Severe Drug induced thrombotic vasculopathy in a female patient after a single dose of Taxotere

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Abstract:
Drug induced thrombotic vasculopathy can be rare side effect of several chemotherapy agents with a wide range in severity and presentation. In this case report, we discuss a patient who had a severe form of that rare outcome in association to medication that has only been reported a small handful of times. A 73 year old female was given a single dose of Taxotere, then developed severe vaso-occlusive vasculopathy which resulted in necrosis in a large portion of her body surface area of her arms and legs. After hospitalization and high dose steroids, the patient slowly recovered.

Introduction
With increasing age and increase size of the world population, the incidence of cancer is rising. In 2012 there were 14.1 million new cancer cases. That number expected to rise to 23.6 million new cases by 2030(6). Many of these new cancer cases will be treated using classical and new anti-cancer agents. Anti-cancer agents have been associated with many side effects from alopecia to xerosis(1). One of the potentially more serious side effects of these medications is vasculopathy.

Cutaneous vasculitis is a disease primarily of small and medium vessels with wide variance in presentation and severity. Drug induced is the most common cause of vasculitis but other causes include infectious, immune mediated, physiologic, and neurologic(1). The majority of drug induced cutaneous vasculitis cases can be described as direct cytotoxic damage (type II) or immune complex mediated damage (type III) (8). Severity ranges from transient purpuric lesions to widespread ischemic necrosis (8). While cutaneous findings are usually present, systemic involvement can also be present (4,5). Taxotere is a non-anthracicly anti-cancer agent. Its use has been increasing in frequency in advanced breast cancer treatment (1,2). As breast cancer disease progresses it can become anthracycline resistant, this new agent has shown to improve clinical outcomes and disease state (2). Adverse effects that are associated with Taxotere use are erythrodysesthesia, alopecia, hyperpigmentation, recall reactions, nail changes, dermal sclerosis, morbilliform rash, neutropenia, and urticaria (3,5-7). There are very few published reports of vasculitis or other vasculopathies post Taxotere administration.

Management and clinical Course:
The patient was immediately referred for inpatient care. Biopsy at that time showed vaso-occlusive disease with possible fibrin thrombi in dermal capillaries and eccrine necrosis consistent with recent chemotherapy. During hospital admission the patient was given high dose IV steroids and it was recommended that she transfer to the burn unit. The patient then refused transfer, and her condition was closely managed by a multidisciplinary team including oncology, internal medicine, hematology, pharmacy, and infectious disease until discharge. The patient underwent extensive laboratory evaluation to rule out disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, paroxysmal nocturnal hemoglobinuria, antiphospholipid syndrome and purpura fulminans which were all effectively rule out. The patient was closely monitored with strict I/Os, hydration and electrolyte monitoring, infection precautions, and antibiotic management. After the patient’s condition stabilized and improved, the patient was switched to oral steroids and discharged to outpatient management. Since discharge, the patient has continued recovery with close monitoring by several specialists including oncology, dermatology, and surgery. Close observation and follow up for infection was minimally complicated by an allergy to several antibiotic medications. During recovery, patient was offered surgical or chemical debridement of her eschars which she has elected not to pursue at this time. The patient’s sensation of her arms and legs was noted to have necrosis with eschar distributed on the arms and legs.

Discussion:
Drug induced vasculitis (DIV) is widely recognized as an adverse event to medications. Phenytoin and Hydralazine are two medications very well documented to cause vasculitis (q). The symptom severity ranges from transient purpuric lesions to widespread ischemic necrosis (8). DIV is characterized by cutaneous findings but can unusually feature systemic involvement (8). Symptoms generally arise within 7-21 days after drug administration but can reappear within 3 days upon re-exposure to the offending agent (8). The mainstay of classical treatment for DIV is systemic corticosteroids and strict discontinuation of the inciting medication (8).

In this patient Taxotere was added to further control her underlying breast cancer. Taxotere is a non-anthracicly chemotherapy medication which is becoming more widely used (1,2). The cutaneous findings in this patient where quickly identified by the administering physician and the patient was admitted to the hospital for high dose steroids and supportive care. Vascular damage can be due to direct damage to vascular epithelium with cytotoxic substances (type II) or secondary to immune complex formation when the medication acts as the hapten (type III). In this patient the managing physicians felt this case was more likely mediated by cytotoxic epithelial damage rather than antibody formation, which was mildly supported by histopathologic examination. The differential diagnosis included several other conditions including paraneoplastic eruptions, hematologic disease, and infectious disease. These conditions were all effectively ruled out through laboratory workup while admitted. Because of the extensive area of necrosis, special care was given to prevent secondary infection.

This likely represents a very rare side effect of Taxotere which is sparsely published elsewhere. Given the potentially serious nature of the adverse event, greater awareness of adverse events like these can aid physicians in the future care for their patients and avoid a more serious outcome.

Conclusion:
This case report and the very limited number of similar cases suggest that Taxotere may cause drug induced thrombotic vasculopathy. With continued research, a better understanding of this medication and its side effects can be better understood and increase awareness of its more serious side effects.

References:

Disclosures:
The authors and institutions involved in this case have no conflict of interests to disclose.