

Ophthalmologic Manifestations of Cutaneous Conditions

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Abstract

Many cutaneous conditions have associated ophthalmologic findings, which are important to recognize for both dermatologists and ophthalmologists. This review highlights some important ophthalmologic manifestations associated with neurocutaneous syndromes and inherited connective tissue diseases.

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Neurocutaneous Syndromes

Type 1 neurofibromatosis (NF; von Recklinghausen's disease) is an autosomal dominant condition with variable expressivity that is linked to chromosome 17. Among its diagnostic criteria, two are ophthalmologic: Lisch nodules (more than 2 are required to fulfill one criterion) and optic nerve or pathway glioma. Lisch nodules (iris hamartomas) appear as small sharply demarcated hyperpigmented excrescences on the iris ranging in color from tan to dark brown and are present in up to 97% of patients who are 6 years old or more [1]. These are best visualized

using a slitlamp. Approximately 50% of patients with NF-1 have choroidal lesions, evident ophthalmoscopically as yellow-white to dark brown spots in the posterior pole. Hyperpigmentation of the conjunctiva and uveal tract, as well as glaucoma may also occur [1, 2]. In patients with glial cell tumors, astrocytomas may also compress the optic nerve and chiasm and cause proptosis and visual loss [1]. Furthermore, plexiform neurofibromas of the upper eyelid can result in significant eyelid disfiguration and ptosis [2].

Type 2 NF is characterized by bilateral vestibular schwannomas and other central nervous system tumors. Like NF-1, it is inherited in an autosomal dominant pattern but is linked to chromosome 22. While cutaneous lesions are infrequent in NF-2, the development of cataracts has been reported to occur in up to 67% of cases [3]. Although many NF-2 patients lack Lisch nodules, their presence, especially in the younger age groups, may be an indicator of a more severe NF-2 phenotype [4]. Moreover, retinal hamartomas and ocular motor abnormalities can occur, although rarely. Ocular changes in NF-2 often appear before related skin changes, central nervous system tumors or vestibular schwannomas and therefore may be a useful diagnostic tool [4].

Tuberous sclerosis (TS), also known as Bourneville syndrome, is an autosomal dominant condition of cellular differentiation and proliferation characterized by hamartomatous formation in many organs (e.g. skin,

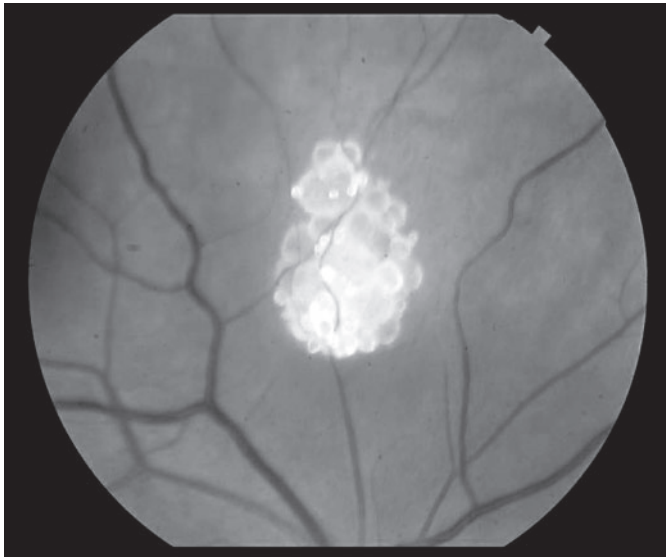


Fig. 1. Retinal phakoma resembling a well-demarcated yellow-white mass in the retina of a patient with TS.

brain, eye, kidney, heart). TS has been linked to chromosome 9. Mental retardation, seizures and various dermatologic findings including hypomelanotic macules and facial angiofibromas, comprise the triad commonly associated with TS. Consensus diagnostic criteria of TS have recently been revised [5]. Retinal phakomas, which represent hamartomatous growth of nerve fibers on the retina, are the most characteristic ophthalmic finding in TS (fig. 1). These may appear as a flat translucent gray-white lesion with indistinct margins (most common), a well-demarcated yellow-white elevation resembling tapioca grains or an intermediate lesion with characteristics of both [2, 6]. Hyper- and hypopigmented lesions in the uveal tract are also characteristic of TS, but are not known to have any clinical significance [6].

Von Hippel-Lindau syndrome is a rare autosomal dominant disorder characterized by vascular tumors (hemangioblastomas) of the central nervous system and retina, a high incidence of clear cell renal cell carcinoma and pheochromocytomas, as well as multiple visceral cysts of the kidney, pancreas and liver. Retinal hemangioblastomas are estimated to occur with a prevalence of 30–58% [7]. Initially, the lesion appears as an erythematous spot in the fundus that gradually enlarges into a pink globular mass with prominent vessels running between the lesion and the disc [2]. Argon laser photocoagulation or cryotherapy can be successful in controlling 74% of

extrapapillary hemangioblastomas [8], but there is controversy as to the consequences of nontreatment. Singh et al. [8] noted that 82% (63 lesions) remained stable for a median follow-up time of 84 months, and those that progressed were successfully controlled with photocoagulation or cryotherapy. However, untreated hemangioblastomas can eventually lead to retinal detachment and blindness in some patients [7]. A careful follow-up is required to determine the timing of treatment.

Sturge-Weber syndrome is a rare embryonic developmental disorder characterized by cerebral calcifications, seizures and facial cutaneous angiomas [2]. Ocular manifestations of Sturge-Weber syndrome include glaucoma (42%), vascular malformations of the retina, choroid, episclera and conjunctiva, and melanosis of the iris [2, 9]. Glaucoma is by far the most serious ocular complication of Sturge-Weber syndrome [2], and it is often refractory to topical agents (i.e. β -blockers, carbonic anhydrase inhibitors) [9]. There are multiple mechanisms for glaucoma in Sturge-Weber syndrome including raised episcleral venous pressure, angle closure due to anterior rotation of the ciliary body as a result of choroidal effusions, congenital angle anomalies and ciliary body hypersecretion due to the presence of a choroidal cavernous hemangioma. Moreover, choroidal angiomatosis is progressive and frequently results in retinal detachment. A timely diagnosis of both glaucoma and choroidal angiomatosis is essential, and more aggressive surgical management is often warranted to prevent visual loss and blindness [2, 9].

Hereditary Connective Tissue Disorders

Ehlers-Danlos syndrome (EDS) represents a group of disorders characterized by skin hyperextensibility, joint hypermobility, easy bruising and poor wound healing. The most common ocular manifestation of EDS is the presence of prominent epicanthal folds [10], which allows for effortless eversion of the upper eyelids (Metenier's sign) [11]. Almost all types of EDS are characterized by ocular fragility (resulting in corneal and or scleral rupture), ectopia lentis (fig. 2) and retinal detachment following minimal trauma. Other ocular abnormalities include strabismus, blue sclera, myopia, angioid streaks (fig. 3) and glaucoma [10, 11]. Autosomal recessive EDS type VI, also known as oculoscoliotic EDS, is specifically associated with ocular fragility and skeletal scoliosis [11].

Marfan's syndrome is an autosomal dominant inherited disorder characterized by musculoskeletal, cardio-

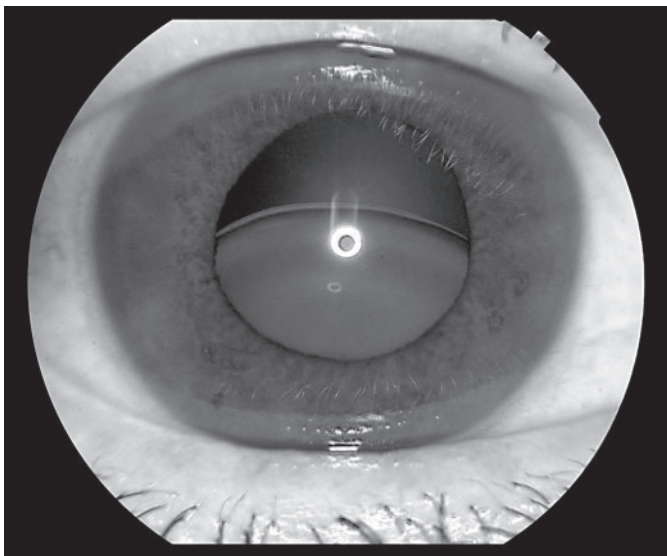


Fig. 2. Ectopia lentis in EDS and Marfan's syndrome.



Fig. 3. Angioid streaks visible as a reddish brown network in the choroid and retinal pigment epithelium in a patient with pseudoxanthoma elasticum.

vascular and ocular abnormalities. The most typical ocular manifestation in this syndrome is bilateral ectopia lentis in up to 80% of patients, often occurring in early childhood (fig. 2) [12]. Additional ocular findings in Marfan's syndrome include amblyopia, cataracts, glaucoma, megalocornea, myopia, strabismus and retinal detachment [12].

Osteogenesis imperfecta encompasses a range of inherited conditions with ocular and bony manifestations secondary to a defect in type I collagen. It typically presents with cutaneous atrophy and easy bruising, bone fragility and deafness [12]. The most common ocular manifestation in most forms of osteogenesis imperfecta is blue sclera [13], which has been attributed to enhancement of the uveal pigment secondary to increased scleral translucency [12]. Other ocular features include decreased central corneal thickness and glaucoma [13].

Pseudoxanthoma elasticum (PXE) is an inherited disorder characterized by the destruction and calcification of elastic fibers resulting in damage to cutaneous, ocular and vascular systems [12]. Angioid streaks, which affect approximately 85% of patients with PXE [12], resemble reddish brown pigment originating from the optic nerve (fig. 3). They are caused by breaks in collagen and elastic tissue in Bruch's membrane [14]. When angioid streaks are present in combination with thickened, pebbled, yellow plaques of inelastic intertriginous skin, the condition

is known as Grönblad-Strandberg syndrome [12]. Although angioid streaks are characteristic for PXE, they are not pathognomonic and can be encountered in a variety of metabolic and heritable disorders, including Paget's disease of the bone, sickle cell anemia, thalassemia, EDS and lead poisoning. They can also be idiopathic. Additional ophthalmologic findings in PXE can include mottled hyperpigmentation (referred to as 'peau d'orange'), optic drusen and 'owl's eyes' (paired hyperpigmented spots), disciform hemorrhagic maculopathy, chorioretinal arteriovenous abnormalities and yellowish deposits at the periphery of the fundus (salmon spots) [12].

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