

# An atypical presentation of pseudoxanthoma elasticum (PXE) without angioid streaks or peau d'orange

Choi Mun Chan, MBBS<sup>1</sup>; Amer Omar, MD<sup>2</sup>; Maria Pefkianaki, MD, PhD<sup>2</sup>; Ranjan Rajedram, MD<sup>2</sup>; David Paige, MBBS<sup>3</sup>; Rino Cerio, FRCP<sup>3</sup>; Michel Michaelides, MBBS, MD<sup>2</sup>

<sup>1</sup> Singapore National Eye Centre, Singapore

<sup>2</sup> Moorfields Eye Hospital, National Health Service Foundation Trust, London, UK

<sup>3</sup> The Royal Hospital London, National Health Service Foundation Trust, London, UK

## Abstract

Pseudoxanthoma Elasticum (PXE) is an inherited multi-system disorder with potentially fatal complications. Biallelic mutations in the *ABCC6* gene, which encodes an ATP-binding cassette transporter, have been identified to underlie this disease. Patients with pseudoxanthoma elasticum (PXE) classically have angioid streaks and peau d'orange. In this report, we present the case of a 9-year-old girl with histologically confirmed PXE, who did not have either angioid streaks or peau d'orange in either eye. Her only ophthalmic finding was the presence of bilateral optic disc drusen. This atypical presentation of PXE highlights that the presence of optic disc drusen in the absence of other signs should alert the physician to consider PXE.

## Introduction

Pseudoxanthoma Elasticum (PXE), also known as Gronblad-Stranberg syndrome, is a genetically inherited multi-system disorder with potentially fatal complications. Biallelic mutations in the ATP-binding cassette sub-family C member 6 (*ABCC6*) gene, which encodes an intracellular transporter protein, multidrug

resistance-associated protein 6 (MRP6), have been identified to underlie this disease, though the mechanism by which these mutations result in pathology remains unknown. Progressive accumulation of calcium and other minerals in the elastic fibers of connective tissue, particularly within the skin, blood vessels, and retina, results in pathology. In the retina, damage to the elastic layers of Bruch's membrane (the thin 2 to 4 micron thick acellular layer, which consists of the basement membrane of the retinal pigment epithelial cell layer of the eye, between the retina and the choroid) results in linear breaks in Bruch's membrane, known as angioid streaks. Diffuse partially confluent deposition of calcium and other minerals at the level of Bruch's membrane results in the peau d'orange appearance of the retina.<sup>1,2</sup> Angioid streaks and peau d'orange are readily visible on ophthalmoscopy and retinal autofluorescence imaging may assist in the diagnosis by demonstrating stippled autofluorescence typical of peau d'orange and hypoauflorescent fissures typical of angioid streaks.<sup>3</sup>

## Case Report

An asymptomatic 9-year-old girl was referred to

### Correspondence:

Choi Mun Chan, MBBS  
Singapore National Eye Centre  
11 Third Hospital Avenue  
Singapore 168751  
E-mail: chan.choi.mun@sneec.com.sg  
Phone: (65) 6322-8330

**Conflict of Interest:** The authors report no conflicts of interest.

**Contributions:** All authors contributed equally.

**Accepted for Publication:** May, 2018

This work is licensed under a Creative Commons Attribution Non-Commercial 3.0 License (CC BY-NC 3.0).

©Copyright Chan et al., 2018.

Licensee Ophthosience Publishers, USA

a tertiary ophthalmological institution for evaluation of possible papilledema. On examination, her best-corrected visual acuity was 20/20 in each eye, with 0.75 Diopter spherical correction in each eye. Visual fields were full and color vision was normal.

Dilated fundus examination revealed bilateral full optic discs with irregular, elevated and hyperemic neuroretinal rims, more so in the right eye than the left. Both retinae had a predominantly confluent yellow appearance, which was centered on the posterior pole and extended to the mid-periphery, sparing the peri-papillary area (Figure 1). Angioid streaks were absent.

B-scan ultrasonography demonstrated small hyperechoic lesions over the optic nerve heads, consistent with optic disc drusen. Fundus autofluorescence imaging confirmed the diagnosis of optic disc drusen which appeared hyperautofluorescent (Figure 2), though revealed the absence of the stippled autofluorescence typical of peau d'orange and the hypoautofluorescent fissures typical of angioid streaks. Macular spectral-domain

optical coherence tomography revealed intact retinal architecture. Electrophysiological testing showed normal symmetrical photopic, scotopic and macular responses.

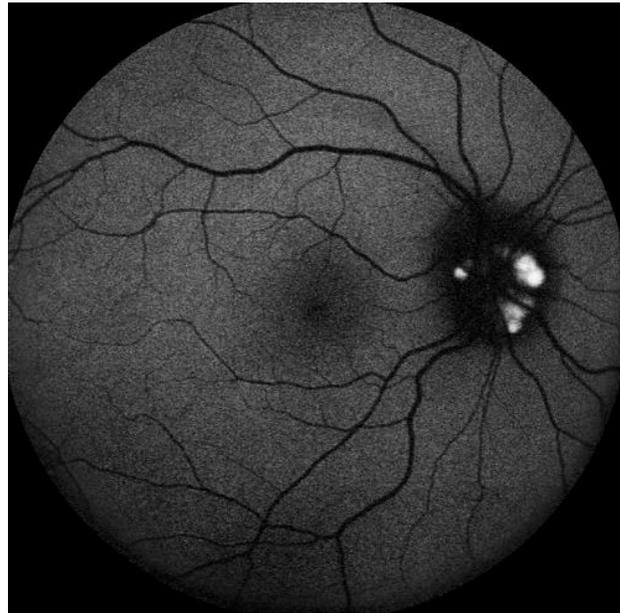
Dermatological assessment revealed tiny yellowish papules on the neck and a solitary axillary café-au-lait lesion. Biopsy of a papule established the diagnosis of PXE; histology demonstrated degeneration of the elastic fibers within the dermis (Figure 3) with evidence of calcium deposition on Von Kossa stains (Figure 4).

## Discussion

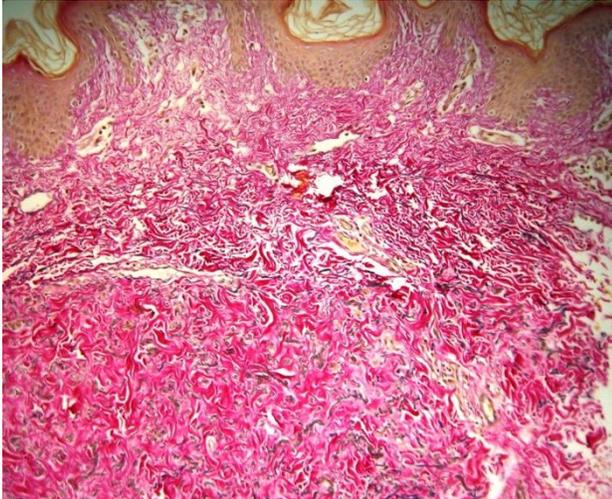
PXE should be considered in the differential diagnosis of bilateral optic disc drusen, even in the absence of angioid streaks and peau d'orange. Optic nerve head drusen appear to occur more frequently in PXE patients, with a reported prevalence of 6% to 20%, compared to 0.3% in the general population.<sup>4,5</sup> It has



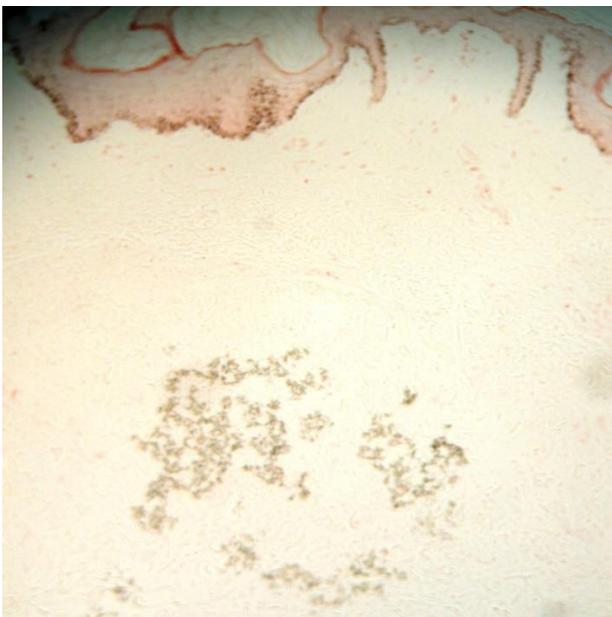
**Figure 1**  
*Fundus photograph demonstrated a full optic nerve head with irregular elevation and hyperemia, as well as a predominantly confluent yellow appearance of the posterior pole, without peau d'orange.*



**Figure 2**  
*Retinal autofluorescence imaging demonstrated hyperautofluorescent optic drusen. There is no stippled autofluorescence typical of peau d'orange and no hypoautofluorescent fissures typical of angioid streaks.*



**Figure 3**  
Hematoxylin and eosin staining of a skin papule demonstrated degeneration of the elastic fibers within the dermis.



**Figure 4**  
Von Kossa staining of a skin papule demonstrated calcium deposition.

been postulated the increased frequency may be due to calcification or increased rigidity of the lamina cribrosa.<sup>4</sup>

As this case demonstrates, angioid streaks and peau d'orange may not be present in PXE. It is

noteworthy that these features are rare in children and not consistent among adults. The predominantly confluent yellow appearance of this patient's retinae, which was centered on the posterior pole and extended to the mid-periphery, is consistent with confluent deposition of calcium and other minerals at the level of Bruch's membrane, and has been observed in cases of PXE. However, the peau d'orange appearance of the retina results from the subconfluent, or partially confluent, deposition of calcium and other minerals that surrounds the more central confluent deposition.<sup>1,2</sup> This young patient did not have this subconfluent deposition surrounding the confluent deposition, and thus did not have the peau d'orange appearance of the retina.

This atypical presentation of PXE highlights that the presence of optic disc drusen in the absence of other signs should alert the physician to consider PXE. It is important not to miss a diagnosis of PXE as this is an inherited multi-system disorder with potentially fatal complications. Timely diagnosis is critical to initiate screening for the associated cardiac and gastrointestinal manifestations and to act upon them accordingly.

## References

1. Gliem M, Zaeytijd JD, Finger RP, et al. An update on the ocular phenotype in patients with pseudoxanthoma elasticum. *Front Genet* 2013; 4:14, 1-13.
2. Spaide RF. Peau d'orange and angioid streaks: Manifestations of Bruch membrane pathology. *Retina* 2015; 35: 392-7.
3. Sawa M, Ober MD, Freund KB, Spaide RF. Fundus autofluorescence in patients with pseudoxanthoma elasticum. *Ophthalmology* 2006; 113(5): 814-20.
4. Finger RP, Charbel Issa P, Ladewig M, et al. Fundus autofluorescence in pseudoxanthoma elasticum. *Retina* 2009; 29(10): 1496-505.
5. Pierro L, Brancato R, Minicucci M, Pece A. Echographic diagnosis of drusen of the optic nerve head in patients with angioid streaks. *Ophthalmologica* 1994; 208(5): 239-42.