Case Report

Pseudoxanthoma elasticum: A case report

Ruchika Agarwal

Abstract

Pseudoxanthoma elasticum (PXE) is a rare genetic disorder that mainly involves the skin, eyes, and cardiovascular system. We are reporting a case of pseudoxanthoma elasticum which involves neck, together with angioid streaks of fundi, but without cardiovascular events. Skin biopsy specimen was taken and was stained with hematoxylin and eosin (H&E) that revealed clumping and fragmentation of elastic fibers. These features confirmed histopathological diagnosis of PXE.

Key words: Pseudoxanthoma elasticum (PXE).

Introduction

Pseudoxanthoma elasticum is a rare inherited multisystem disorder that is characterized by a pathological mineralization of the elastic connective tissue, which involves predominantly the skin, eyes and cardiovascular system. Skin and ocular manifestations of pseudoxanthoma elasticum are referred to as Grönblad-Strandberg syndrome. The condition was named by Darier in 1896, who sought to differentiate PXE from common xanthomas. Cutaneous changes are usually the first manifestation of pseudoxanthoma elasticum, but do not become recognizable until the second or third decade of life [1]. Pseudoxanthoma elasticum can be transmitted as an autosomal dominant trait (Type I and Type II) or an autosomal recessive trait (Type I and TypeII). PXE has been estimated to have a prevalence ranging from 1 in 70,000 to 1 in 1 million [2, 3].

In some families the cutaneous changes may be predominant with relatively mild eye or cardiovascular.involvement, while in other families the involvement of eye and cardiovascular system may be severe with limitedskin findings .Its cause lies on mutations in the ABCC6 gene, which lead to reduction or absence of the transmembrane transport ADP dependent protein (MRP6), causing an accumulation ofextracellular material and subsequent deposition of calcium and other minerals in the elastic tissue. The first lesions to be noted are on the skin in the lateral part of the neck. Skin lesions begin in childhood but they are not usually noted until adolescence. Small, yellow papules are seen in a linear or reticular pattern and may coalesce to form plaques [4-8].

Case Report

A female 24 yr old was diagnosed as pseuso xanthoma elasticum by Skin and VD department MLB Medical College Jhansi and referred to ophthalmic department MLB Medical College Jhansi for fundus examination. There was no visual complaint.

On examination patient had thickening, wrinkling over the nape of neck. The skin abnormally came as rubber on pulling out to acertain extent (loss of elasticity).

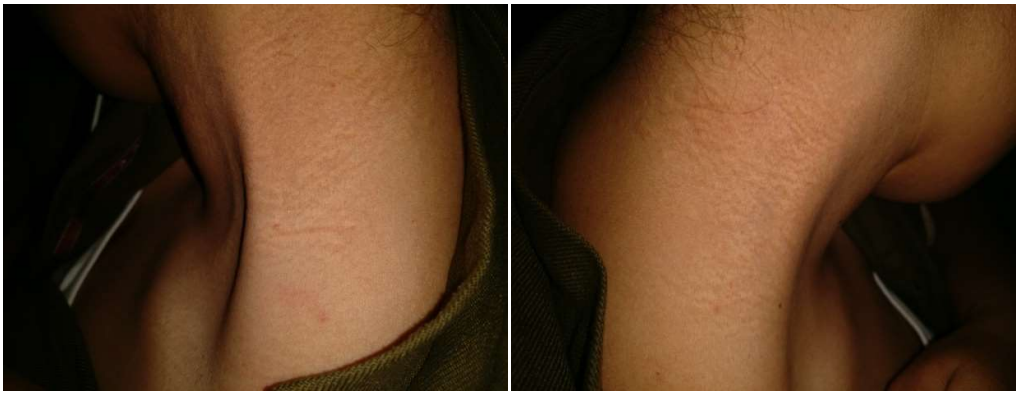

Figure 1-Skin lesions showing reticular pattern wrinkling at the nape of the neck

Rama Medical College, Hospital and Research Centre, Mandhana, Kanpur, Uttar Pradesh-209217, India.
Email id: ruchidrjain@gmail.com

Left- eye: Adenexa and anterior segment were normal. Tension was normal. Vision was 6/6

Fundus: The disc was normal in colour and was surrounded by a light grey zone of 1/4 disc diameter in

width from which small grey streaks of less than 1/4 disc diameter width, ran peripherally in radial direction with tapering ends. They were deeper to the retinal vessels, some were continuous and some were interrupted. Retinal vessels were normal.

Right Eye: Adnexa and anterior segment were normal. Tension was normal. Vision was 6/6.
Fundus: Almost a similar picture to that of the left eye with angioid streaks.

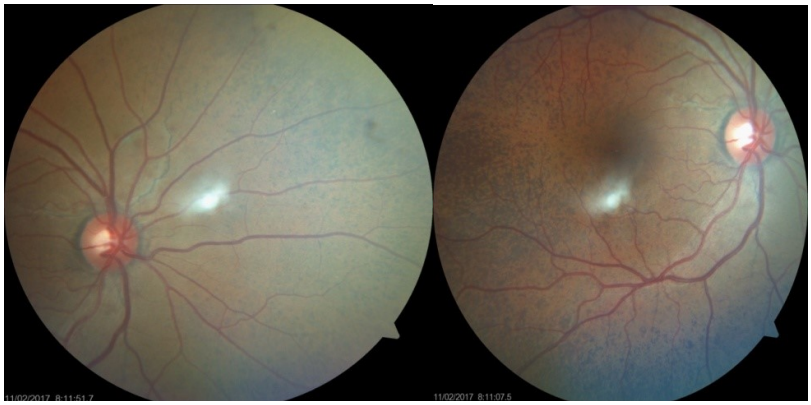

Figure 2.Fundus Photograph showing Angiod streaks running in radialy in the parapapillary region.

Investigations

Routine investigations were normal.

Discussion

Pseudoxanthoma elasticum is a rare inherited multisystem disorder that is characterized by a pathological mineralization of the elastic connective tissue, which involves predominantly the skin, eyes and cardiovascular system. Skin and ocular manifestations of pseudoxanthoma elasticum are referred to as Grönblad-Strandberg syndrome. The basic fault in PXE appears torelate to the mutations in the transporter genes MRP6 or ABCC6, which has been mapped to chromosome 16p13. Mutations in the ABCC6 gene cause absence or non-functional MRP6 protein which may cause impairment of release of ATP from cells. As a result calcium and other minerals accumulate in elastic fibers of the skin, blood vessels, eyes, and other tissues affected by PXE [9]. There are two types of autosomal dominant pseudoxanthoma elasticum; type I is characterized by a classic skin lesions, intermittent claudication, severe recurrent angina, and severe chorioretinitis, even blindness, and type II is a much milder form, with a macular rash, mild retinal degeneration and no vascular complications [2]. Autosomal recessive pseudoxanthoma elasticum also has two types: recessive type I has the characteristic flexural distributed skin rash, moderately severe ocular disease, and increased risk to gastrointestinal bleeding, and recessive type II is much rarer and affects the entire skin which is soft, lax and wrinkled. It shows extensiveinfiltration with degenerated elastic fibers [3]. Cutaneous changes are usually the first manifestation of pseudoxanthoma elasticum. These lesions starts during childhood and progresses sluggishly during adulthood. Small, yellowish papular lesions in a linear or reticular pattern is seen on the neck, axillae, groin, and flexuralcreases. On advancement of the disease, the skin may become loose, lax and redundant and it hangs down infolds producing the typical plucked chicken appearance [10].The main ocular manifestation consists in the presence of angioid streaks visualized by ophthalmoscopy,which represent the calcium deposit in the retina Bruch's membrane and may lead to the rupture of vessels, with subsequent neovascularization that is associated with retinal hemorrhages and may lead toprogressive loss of visual acuity. The cases of ocular involvement must be monitored by periodical fluorescein angiography and ophthalmoscopy. [2, 6] During fluorescein angiography, angioid streaks from increased visibility of the choroid due to the local defect in Bruch's membrane and in the later phase dueto the leakage from the adjacent choriocapillaris. The frequent clinical association of angioid streaks anddisciform degeneration at the macular area and the similarity of the histopathological changes indicate somepathogenetic link between them. Macular involvement with loss of vision usually appears after age 40 years.Angioid streaks may progress slowly or remain stationary for years. Two possibilities are suggested to be the cause of angioid streaks: [1] Degenerative changes in Bruch's membrane which are incidental to several other pathological conditions; [2] Primary degeneration of the Bruch's membrane which is bilateral and inheritedwith elastic tissue degeneration in other tissues of the body. Bruch membrane defects predispose to choroidalneovascularization, which may cause subretinal hemorrhage and ultimately disciform degeneration. Lossvisual field due to optic disk drusen has been reported in some patients with pseudoxanthoma elasticum who have angioid streaks.

The prognosis is often very poor because of choroidal ruptures and retinal hemorrhages which may occur in patients with pseudoxanthoma elasticum due to minor ocular trauma [13, 14]. Choroidalneovascularization reveal (CNV) can be treated with surgery, photocoagulation, and photodynamic therapy withvarying success [15]. Intravitreal antivascular endothelial growth factor (anti-VEGF) agents should be considered for patients with choroidal neovascularization. Intravitreal injection of aflibercept or ranibizumab or the off-labeluse of bevacizumab seems to maintain visual acuity.

In the cardiovascular system the calcification of artery walls of small and medium caliber is observed, which results in early atheromatosis. It can present itself through gastrointestinal hemorrhages, hypertension, acute myocardial infarction, cerebrovascular accident and peripheral arterial occlusion. [1,2,7,8]. The diagnosis is clinical, associated with anatomopathologicalm examination, which is characteristic and reveals fragmented and distorted elastic fibers in the reticular and deep dermis. These changes are more evident in the Verhoeff, Van Giesson and Calleja stains, specific for the elastic tissue. The calcification of fibers can be clearly identified in stains for calcium, as the Von Kossa. [1, 2]

To this day, there is no specific treatment and the therapeutical management is based on prevention, tracking and monitoring of complications associated with the disease. Complementary exams such as blood count, lipid profile, echocardiogram, and ophthalmologic monitoring should be made whenever necessary. The diet supplemented with magnesium and vitamin K may extend the progression of the disease and improve the quality of life of the patients. Surgery for aesthetic improvement of cutaneouslesions is not routinely performed due to the risk of complications with formation of keloids, dehiscence

And extrusion of calcium particles through the surgical wound. [9, 10] The reported cases presented typical clinicalmanifestations of pseudoxanthoma elasticum, and the diagnosis was confirmed after anatomopathologicalexamination. The ocular involvement confirmed by fluorescein angiography, which revealed the presence of hyperfluorescent angioid streaks arising from changes to retina, Bruch's membrane by deposition of calcium. However, a significant involvement of the cardiovascular system was not detected in the case. In conclusion, despite the rarity of this pathology, one must be aware of the need for early diagnosis, recognizing the typical cutaneous manifestations of the disease, for adequate handling and better management of the associated complications when these are present, making periodical ophthalmologic and cardiovascular follow-ups imperative.

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