long chronic dissection of the ascending aortic arch was found adjacent to a mild calcified plaque. No areas of hemorrhage, softening, or discoloration were noted in the heart or aorta.

Sectioning of the lungs demonstrated moderate palpable consolidation and parenchymal mottling in the lower lobes. A moderate amount of congestion and edema were reported. Sputum cultures during hospitalization were positive for Haemophilus influenzae and gram-negative rods.

No other significant traumatic injuries or active diseases were observed in the extremities, pelvis, or abdomen that would have contributed to the cause of death.

Discussion

A review of the patient's initial intake reports at the hospital elucidates indications of the patient developing Pott's puffy tumor (PPT). The patient's longstanding comorbidities of hypertension, dilated cardiomyopathy, polysubstance use, and obesity compounded into chronic compensation, which compromised his immune response. Polysubstance use and severe obesity are risk factors seen in other PPT cases.[1,15] The URI provided an opportunistic infection for commensal bacteria to replicate excessively, leading to frontal sinusitis.[6] Hospital intake notes also describe the patient experiencing periorbital localized swelling, a common symptom associated with PPT's potential to spread to surrounding areas. Had the patient been able to communicate symptoms as they progressed, the care team may have identified the concurrent cephalic infection; unfortunately, his continued sedation and intubation were necessary to maintain relative stability.

The postmortem examination revealed manifestations of the patient's extensive cardiac history. Notably, chronic hypertension and dilated cardiomyopathy had burdened the heart with pressure overload. The clinically documented cardiac arrests and resuscitation efforts further compounded this cardiac strain. These underlying chronic and acute conditions likely contributed to the gross manifestations of cardiomegaly, ventricular dilation, and replacement fibrosis. Delayed diagnosis, compromised immune systems, extensive bone necrosis, and inadequate antibiotic therapy or surgical debridement can also increase the odds of unresolved acute osteomyelitis.[8] Similarly, the lung findings in autopsy are also consistent with the patient's history of substance use, prolonged respiratory infection, and heart disease.

This case exemplifies the complex interplay of various medical factors, with infection being a precipitating factor for decompensated heart failure. Infection significantly contributes to acute heart failure (AHF) by triggering widespread activation of the immune system through systemic inflammation. Excessive cytokine production, triggered by pathogen recognition, can lead to myocardial injury and left ventricular dysfunction by influencing both cardiostimulatory and cardiodepressant mechanisms. Moreover, cytokine overproduction disrupts signaling pathways, impairing endothelial cells which are normally responsible for microcirculation homeostasis, including blood flow distribution, tissue hypoxia, and peripheral perfusion.[19]

If PPT is suspected or discovered upon postmortem examination, the PA must carefully examine the skull and the brain, submitting sections of areas with signs of infection and adjacent normal tissue. Infection from the frontal sinus or skull can spread directly, leading to complications such as epidural or subdural empyemas, meningitis, and intracranial abscesses.[5,8] Gross examination may reveal a collection of pus within a translucent membrane, macroscopically presenting as generalized opacity or multifocal areas of thick exudate. Brain abscesses are characterized by localized areas of liquefactive necrosis, granulation tissue, and edema.[8] Understanding the characteristic gross examination findings aids in effective prosection and specimen submittal.

The discovery of PPT during autopsy was instrumental in determining a final diagnosis for this patient who initially presented with a URI. In complex cases of comorbidities, such as this, it becomes essential for the prosector to utilize a combination of medical knowledge and macroscopic expertise to draw successful conclusions. This integrated approach proves invaluable not only in this case, but also in making timely and accurate diagnoses in future cases of PPT.[20] ■

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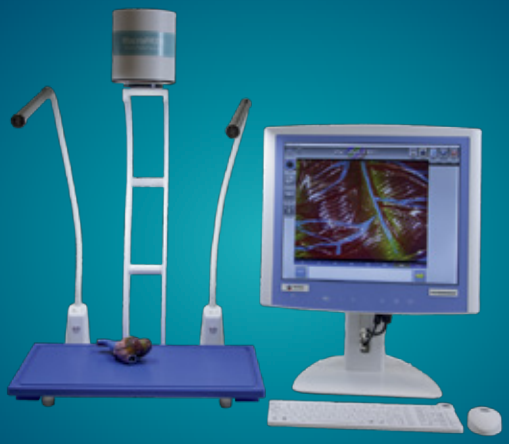

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A Case of Synchronous Clear Cell Renal Cell Carcinoma and Contralateral Adrenal Cortical Carcinoma

Samantha Pan, MHS, PA(ASCP)
West Virginia University

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Abstract
There are currently only two documented cases of synchronous renal cell carcinoma (RCC) and adrenal cortical carcinoma (ACC). This is a case of a 63-year-old male who represents a third such case. This is an unusual case due to the rarity of ACC, in addition to the rarity of a simultaneous additional primary carcinoma. RCC is known to metastasize to the contralateral adrenal gland and ACC is known to invade the adjacent kidney. Due to the similar presentation of metastatic RCC and invasive ACC there may be challenges when diagnosing these types of tumors.

Keywords
Adrenal cortical carcinoma, renal cell carcinoma, synchronous primaries

Introduction
Adrenal cortical carcinoma (ACC) is an extremely rare tumor with an incidence believed to be 1 to 2 people per million, per year.[1] Synchronous renal cell carcinoma (RCC) and adrenal cortical carcinoma is therefore thought to be extremely rare. In fact, only two cases have been reported in the literature.[2,4] In this article, we examine a third such case and discuss the pathologists' assistants' role in grossing the specimens correctly which leads to correct diagnosis and staging.

Because the adrenal gland lies adjacent to the kidney, it is not uncommon for ACC to involve the renal parenchyma. Moreover, renal cell carcinoma may metastasize to the contralateral adrenal gland.[4] Therefore, when a patient presents with a kidney mass and an additional mass in the contralateral adrenal gland, it is important to distinguish these differentials from synchronous primaries.

Patient History
The patient is a 63-year-old male who presented to the emergency department with complaints of right upper and lower abdominal pain. His prior medical history was significant for diabetes mellitus type 2, hyperlipidemia, chronic kidney disease and slowed mentation. On ultrasound two years prior, a solid mass thought to represent an angiomyolipoma was seen in the left lower pole of the kidney. A magnetic resonance image (MRI) was recommended but not pursued.

Hospital Course
On admission to the emergency department, a computed tomography (CT) scan revealed a left kidney lower pole mass concerning for renal cell carcinoma and a right adrenal mass concerning for metastatic disease. A CT-guided biopsy of the right adrenal mass revealed a primarily necrotic specimen favoring a primary adrenocortical tumor. A surgical course was recommended, and a right radical nephrectomy-adrenalectomy and left adrenal-sparing nephrectomy were performed.

Methods and Materials
The pathology department received the case in two parts: a left nephrectomy specimen and a right nephrectomy-adrenalectomy specimen.

Left Nephrectomy
The left kidney was bivalved to show a 16.0 x 10.0 x 5.0 cm kidney with a 4.1 x 2.9 x 2.6 cm well-encapsulated, golden-yellow, lower pole mass with central hemorrhage. The mass abutted but did not grossly transect the kidney capsule. The mass was confined to the renal parenchyma without extension into the renal sinus or pelvis and was 4.0 cm from the ureter and vascular margins. The remaining kidney parenchyma showed a distinct corticomedullary junction and fatty replaced renal hilum. Sections included the ureter and vascular margins, mass to kidney capsule, uninvolved renal parenchyma, and multiple sections of mass to renal pelvis and sinus.

Right Nephrectomy and Adrenalectomy (Fig. 1)
The right kidney and adrenal specimen was received with traces of possible liver parenchyma and diaphragm. The specimen was bivalved to show a 7.5 x 4.5 x 2.5 cm kidney and a 12.0 x 11.0 x 10.5 cm necrotic, grey-tan, centrally hemorrhagic mass which largely replaced the right adrenal gland. The mass invaded the right kidney and surrounding perinephric/periadrenal soft tissues without extension into the attached diaphragm or liver. The mass was 5.0 cm from the vascular and ureter margins and abutted the soft tissue margin.

In addition to the adrenal tumor invasion, the right kidney demonstrated a dilated pelvis and atrophic but distinct corticomedullary junctions. Sections included the ureter and vascular margins, mass to soft tissue margin (inked black), mass to kidney, mass to possible diaphragm and liver, representative mass, uninvolved kidney, and uninvolved adrenal gland.

Results
Histologic sections of the left kidney mass showed clear cells with occasional nucleoli compatible with clear cell renal cell carcinoma (**Fig. 2**). Immunohistochemical (IHC) stains showed tumor cells were positive for CAIX and negative for CK7 further confirming a clear cell type renal cell carcinoma (ccRCC). The multiple sections of mass to renal sinus and pelvis confirmed there was no invasion so the ccRCC was staged based on its 4.1 cm size as a pT1b cancer.[7]

The prior biopsy of the right adrenal mass was largely necrotic with foci of viable cells which showed patchy weak to moderate staining with synaptophysin, weak to moderate staining for inhibin, focal weak positive staining for Mart[1] and strong positivity for vimentin. The morphology, immunohistochemical findings, necrosis, and clinical correlation of tumor size suggested a malignant process.

Sections of the right adrenal gland mass again showed abundant necrosis. This time, however, viable tissue demonstrated a poorly differentiated mass with high nucleus-cytoplasm (N:C) ratio, very frequent mitoses, irregular nucleoli and lymphovascular invasion, all of which are features characteristic of a malignant neoplasm (**Fig. 3**). Steroidogenic factor 1 (SF1) demonstrated strong tumor cell nuclear staining supporting an adrenal cortical origin. Other immunohistochemical stains showed tumor cells were positive for inhibin, weakly positive for synaptophysin, focally positive for Mart1/melA and negative for AE1/3, S100, chromogranin, and GATA3. Furthermore, Ki-67 demonstrated a proliferation index of 50%.

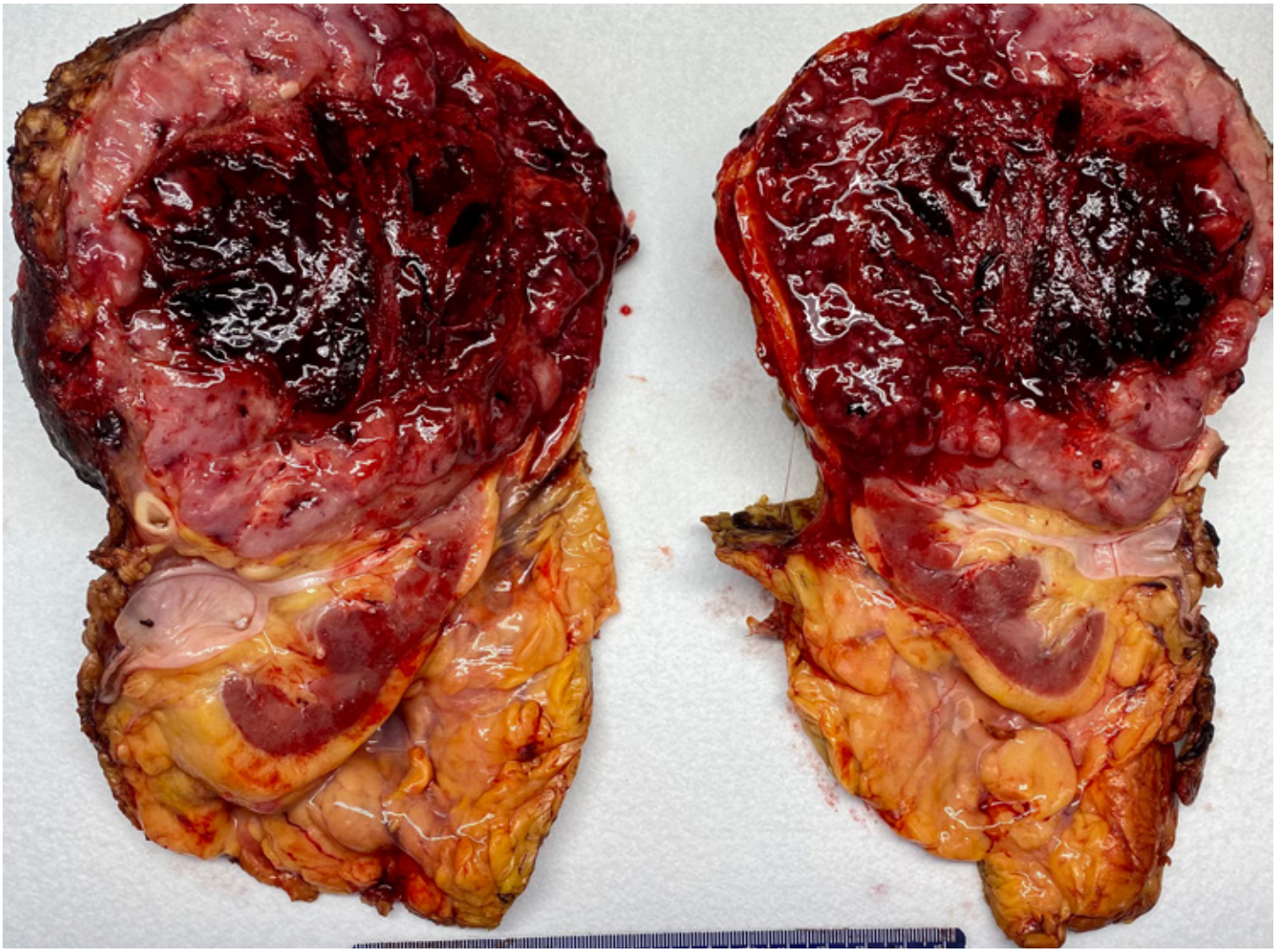

Fig. 1: Right nephrectomy and adrenalectomy showing a 12.0 x 11.0 x 10.5 cm necrotic, grey-tan, centrally hemorrhagic mass largely replacing the right adrenal gland.

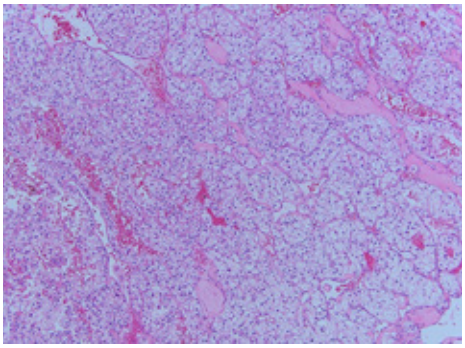

Fig. 2: Section of left renal mass demonstrating clear cells with occasional nucleoli compatible with clear cell renal cell carcinoma.

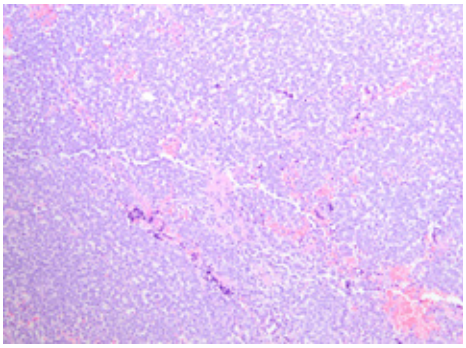

Fig. 3: Section of the right adrenal mass showing poorly differentiated cells with high N:C ratio, very frequent mitoses, and irregular nucleoli.

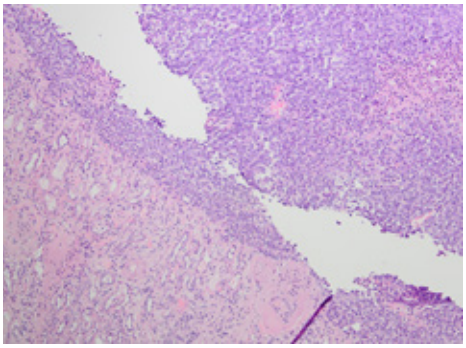

Fig. 4: Section of the right adrenal mass invading renal parenchyma.

Ultimately, this supported the diagnosis of a primary adrenal cortical carcinoma.

Microscopically, the adrenal mass did not invade the attached diaphragm or liver. However, the mass did invade the right kidney (**Fig. 4**) assigning the cancer stage of pT4.5 All surgical margins were negative for malignancy, though the soft tissue margin was difficult to assess due to friable tumor presumably transferred on top of the ink giving a "stuck on" appearance.

Discussion

ACC and RCC can go undetected for long periods of time due to their indolent growth. Most patients present clinically with either symptoms of hormone excess or symptoms due to local tumor growth, such as abdominal or flank pain, abdominal fullness, or early satiety. Other cases are incidentally diagnosed on imaging for other unrelated medical issues. ACC has a median age of diagnosis in the fifth to sixth decade with a predilection for the female population. Grossly, it appears as a well-delineated mass with yellow to brown color due to its lipid content. Currently, the only curative approach for ACC is adrenalectomy with complete tumor resection. Adjuvant therapy is then used to prevent recurrence though overall prognosis is poor.[1]

Renal cell carcinoma has been known to metastasize to the most unlikely of places, including the contralateral adrenal gland.[4,6] Therefore, it was important to differentiate

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between a metastatic renal cell carcinoma and two synchronous tumors. The tumors can be differentiated using IHC. ACC stains positive for Vimentin, Inhibin, Melan-A, C-Kit, NSE, and Synaptophysin and negative for EMA, Keratin, CEA, Chromogranin, P-53, Bcl-2, Cyclin-D1, and Calretinin.[4] Furthermore, SF1 stands out as the most reliable biomarker in the confirmation of adrenal cortical origin.[5] And moreover, ACCs typically have a Ki-67 of >5%.[1]

RCC stains positive for AE1/3, PAX8, CAIX and EMA and negative for Inhibin, CK7 and MelanA.[8] The RCC stains oppose the ACC stains allowing for pathologic differentiation.

An adrenal mass biopsy was performed with high suspicion of an RCC that had metastasized. The biopsy, however, favored a separate adrenal gland primary, so an adrenalectomy and bilateral nephrectomies were performed.

The adrenal mass resection was positive for inhibin, synaptophysin, Mart1/melA (Melan-A) and negative for chromogranin and AE1/3 (keratin). The prior biopsy was also stained with vimentin which was positive. Additionally, the mass was positive for SF1 confirming an adrenal cortical origin and the Ki-67 was 50%. All of these findings are suggestive of ACC. Therefore, the patient was diagnosed with two synchronous primaries.

Adrenal cortical carcinoma is an infrequent malignancy that is best prognostically defined by its tumor stage.[3] The College of American Pathologists (CAP) stages adrenal tumors based on size and extra-adrenal invasion. A pT4 is defined as a tumor of any size with invasion of adjacent organs to include the kidney, diaphragm, spleen, pancreas, liver or large blood vessels.5 So, due to the renal invasion in this case, the ACC was staged as a pT4. Renal cell carcinoma is a more prevalent type of cancer that receives its tumor stage based on size and renal sites involved. This tumor measured 4.1 cm and was confined to the renal parenchyma making it a pT1b stage.[7]

In conclusion, the presentation of a kidney mass with contralateral adrenal gland mass is suspicious for renal metastasis, but the specimens must be thoroughly examined for two possible primaries. This is best achieved via accurate gross examination and prosection by the pathologists' assistant and subsequent immunohistochemical stains. The outcome of the diagnosis can alter the prognosis and treatment outcomes for the patient.

Special Thanks
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Congratulations to the 2024 Journal Award Winners!

Editor in Chief of The Cutting Edge Beth Felicelli, PA(ASCP)^{CM}, and Assistant Editor Alice Levin, PA(ASCP)^{CM}, have thoughtfully selected the top three journal articles to receive cash prizes this year! All articles published in The Cutting Edge 2023 Issue 4 to 2024 Issue 3 were eligible.

The winning articles are as follows:

1st place with a $1,000 prize:
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Michaela Lewia, PA(ASCP)^{CM}, 2024 Issue 1

3rd place with a $500 prize:
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Epithelioid Angiosarcoma cont. from page 5 >

with the pathologist who will be signing out the case; it is always easier to view an intact specimen together, than try to put a sectioned specimen back together. ■

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PAs Promoting the Profession: ASCP 40 Under Forty Honorees

Nea (Moyer) Fride, MD, PA(ASCP)^{CM}

Nea (Moyer) Fride, MD, PA(ASCP)^{CM}, is a PGY1 resident pathologist at University of Wisconsin – Madison and a board-certified pathologists' assistant. She completed her master's degree at University of Maryland – Baltimore and her medical school at University of Minnesota – Duluth. She received dual bachelor's degrees in management and classical literature at Tulane University. She is a member of ASCP and the Association for Molecular Pathology. Dr. Fride continued to work as a pathologists' assistant during her medical training. She provided crucial frozen section coverage to rural Wisconsin as well as implemented digital pathology centers in rural Minnesota and Wisconsin to allow for remote frozen viewing and consultations. She is passionate about decentralized medicine and providing pathology resources for rural and underserved communities. In the era of digital pathology, she believes there are new and innovative ways that pathologists can support these continuously neglected communities. With her 10 years of experience at the gross bench, Dr. Fride focuses on fostering a collaborative environment, promoting streamlined communication, ensuring laboratory safety, and elevating the roles of pathologists' assistants, histologists, and other laboratory professionals. Dr. Fride can be found on X and Instagram as @neafride.

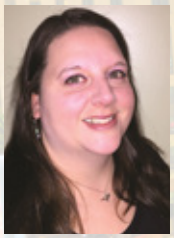
Kaysi Glasgo, MS, PA(ASCP)^{CM}

Kaysi Glasgo MS, PA(ASCP)^{CM}, is a lead pathologists' assistant at The Ohio State University Wexner Medical Center in Columbus, OH. Her current role allows her to serve as a mentor to her colleagues, fellow staff members, pathology residents, pathologists' assistant students, and future pathologists' assistant students through coordinating shadowing opportunities. Kaysi has served as the chair of the Staff Advisory Committee for Ohio State's College of Medicine throughout fiscal year 2024, having led the group in initiatives pertaining to staff support, development, and recognition. Mrs. Glasgo is passionate about people's positive experiences in the workplace by advocating for the professional development, benefit, and wellbeing of staff and learners. She received her Bachelor of Science degree in Biological Sciences at Ohio University with a Mathematics minor and completed her Master of Science in Pathologists' Assistant training at Drexel University. A member of ASCP, she is also a fellow of the American Association of Pathologists' Assistants (AAPA), where she currently serves as the vice chair of the Education Committee, chair of the Grossing Videos Subcommittee, Student Liaison for Drexel University, and as a lead content creator of the forthcoming Preceptor Program. Mrs. Glasgo enjoys sharing her passion for pathology by advocating for clinical laboratory careers in her community and alma mater, being frequently invited back to Ohio University to discuss her PA career journey. She is also an amateur ballroom dancer, avid book reader, competitive volleyball player, video and board game enthusiast, and a dog/cat/plant mom! Kaysi can be found on LinkedIn, welcoming conversation and collaboration!

Steven Springer, MS, MLS(ASCP)^{CM}, PA^{CM}, MB^{CM}

Steven Springer, MS, MLS(ASCP)^{CM}, PA^{CM}, MB^{CM}, serves as the senior director of Laboratory Operations and site head at Foundation Medicine in San Diego, CA. He holds a Bachelor of Science degree in Clinical Laboratory Sciences from the University of Iowa and dual master's degrees in Pathologists' Assistant Studies and Healthcare Administration from Rosalind Franklin University, in North Chicago, IL. Mr. Springer has consistently demonstrated a passion for innovation and entrepreneurship within the laboratory medicine field. His contributions include participating in focus panels for early-stage companies developing cutting-edge pathology devices, running a consulting firm that advises innovative biotech companies, mentoring students transitioning into the workforce, and guest lecturing at universities on the business aspects of laboratory medicine. Mr. Springer actively engages in professional organizations, serving as the vice chair of the American Association of Pathologists' Assistants Legislative Committee and as a member of ASCP's Council of Laboratory Management and Administration. Additionally, he is involved in the San Diego life sciences community, fostering opportunities for young professionals.

2025 Spring Meeting



Becky Stankowski, PA(ASCP)^{CM}
Spring Meeting Chair

The next Spring Meeting will be March 10-12, 2025, at the Embassy Suites Seattle Downtown Pioneer Square. The Pioneer Square neighborhood is full of restaurants, shops, galleries, wine tasting rooms, and fun areas to explore. Check out funky and free sites like the Waterfall Garden Park, the Last Resort Fire Department Museum, and the Klondike Gold Rush National Historical Park. Check out views from the 35th floor open air observatory at Smith Tower or the 73rd floor Skyview Observatory at Columbia Center, or head down instead of up, and take a tour of the underground storefronts and sidewalks beneath Pioneer Square, which were buried when the city rebuilt after an 1889 fire.

The hotel is just steps from Chinatown and the International District, where you will find blocks full of shops and restaurants. Visit the huge Asian supermarket Uwajimaya, which also has a food court offering a wide variety of quick-service dining options, and additional retailers, such as the Kinokuniya bookstore.

Head across the street from the hotel and take the Link light rail to explore more of Seattle. You can take the Link a few stops to the Westlake station, then take the monorail to the Space Needle, which is surrounded by museums such as the Pacific Science Center, the Chihuly Garden and Glass museum, the Seattle Children's Museum, and the Museum of Pop Culture. Pike Place Market is about a mile from the hotel, near the waterfront. You can also find the Seattle Aquarium, The Seattle Great Wheel, and docks for ferries, cruises, and other water activities along the waterfront.

Your registration for the Spring Meeting includes breakfast Monday through Wednesday, lunch on Monday and Tuesday, and coffee breaks each day. Our attendees who have limited or no reimbursement from work have found the Spring Meeting to be a great value for their conference funds. This is our "no frills, back to the basics" meeting, focused solely on CEs. Fifteen lectures for continuing education credit will be offered. Monday and Tuesday will also feature daily sponsors who will host tables to showcase the latest in pathology goods and services. This smaller meeting provides wonderful opportunities to meet up with old friends and classmates, network with new acquaintances, and chat with sponsors. Evenings are open to sightsee, find a great meal, or build relationships with PA peers.

While we are still finalizing speaker details, we expect to hear from both pathologists and pathologists' assistants on grossing topics such as liver tumors, renal tumors, esophageal and gastric tumors, breast tumors, uterine cancer, thyroid, and prostate. In addition to these topics, many of which will qualify for advanced AP credits, we are also looking forward to some lectures discussing medical education, autopsy, grossing technologies, and DEI. We expect registration to open before the end of the year. We hope to see you at the 2025 AAPA Spring Meeting in Seattle. Space is limited to the first 125 registrants, so be sure to register early to guarantee your spot! ■

Becky Stankowski works as a PA at Wisconsin Diagnostic Laboratories in Milwaukee, WI. She has been a member of AAPA since 2009, and has served as a member of the AAPA Conference Committee from 2010-2013, and as the Spring Meeting Chair since 2014.

Congratulations to the pathologists' assistants who were recognized on The Pathologist Power List 2024! The Power List celebrates laboratory medicine professionals who are at the forefront of innovation and achievement in pathology. The following nine AAPA members were honored this year:

Niki Boisso
Eric Daley
Janelle Fabian
Beth Felicelli
Ashley Illingworth
Emily Nangano
Christina Narakorn
Brenna Rondeau
Becky Stankowski

To read more about each honoree, go to **https://thepathologist.com/power-list/2024**

AAPA Calendar

December 15

- Free CE Release

January 1, 2025

- Journal Submission Deadline
- Fellow Travel Grant Deadline

January 15

- Free CE Release

January 31

- AAPA Membership Renewal Due

February 1

- Free CE Release
- Membership Renewal Standard Rate Begins

March 1

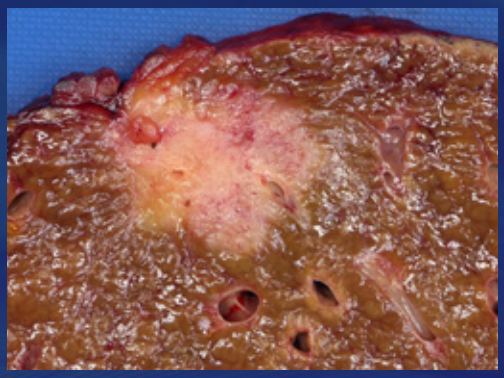
- Free CE Release
- Student Non-Delegate Travel Grant Opens

March 10–12

- AAPA Spring Meeting Seatlle, Washington

Gross Photo Unknown

Quiz Case:



This case is that of a male in his 50s with history of ETOH liver cirrhosis complicated by a segment 6 liver lesion. The patient was on the transplant list due to stage 4 cirrhosis and liver failure. A total hepatectomy was received for gross examination. Sectioning demonstrated a single, 2.8 x 2.7 x 2.1 cm, well-demarcated, white-pink, indurated, mildly nodular mass in the periphery of the right lobe, <0.1 cm to the hepatic capsule. The background liver parenchyma was diffusely micronodular. Histologically, the mass did not involve the visceral peritoneum and did not demonstrate vascular invasion.

Quiz:

1. Based off the gross and microscopic findings, this tumor is best staged as a:
    - A. pT1a
    - B. pT1b
    - C. pT2
    - D. pT3

2. This tumor mostly likely depicts a:
    - A. Hepatocellular carcinoma
    - B. Intrahepatic cholangiocarcinoma
    - C. Extra hepatic cholangiocarcinoma
    - D. Hepatic adenoma

3. This tumor can present as:
    - A. Mass forming
    - B. Periductal infiltrating
    - C. Mixed mass-forming and periductal infiltrating
    - D. All the above

Answers found on page 23

Hot Topics in Pathology

American Association of Pathologists' Assistants 49th Annual Conference

2024 Annual Conference Recap

Janelle Fabian, PA(ASCP)CM
Annual Conference Chair

We missed you in Fort Lauderdale if you didn't make it this year! The host hotel was steps from the beach and attendees enjoyed dipping their toes in the sand and lounging by the pool bar after lectures. It was another successful Fall Conference with stellar lecture topics in a beautiful backdrop.

The week kicked off Sunday night at our beach-themed Welcome Party with a sliders bar and taco bar accompanied by Tropical Rum Punch. Attendees dressed in beach attire and the room was packed! As always, it was a great time for networking and catching up with old and new friends.

On Monday we welcomed Sanjay Mukhopadhyay, MD, as our Keynote speaker who presented three lively lectures on lung cancer updates, non-neoplastic lung disease, and social media resources. Dr. Mukhopadhyay has an active presence on X (formerly Twitter) with a large following and it was fascinating to hear his take on social media and how it can advance our field.

Following our Keynote, Rob Terranova spoke on what it means to be a traveling PA. Many of you have been intrigued by the idea of traveling contracts, and he provided details of how that works. As always, we enjoyed lectures from fellow PA colleagues: Diane Spicer, PA(ASCP)CM, on normal heart anatomy; Julie Mastrodomenico, PA(ASCP)CM, on grossing breast specimens; Emma Wessner, PA(ASCP)CM, on mesothelioma; and a few others on our Education panel.

Danielle Fortuna, MD, also presented three engaging lectures on Tuesday and was a member of the Education panel. Her second lecture titled "It's Time to TNM! An Interactive Exploration of the Pathologic Tumor Staging" was a Family Feud game-style lecture with two teams battling it out over questions on staging. Name another conference where you can find this engagement!

Poster sessions offered on Monday, Tuesday, and Wednesday were packed with attendees. Thank you for supporting our student and fellow poster presenters. Tuesday evening was our Happy Hour with Exhibitors where attendees visited vendor booths and experienced new products.

Wednesday evening after lectures was our Annual 5K Fun Run and Walk sponsored by Cancer Diagnostics. Participants walked or jogged along the beach and finished up with a happy hour back at the hotel.

If you didn't make it this year, we truly missed you and hope you can join us next year. Check back in the next few months for more details about our Denver meeting, and we hope to see you in the mountains! ■

Janelle Fabian is a Technical Supervisor/ Pathologists' Assistant at Fox Chase Cancer Center in Philadelphia, PA. She has been a member of the AAPA since 2009, served as the AAPA Ad Sales Subcommittee Chair from 2014-2019, and as Fall Conference Vice Chair 2017-2019, before moving up to Chair in 2020.

Mark Your Calendar!

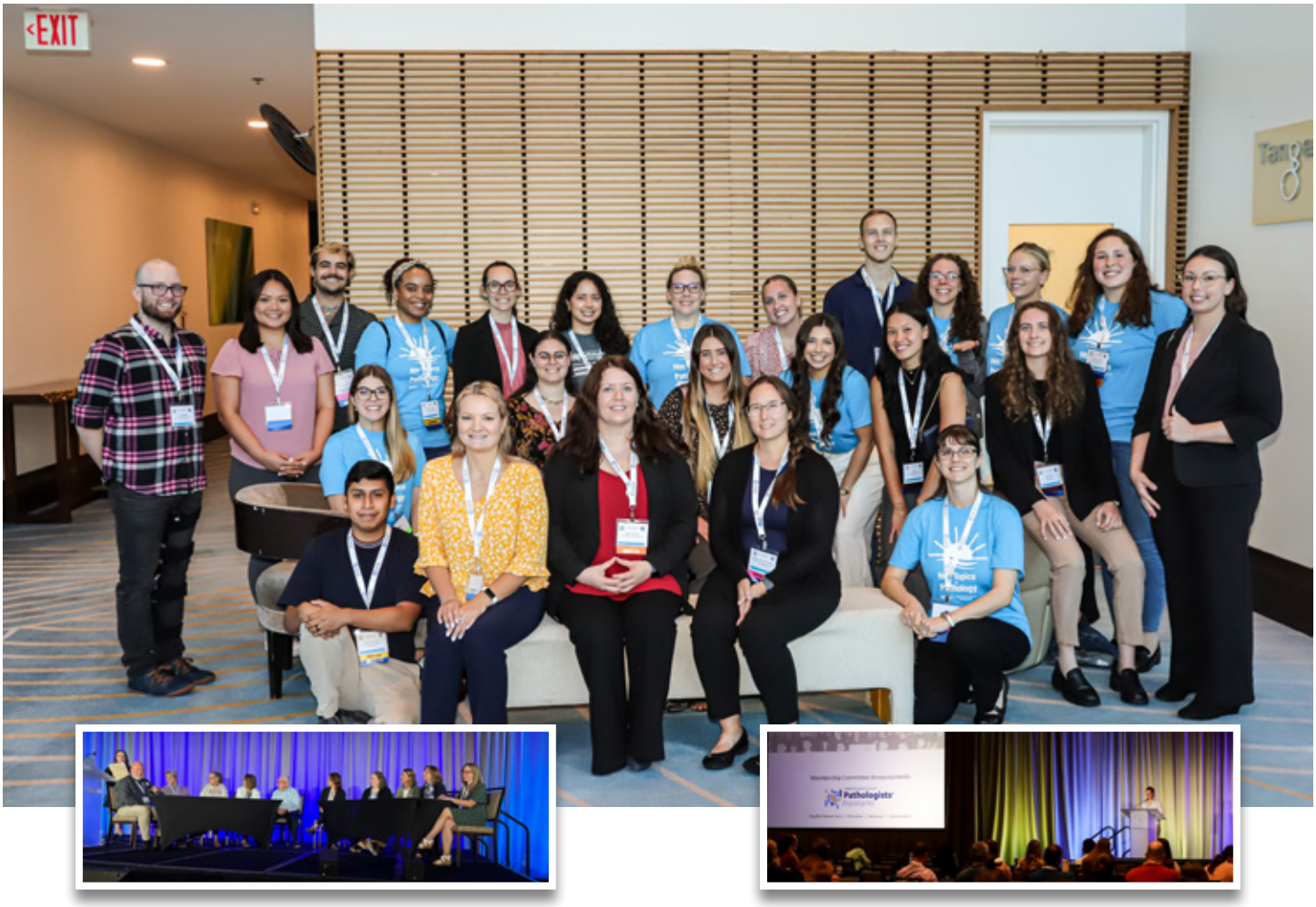
2025 Spring Meeting
March 10 - 12, 2025
Embassy Suites Downtown
Pioneer Square
Seattle, WA

2025 Summer Meeting
June 20 - 22
Virtual

50th Annual Conference
September 7 - 11, 2025
Hyatt Regency Convention Center
Denver, CO

2026 Spring Meeting
March 9 - 11, 2026
Embassy Suites at Centennial
Olympic Park
Atlanta, GA

51st Annual Conference
September 13 - 17, 2026
Sheraton Downtown
Phoenix, AZ



Board of Trustees Chair's Report

Jennifer Perez, MS, PA(ASCP)CM

I would like to thank Janelle Fabian, PA (ASCP)CM, our Annual Conference Committee Chair and the entire Education Committee for a wonderful conference this past fall in Fort Lauderdale. The conference was filled with great lectures and fun activities. If you were unable to attend this year's meeting, my hope is that you will be able to join us in Denver in 2025 or another future meeting. This year, the AAPA partnered with Kubtec Medical Imaging to host an X-ray imaging contest. Congratulations to our winner William Tsui, PA(ASCP)CM, with "Chondrosarcoma-Right proximal femur and acetabulum". Thank you to Kubtec for sponsoring this contest for our members.

As we come to the end of the year, I would like to thank our outgoing Board of Trustees (BOT) members, Mike Sovocool, PA(ASCP)CM, and Charlene Gettings, PA(ASCP)CM.

Mike Sovocool, PA(ASCP)CM, was elected to the board to complete the remainder of a three-year term following a vacancy. Mike has been serving as oversight to the Administration Committee. He was also part of the association management company RFP Search Committee. Charlene Gettings has served two, 3-year terms on the BOT. She has been serving as oversight to the Marketing/Communications (MarComm) Committee. Thank you both for your leadership and dedication.

This January we will be welcoming our newly elected board members. Congratulations to returning board member Jesse McCoy, PA(ASCP)CM. Jesse has been serving as the executive council's CFO and will continue in her role this coming year. Jesse will be serving her second 3-year term on the board.

Congratulations as well to our two first-time board members, Rachel Poon, PA(ASCP)CM, and Marissa Spencer, PA(ASCP)CM.

Rachel Poon has been the Education Committee's Ad Sales Chair for the last six years. As Ad Sales Chair, Rachel has maintained relationships with existing sponsors and vendors as well as recruiting new potential exhibitors for all our meetings. Ad Sales also works with Sustaining Members who support our association annually. Rachel has helped to promote the profession by staffing AAPA booths at conferences hosted by PA-relevant organizations such as the Association of Pathology Chairs (APC), United States and Canadian Academy of Pathology (USCAP), and American Society of Clinical Pathology (ASCP). She also assisted the Conference Committee with speaker recruitment for conferences in Chicago. Beyond the AAPA, Rachel has been a CAP inspector since 2019.

Marissa Spencer is a pathologists' assistant at Long Island Jewish Medical Center in New York. Marissa has been an active member of the AAPA since 2015, acting as the External Marketing Subcommittee Chair from 2019 to 2023 and currently as the MarComm Committee Chair. Marissa has a strong passion for advocacy of the pathologists' assistant profession and the patient care it provides. In addition to her volunteer work with the AAPA, she has held numerous leadership roles in volunteer organizations outside of the PA profession.

We are very fortunate to have such talented and dedicated individuals on the BOT. Please join me in welcoming them!

I would like to give a warm welcome to Kellen, our new association management company. The transition from ADS to Kellen occurred October 15. Kellen has hit the ground running and is meeting with all our committees. A transition team comprised of the Executive Commitee and Kellen staff has been meeting weekly to ensure a smooth transition takes place. I would like to welcome Christy Levine as our new Executive Director. Christy is a long-standing association management professional with over 20 years of experience specializing in the management of medical associations. Throughout her career, Christy has been responsible for developing and driving strategic growth and providing oversight of membership program and services.

I will close by thanking our membership and our impressive number of volunteers for the work they do for both our association and the medical community. I hope you have a very happy and healthy new year! ■

Jennifer Perez is the Lead PA at Comprehensive Pathology Associates in Miami. She has been a member of the AAPA since 2004 and is currently serving as the Chair of the Board of Trustees. Jennifer has served on the BOT since 2019 and had previously served as both Education Chair and Vice Chair for several years prior to moving up to the BOT.

Call for Speakers

Do you have a topic you are passionate about? Are you planning to attend an AAPA upcoming meeting? Share your knowledge and expertise with other pathologists' assistants (PAs) by presenting a one-hour lecture! Topics we are interested in include current trends in grossing, staging updates, autopsy, surgical pathology, laboratory safety, medical ethics, lab management, surgical procedures, malignancy and metastasis, and workplace communication. In addition to an honorarium for presenting, you can earn up to 3 CMP points for the research and preparation for the presentation.

Who should present a lecture at an upcoming meeting?

- PAs whose employers require them to present at a meeting to get approval/reimbursement
- PAs who have contributed to *The AAPA Macroscopic Examination Guidelines: Utilization of the CAP Cancer Protocols at the Surgical Gross Bench*
- PAs who have presented a poster at the Annual (Fall) Conference
- PAs who have had a peer-reviewed article published in *The Cutting Edge* or other publication
- PAs who have knowledge or expertise they would like to share with their peers!

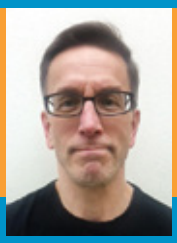
Additionally, please send us any recommended presenters for future meetings, including pathologists, surgeons, lab managers, and researchers.

50th Annual Conference in Denver
September 7-11, 2025

2026 Spring Meeting in Atlanta
March 9-11, 2026

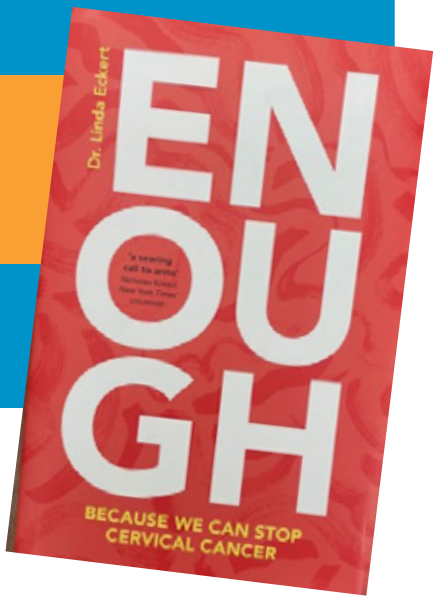
51st Annual Conference in Phoenix
September 13-17, 2026

AMERICAN ASSOCIATION OF Pathologists' Assistants



ENOUGH
Because We Can Stop Cervical Cancer

Written by Linda Eckert, MD
Review by Chet Sloski, PA(ASCP)CM



Dr. Linda Eckert is on a mission. The mission is to eradicate cervical cancer worldwide, much like we have eradicated smallpox. And since we now have an effective HPV vaccine, the comparison is apt. Although, as Dr. Eckert will explain, an HPV vaccine alone will not stamp out cervical cancer.

Dr. Eckert is a professor of obstetrics and gynecology with an infectious disease fellowship at the University of Washington. She is an internationally recognized expert in immunizations and cervical cancer prevention. She has traveled around the world in her quest to squelch cervical cancer, and her journeys have afforded her a bird's eye view of the thorny cultural, monetary, and logistical hurdles that must be overcome before we can put an end to cervical cancer.

Dr. Eckert tells us that in 1983, researchers discovered that the human papillomavirus was the cause of cervical cancer. Between 1998 and 2002, a placebo-controlled vaccine trial conducted in the United States tested a new HPV-16 vaccine in girls and women aged sixteen to twenty-three. The trial found that the vaccine prevented 100 percent of cancer-causing HPV-16 infections in all women who got the vaccine. None of the nearly 2,400 girls and women vaccinated went on to develop persistent HPV-16 infection associated with pre-cancer of the cervix. Of those who received a placebo vaccine, 41 became infected with HPV-16.

Eckert tells us that of the more than 100 types of HPV, only about 12 cause the changes in cervical cells that lead to pre-cancer. These are called "oncogenic HPV" or "high-risk HPV" types. Among these, HPV-16 causes the most cervical cancers worldwide, accounting for 50 percent of cases. It is estimated that 80 percent of sexually active people will contract one or more HPV infections in their lifetime. Luckily, about 85 to 90 percent of the time the body clears the HPV infection including those infections caused by high-risk HPVs.

The vaccine was an amazing scientific advance to be sure. But even though it has been decades since the vaccine's discovery and implementation, cervical cancer has not only not been wiped out, it is increasing. The International Agency for Research on Cancer reported in 2020 there were more than 600,000 cases of cervical cancer worldwide with more than 340,000 deaths. Without significant intervention, by 2030 that number is expected to increase to 700,00 and 400,000 respectfully. How can this be so?

A major hurdle is that the cost of the HPV vaccine, along with its associated shipment and storage costs, is prohibitive for the governments of poorer nations. Statistically, 90 percent of cervical cancer deaths occur in lower-income countries. Eckert tells us that cervical cancer is largely a disease of poor women. Currently, only 13 percent of the world's nine to fourteen-year-olds receive the HPV vaccine.

Another hurdle involves vaccine supply constraints. There is simply not enough vaccine to go around. A 2020 WHO Global Market Study showed that boys account for one-tenth of vaccine use despite tracing the number of HPV cancers in males globally to just under 60,000 vs around 570,000 for women. Ideally, both boys and girls should get immunized, but due to a global shortage of vaccine, Eckert tells us it would be prudent to focus first on the gender with the most significant cancer burden.

The same situation holds when it comes to vaccinating older women. The vaccine is most effective for young girls. According to Eckert, in the United States it takes 6,500 vaccinations of women aged 40 to prevent one case of cervical cancer. By contrast, when the vaccine is given to girls at age nine before they are sexually active, only 70 of those girls need vaccination to prevent one case of cervical cancer.

Eckert is often put in a difficult situation when her older patients in America request the vaccine. Eckert's conscience is operating on a global level in that she realizes every dose of vaccine given to a 40-year-old American is a dose of vaccine that can't be given to an eleven-year-old in sub-Saharan Africa.

The good news is that Merk, one of the makers of the vaccine (the other being GlaxoSmithKline), has plans to build two new manufacturing facilities. A Chinese manufacturer has recently developed an approved HPV vaccine and India is working on its own vaccine. Hopefully, the increase in supply will also bring the price of the vaccines down to where poorer nations can more easily afford it.

A third hurdle is the cultural stigma surrounding sexual transmitted diseases including HPV infection. Leaving aside third world countries and their cultural and social taboos, even parents in America are sometimes hesitant about vaccinating their twelve-year-old daughters for a sexually transmitted disease. As Eckert says, "You can't take the sex out of 'sexually transmitted.'" One of the parents' fears is that being vaccinated will lead to promiscuity. Eckert tells us that this is not the case and cites studies debunking this claim. If we are going to get the maximum number of girls vaccinated, we have to get rid of the social stigma that comes with HPV and HPV infection.

As stated, the vaccine alone will not wipe out cervical cancer. Even if we achieved a 100 percent vaccination rate for young girls, we would still have the scourge of cervical cancer with us. Eckert tells us that it typically takes from ten to twenty years for an HPV infection to cause cervical cancer. And once you are infected with an oncogenic HPV strain, a vaccine is impotent. Many women around the world would still develop cervical cancer in the next twenty years and this issue needs to be addressed.

One way to help women already infected with HPV is affording them ready access to proper cervical cancer screening tests such as PAP smears, HPV-DNA testing, and visual inspection with acetic acid. PAP smears alone have cut U.S. cervical cancer rates in half over the past thirty years. But in America many lack healthcare because their jobs do not offer it or they can not afford it on their own. This is especially true in rural areas where there is the additional roadblock of proximity to adequate healthcare facilities. According to Eckert, access to cervical cancer screening is heavily dependent on which state a woman lives in. Nonprofit organizations such as Planned Parenthood are doing their part in helping women gain access to healthcare including cervical cancer screening. Universal healthcare offers a potential solution for access and affordability.

Secondary to saving countless lives, screening for cervical cancer also makes fiscal sense. The cost for advanced cervical cancer treatment which can include surgery, chemotherapy and radiation, is significant and will cumulatively dwarf any costs associated with cervical cancer screening.

Abolishing cervical cancer worldwide is, indeed, a herculean task. But we have faced such tasks before and know it can be done. It will take time, money, and dedicated people working around the world, ranging from ordinary citizens to social workers to physicians. But most of all, it will take people like Dr. Eckert. ■

Chet Sloski works as a PA at North Coast Pathology in Oceanside, CA. He has been a member of AAPA since 1993, and he has been reviewing books for The Cutting Edge since 2001.

RATING: 5 out of 5 scalpels

**Disclaimer: The views and opinions expressed in this article do not necessarily reflect the views and opinions of the AAPA.*

2024 AAPA Award Winners

Jennifer Hudson, MS, PA(ASCP)CM

Rising Star Award Winner

The Rising Star award was designed to honor a member who although relatively new to volunteering for the AAPA has jumped right in and made a huge impact. Jennifer graduated from the University of Maryland in 2014 and immediately started doing great things. She has had an impactful effect on the legislative committee. Jennifer's model for running a subcommittee is one of organization, and more importantly results. She sets goals with the committee and then works in a systematic manner to achieve these goals. She is perfect example of a successful volunteer, and the AAPA is beneficiary of all her efforts.

Service Highlights

- 2020 – Joined the Legislative Subcommittee
- 2023 – Became Legislative Subcommittee Chair
- 2024 – Spearheaded "Why Licensure" campaign and will be led the licensure-focused CE webinar

Emily Nangano, MS, PA(ASCP)CM

BOT Award Winner

This award was designed to recognize a member for their steadfast work and contribution to the association, and Emily certainly fits that description. Emily has been deeply involved with the Education Committee. Emily started volunteering on the speaker recruitment team. She truly hit the ground running. She has advanced through various roles within education and most recently has become the Chair of the Education Committee. In addition to her committee work, Emily has contributed content to the Preceptor Program's Behavioral Module, conducted mock interviews for student delegates, and served as a program liaison for Drexel University. She has presented lectures at conferences, moderated panel discussions, Town Hall meetings and State of the Association meetings. She is truly such a pleasure to be around and does so much for the association.

Service Highlights

- 2017 – Joined Speaker Recruitment team
- 2021-2024 – Education Committee Vice Chair
- 2024 – Appointed as Education Committee Chair
- 2024 – Began serving as co-Student Liaison for Drexel
- Our go-to moderator for numerous Town Halls, webinars, and panels
- Lecture and poster presenter

Diane Spicer, PA(ASCP)CM

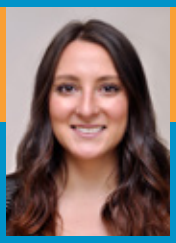
Lifetime Achievement Award Recipient

This award is for a member who has truly dedicated their career to advancing and enhancing the pathologists' assistant profession, and Diane is the embodiment of that. Her historical knowledge of our profession and, in particular the field of congenital heart defects, is incredible. The manner in which she has practiced our profession has made her a much respected professional who is sought after for her content expertise. Many of our profession now benefit from early members like Diane who demonstrated her abilities with confidence and a professionalism which were accepted by the general pathology community. Among her peers, Diane was always welcoming and eager to share her knowledge from which we all benefited and continue to benefit. She truly embodies this award.

Service Highlights

- Published author – a true wealth of knowledge who wants to share what she has learned before she retires
- Highly-regarded supporter and advocate for the PA profession
- Has presented multiple lectures and workshops at AAPA meetings
- Has been involved with speaker recruitment and the Conference Committee
- Established AAPA Congenital Heart Disease Special Interest Group (SIG)

Congratulations to all of our award winners!



Gross Photo Tutorial

Tanja Doty, MS, PA(ASCP)CM
University of Colorado School of Medicine

Discussion

Cholangiocarcinoma (CCA) is the second most common primary malignant tumor of the liver, behind hepatocellular carcinoma (HCC), and arises from the biliary tree, intra-or extrahepatic. It can present as a nonencapsulated, but well-demarcated, tan-white to gray, firm mass. Similarly to HCC, patients with Hepatitis B and C have a higher risk of developing cholangiocarcinoma, although they occur sporadically. The extrahepatic forms are also known as Klatskin tumors, which present at the junction of the right and left hepatic ducts and are the most common type of CCA. Approximately 10% are intrahepatic. Staging is based on size, multifocality, and structure invasion like vasculature and peritoneum. In this case, because the tumor is less than 5 cm and has no vascular involvement, it is staged as a pT1a. If the tumor had involved the visceral peritoneum, the stage would be pT3. Vascular involvement or multifocal lesions is categorized as pT2. CCA can present as a solid mass, ill-defined periductal infiltrating mass, or both. The CAP protocol requires specific documentation of the type of growth pattern. When grossly examining these specimens, it is important to also sample areas around the mass to rule out vascular invasion or multiple growth patterns. Because multifocality plays a big role in staging, serially sectioning the liver in small increments and submitting any suspicious lesions is best practice. ■

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Quiz answers from page 15

1. A
2. B
3. D

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