**Pseudoxanthoma Elasticum Revealed by Bilateral Macular Neovascularization**

Manal Chafik\*, Malik Alkteish, Mohamed Ammar, Said Nado, Soufiane Dhaoui, Fatima-zahra Mabrouki, Siham Chariba, Asmae Maadane, and Rachid Sekhsoukh

Ophthalmology Department, Mohammed VI University Hospital, Morocco.

**\*Corresponding Author:** Email: [manalchafik@hotmail.fr](mailto:manalchafik@hotmail.fr)

**Abstract**

We present the rare case of a 67-year-old male patient, with a history of stunted cardiopathy of unknown etiology especially without associated cardiovascular risk factors, who presented a progressive bilateral visual loss. The best corrected visual acuity was 1/10 on both eyes with normal anterior segment and intra-ocular pressure. Fundus examination showed angioid streaks with bilateral macular neovascular membrane more severe in the right eye.The macular optical coherence tomography showed choroidal neovessels associated with intra-retinal cystoid macular edema in both eyes.A skin examination revealed an advanced pseudoxanthoma elasticum undiagnosed, which is at the origin of the angioid streaks with macular neovascularization, and most likely the cardiopathy.

**Keywords:** Angioid streaks, macular choroidal neovessels, Pseudoxanthoma elasticum.

1. **INTRODUCTION**

Pseudoxanthoma elasticum (PXE) is a rare genetic metabolic disorder characterised by cutaneous, ocular and cardiovascular involvement.

Few studies, in the PubMed database, report cases of PXE revealed by ocular involvement.

The aim of this study is to report the case of a patient with significant visual loss associated with advanced bilateral macular neovascularization revealing a PXE.

1. **CASE REPORT**

A 67-year-old male patient, followed in the cardiology department for a stunted, cardiopathy of undetermined etiology, presented with a progressive bilateral decrease in visual acuity that has developed over the past year. Upon ophthalmological examination, the best corrected visual acuity was 1/10 in both eyes, along with a normal anterior segment and intraocular pressure. The fundus examination showed a clear vitreous, and the presence of dark red angioid streaks, originating from the papillary region, associated with a large macular neovascular membrane in the right eye (RE) and a peri macular bleeding spot in the left eye (LE) **[Figure 1].**

Macular optical coherence tomography (OCT) revealed a subretinal hyper-reflective materiel deposit associated with intra-retinal cystoid macular edema in both eyes **[Figure 2].**

A comprehensive evaluation of the patient was conducted to look for signs that support an etiologic diagnosis of the angioid streaks, including a cutaneous examination which revealed a skin laxity, with multiple red papules on the lateral sides of the neck giving a “plucked chicken skin” appearance, and yellowish skin streaks in the popliteal fossae and axillary creases. The examination also revealed two raised, beaded, reddish skin lesions, with irregular edges located on the posterior side of the right thigh and the upper inner side of the right arm **[Figure 3].**

A skin biopsy was carried out, which established the diagnosis of pseudoxanthoma elasticum, with two perforated PXE lesions.

The patient underwent a cardiology consultation to establish the underlying cause of his cardiopathy and received monthly intravitreal injections of Anti–vascular endothelial growth factor (Anti-VEGF) to manage macular neovascularization.

1. **DISCUSSION**

Pseudoxanthoma elasticum (PXE) is a rare autosomal recessive metabolic disorder characterized by calcification of elastic fibers in the dermis of the skin, the Bruch's membrane of the eye and the walls of medium caliber arteries [1,2].

The disease is secondary to a mutation in the ABCC6 gene on chromosome 16, resulting in abnormal mineralization with excessive calcification [3].

Skin involvement is often early, starting at a young age, but diagnosis is usually not made until there is a systemic complication or ocular involvement, around the 3rd or 4th decade of life [4].

Clinically, the skin is affected in the form of yellowish papules, first on the neck and then on other flexural areas, giving a plucked chicken skin, cobblestone or Moroccan leather appearance. Skin laxity, an exaggerated chin fold or yellowish papules on the mucosa of the lower lip may also be seen [5,6].

Ocular involvement is characterized by the presence of angioïd streaks secondary to rupture of the Bruch's membrane [7], orange peel appearance of the retina, corresponding to the transition between calcified and non-calcified Bruch's membrane, and the comet sign, in the form of whitish lesions with tips pointing towards the optic disc [6].

Angioïd streaks, often seen in PXE, are not specific to the disease, as they are seen in other conditions such as Ehlers-Danlos disease, Paget's disease of the bone, sickle cell disease, or may be idiopathic. They are generally asymptomatic unless they are located in the subfoveolar area, or complicated by subretinal hemorrhages after minor trauma or by macular neovascularization with a life-threatening visual prognosis [7].

Cardiovascular damage secondary to calcification of the medium caliber arteries leads to intermittent claudication, myocardial infarction, aneurysm or stroke in relatively young patients with a life-threatening prognosis [8].

A positive diagnosis is based on revised cutaneous, ocular and genetic criteria, and the disease is classified as confirmed, probable or possible [6].

There is no cure for the disease [5], but symptomatic treatments are available, including intravitreal injections of Anti-VEGF drugs and laser photocoagulation for choroidal neovascularization [9], bypass surgery or angioplasty for arterial stenosis [10], and plastic surgery for skin lesions [11].

Oral supplementation with inorganic pyrophosphates [12] and magnesium [13] appears to have an anti-mineralizing effect, preventing the progression of the disease.

1. **CONCLUSION**

Skin involvement in PXE, although earlier and more obvious, is only the tip of the iceberg in a disease whose prognosis is associated with vision loss and the occurrence of life-threatening vascular accidents. Therefore, regular ophthalmological and cardiovascular monitoring of these patients is important for early detection of any damage and appropriate symptomatic management.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest

**REFERENCES**

1. Li Q, Jiang Q, Uitto J. Ectopic mineralization disorders of the extracellular matrix of connective tissue: Molecular genetics and pathomechanisms of aberrant calcification. Matrix Biol J Int Soc Matrix Biol. 2014 Jan; 0:23‑8.

2. Le Saux O, Martin L, Aherrahrou Z, Leftheriotis G, Váradi A, Brampton CN. The molecular and physiological roles of ABCC6: more than meets the eye. Front Genet. 12 Dec 2012;3:289.

3. Struk B, Cai L, Zäch S, Ji W, Chung J, Lumsden A, et al. Mutations of the gene encoding the transmembrane transporter protein ABC-C6 cause pseudoxanthoma elasticum. J Mol Med. juill 2000;78(5):282‑6.

4. Uitto J, Jiang Q, Váradi A, Bercovitch LG, Terry SF. PSEUDOXANTHOMA ELASTICUM: DIAGNOSTIC FEATURES, CLASSIFICATION, AND TREATMENT OPTIONS. Expert Opin Orphan Drugs. 1 juin 2014;2(6):567‑77.

5. Marconi B, Bobyr I, Campanati A, Molinelli E, Consales V, Brisigotti V, et al. Pseudoxanthoma elasticum and skin: Clinical manifestations, histopathology, pathomechanism, perspectives of treatment. Intractable Rare Dis Res. août 2015;4(3):113‑22.

6. Plomp AS, Toonstra J, Bergen AAB, Van Dijk MR, De Jong PTVM. Proposal for updating the pseudoxanthoma elasticum classification system and a review of the clinical findings. Am J Med Genet A. avr 2010;152A(4):1049‑58.

7. Georgalas I, Tservakis I, Papaconstaninou D, Kardara M, Koutsandrea C, Ladas I. Pseudoxanthoma elasticum, ocular manifestations, complications and treatment. Clin Exp Optom. 2011;94(2):169‑80.

8. Lefthériotis G, Omarjee L, Saux OL, Henrion D, Abraham P, Prunier F, et al. The vascular phenotype in Pseudoxanthoma elasticum and related disorders: contribution of a genetic disease to the understanding of vascular calcification. Front Genet. 12 févr 2013;4:4.

9. Gliem M, Finger RP, Fimmers R, Brinkmann CK, Holz FG, Charbel Issa P. TREATMENT OF CHOROIDAL NEOVASCULARIZATION DUE TO ANGIOID STREAKS: A Comprehensive Review. Retina. juill 2013;33(7):1300‑14.

10. Lefthériotis G, Abraham P, Le Corre Y, Le Saux O, Henrion D, Ducluzeau PH, et al. Relationship between ankle brachial index and arterial remodeling in pseudoxanthoma elasticum. J Vasc Surg. nov 2011;54(5):1390‑4.

11. Ng AB, O’Sullivan ST, Sharpe DT. Plastic surgery and pseudoxanthoma elasticum. Br J Plast Surg. oct 1999;52(7):594‑6.

12. Kozák E, Fülöp K, Tőkési N, Rao N, Li Q, Terry SF, et al. Oral supplementation of inorganic pyrophosphate in pseudoxanthoma elasticum. Exp Dermatol. avr 2022;31(4):548‑55.

13. Kupetsky‐Rincon EA, Li Q, Uitto J. Magnesium Reduces Carotid Intima‐Media Thickness in a Mouse Model of Pseudoxanthoma Elasticum: A Novel Treatment Biomarker. Clin Transl Sci. juin 2012;5(3):259‑64.