INCONTINENTIA PIGMENTI

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Incontinentia pigmenti, also known as Bloch-Sulzberger syndrome, is an uncommon sex-linked inherited syndrome reported primarily in females, as it is often lethal to male fetuses in utero. Most often diagnosed during infancy because of the striking cutaneous findings that typical follow **Blaschko lines**. During childhood persistent abnormalities of other systems (ocular, dental, skeletal, and CNS) occur, leading to blindness, neurological problems, and disabling functional deficits.

Cutaneous lesions generally progress through four stages that may show some overlap, during infancy and early childhood. However, one or more of the stages may be unapparent. The vesicular (blistering) and verrucous (wart-like) stages are inflammatory, while the pigmentary and atrophic stages are ordinarily not inflammatory.

The vesicular stage is seen in almost all cases. It is usually seen at birth, but may be congenital, generally most noted during the first 6-12 weeks of life and overlaps with the verrucous stage that peaks while the vesicular lesions are subsiding. The vesicular lesions generally clear spontaneously, sometimes going from vesicles to pustules that rupture to form crusts in hours to days but may take from 1-4 weeks to clear. These lesions may reactivate in localized crops in certain patients after infections, immunizations, or after trauma to the area. Older patients may experience the same recurrence of lesions, but usually with erythematous whorls without any vesicles. The lesions may be pruritic and can result in post-inflammatory hyperpigmentation, unassociated with the hyperpigmentation stage of the disease process.

Most patients progress, and overlap, with the second stage, the verrucous phase. This is manifested by 0.5mm – 1.0mm verrucous papules and nodules that develop as the vesicular stage is waning, but may present having developed without any vesicular lesions being noted. These warty lesions generally are noted in a linear pattern on one or more of the extremities, most notably on the dorsum of the hands and feet. But for the linear pattern of development and their great numbers, as well as their distribution, these lesions could be clinically confused with common warts. These lesions are histologically, and by nature, inflammatory, but on clinical inspection, very little inflammation may be noted. The verrucous lesions generally resolve in 1-2 years, but may persist into the patient's teen years resolving with a hyperpigmentation independent of the pigmentary and atrophic changes seen in stages 3 and 4.

The hyperpigmentation of the third stage is seen in just about all patients, beginning at 3-6 months of life. In contrast to the vesicular and verrucous lesions, the pigmentary changes are generally truncal in distribution and not proceeded by inflammatory changes. The tan-brown/blue-gray/slate-gray/blue-brown pigmentary lesions are characteristically asymmetrical. They appear as linear, swirled, streaky, and serpiginous patterns and can look artificially induced. The bands of pigmentary patterns may be purpuric appearing at onset and can raise the question of child abuse. The pigmentary patterns generally intensify during the first few years of life and then gradually fade and become persistent for years. Two-thirds of patients see resolution of the pigmentary lesions. If a biopsy of the pigmented area is undertaken, an incontinence of pigment is seen, thus the name of the syndrome: Incontinentia pigmenti. Since the pigment incontinence does not follow the pattern of the vesicular or verrucous stage lesion, it is not considered just a post-inflammatory hyperpigmentation phenomenon.

The fourth stage characterized by hypopigmentation and atrophy is seen in less than one-third of patients. The atrophic streaks, commonly hypopigmented are seen on the arms, thighs, trunk, and particularly the calves of affected individuals, but the atrophy and hypopigmentation is usually most prominent on the extremities, especially the legs. These changes can persist into adulthood and may be the only manifestation of the syndrome available for diagnosis and subsequent appropriate genetic counseling.

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Even though the cutaneous findings are most prominent and oft times diagnostic, it's imperative to remember that involvement of the teeth, eyes, or central nervous systems more often lead to morbidity. Teeth abnormalities occur in about two-thirds of patients with deciduous and permanent teeth both being affected with conical malformations of the crowns of the incisors, canines and bicuspids as well as a decreased number of teeth and/or delayed eruption of teeth.

Cicatricial (scarring) alopecia is seen in one-third to two-thirds of patients and occurs most often at the vertex of the scalp. The alopecia area does not necessarily coincide with prior vesicular or verrucous lesion involvement. With or without hair involvement, up to 50% of patients may experience nail abnormalities or even distal phalanges bone changes noted on X-ray.

Vascular compromise may lead to retinal or cerebral infarction which can cause partial or complete blindness or strokes. Strabismus as well as cataracts, optic atrophy, retinal neovascularization or detachment can occur. A small percentage of patients may even experience bilateral blindness. About 20% of patients with incontinentia pigmenti will have major eye abnormalities, with approximately one-third of patients having some ocular pathology. Ocular examination in infants with incontinentia pigmenti should be done monthly during the first four months and then every three months through the first year of life. Ophthalmological exams should continue twice yearly to age three, and then annually thereafter.

About one-third to one-half of patients have neurological deficits with motor problems such as psychomotor retardation, spasticity, or paralysis, and about 20% will have mental retardation, which can be severe, hydrocephalus, microcephaly, or cortical atrophy. Repetitive strokes have been reported and because of the vesicular eruption, a misdiagnosis of neonatal herpes simplex can result. Seizure disorders are noted in 15-20% of patient.

The diagnosis of incontinentia pigmenti can often be made on clinical grounds due the highly characteristic linear cutaneous inflammation and serpiginous pigmentary findings. **Biopsy** of the vesicular and/or verrucous lesions can also aid in the diagnosis. Because of the multi-system involvement, appropriate consultations should be considered: ophthalmology, neurology, dental, radiology as well as appropriate evaluation and work-up for any boney abnormalities.

There are no definitive curative therapies for incontinentia pigmenti. Treatment of the vesicular lesions can often be accomplished with wet to dry dressings; however, excessive cooling of infants and small children should be avoided. The self-limiting nature of the vesicles usually precludes the need for **topical steroids** or non-steroid anti-inflammatory products such as **tacrolimus**, but with significant inflammation, they may be helpful. Cover-up camouflage makeups can be used in older patients to hide the hyper and hypopigmented areas. Regular dental and eye exams are crucial for all patients with subsequent treatment of abnormalities undertaken when appropriate. Appropriate therapies for seizures and other neurological manifestations should be utilized as well.

Genetic counseling should be undertaken. Any female child can be affected and because of increased spontaneous abortions, there is a decreased chance of bearing any male children.

Prognostically, the cutaneous manifestations of this condition resolve completely in the majority of patients and residual pigmentations can be ignored or camouflaged with appropriate makeups. The neurological, dental, ophthalmic and other non-cutaneous deficits will obviously require ongoing evaluations and care.

For more information please see **www.ipif.org**

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