

Angioid Streaks with Choroidal Neovascularization: An Ophthalmic Window to the Diagnosis of Pseudoxanthoma Elasticum



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ABSTRACT

The most common systemic association of Angioid streaks is Pseudoxanthoma Elasticum (PXE), which is defined by the progressive mineralization of elastic tissue in the epidermis, eyes, and vascular system. We present the case of a 45-year-old female who presented with findings consistent with Angioid streaks complicated by choroidal neovascularization (CNV) in association with PXE. The patient presented with bilateral asymmetric painless vision loss, with an active CNV in the left eye, and a disciform scar in the right eye. Skin biopsy from neck confirmed PXE as the systemic cause. Intravitreal Ranibizumab was given in the left eye, which resulted in significant anatomical and functional improvement. This case demonstrates the need for systemic examination in Angioid streak patients, as well as the efficacy of anti-VEGF therapy in salvaging vision.

Keywords: Angioid streaks, Pseudoxanthoma elasticum, Choroidal neovascularization, Anti-vascular endothelial growth factor therapy, Ranibizumab.

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INTRODUCTION

Angioid or Knapp streaks are bilateral thin crack-like disruptions in Bruch's membrane, which is calcified and brittle. They normally radiate from the optic disc as reddish-brown, uneven bands with varied widths.¹ They may not cause any symptoms if the layers of the retina that cover them are intact, but they are at risk for problems like retinal pigment epithelium (RPE) degeneration and subsequent photoreceptor damage, which can lead to visual impairment.² Angioid streaks frequently afflict people throughout their professional years (20–50 years old), which significantly compromises the patient's quality of life.^{1,2}

The development of choroidal neovascularization (CNV), which has been observed in 70–86% of patients with Angioid streaks and affects the other eye in over 70% of cases, is a major complication that can impair vision.³ CNV may present with metamorphopsia, scotoma, or hemorrhage, and if left untreated, progresses to disciform scarring and irreversible vision loss.³ The pathogenesis involves breaks in Bruch's membrane with ingrowth of fibrovascular tissue, and vascular endothelial growth factor (VEGF) upregulation plays a central role in angiogenesis.^{1,2}

About half of Angioid streak cases are idiopathic; however, they are often associated with systemic connective tissue and metabolic disorders which include Pseudoxanthoma elasticum, Ehlers–Danlos syndrome, Paget's disease and Sickle cell disease. Among these, pseudoxanthoma elasticum (PXE) is the most frequent association, occurring in up to 87% of patients.⁴ PXE is characterized by calcification and fragmentation of mid-dermal elastic fibers, confirmed

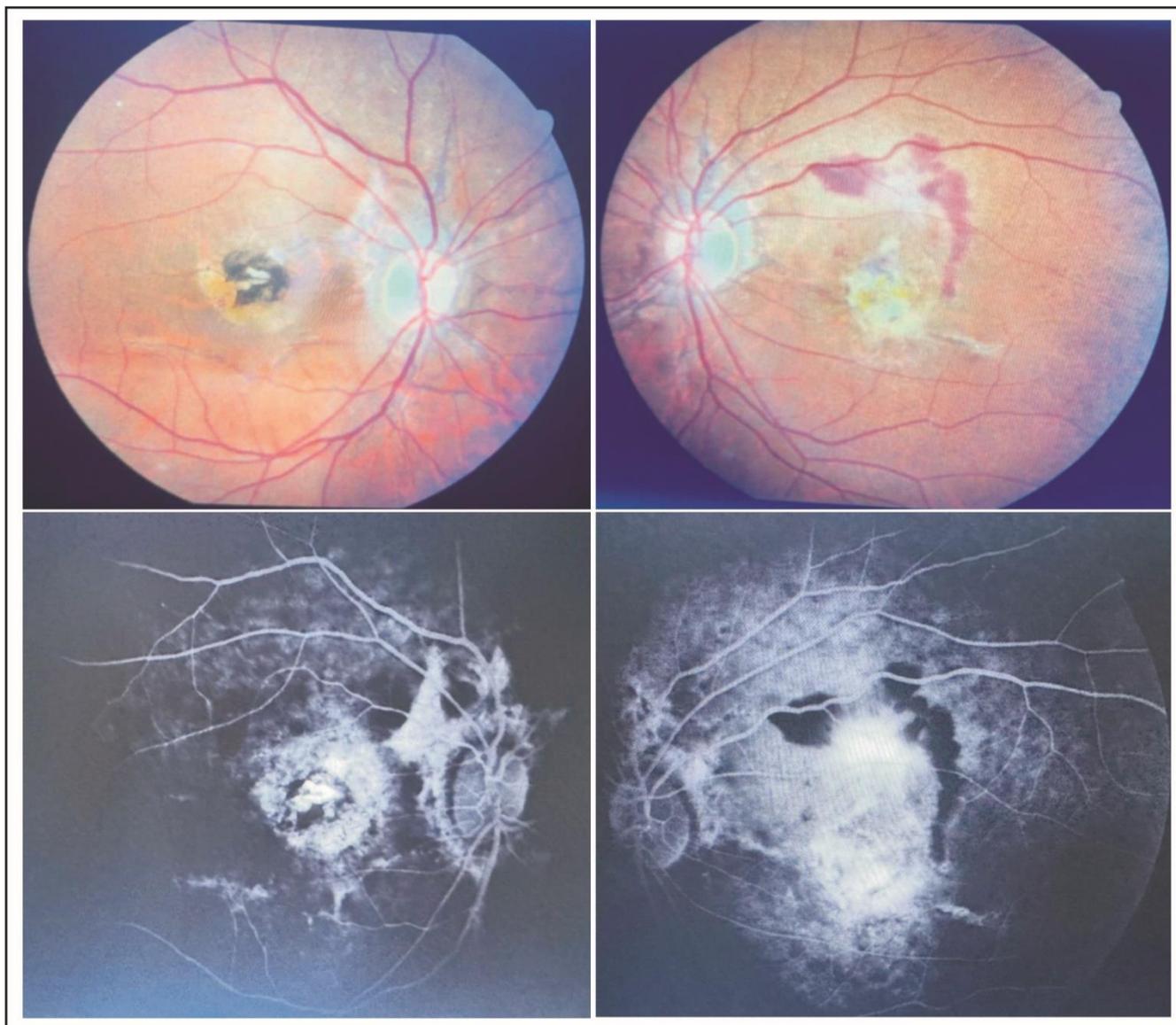


Figure 1 (Top): Fundus Photograph showing Bilateral Angioid streaks along with fibrotic scar in Right eye and CNV with hemorrhage in Left eye. **(Bottom):** FFA images of Late phase showing staining in Right eye and leakage in Left eye.

by skin biopsy.⁵ Systemic manifestations include yellowish papules on flexural skin, gastrointestinal bleeding, and cardiovascular complications such as arterial calcification, hypertension, and cerebrovascular disease, which may be life-threatening. Therefore, all patients with Angioid streaks should undergo systemic evaluation to identify associated conditions, particularly PXE.⁴

Diagnostic techniques like Fundus fluorescein angiography (FFA), fundus autofluorescence (FAF), optical coherence tomography (OCT), and more recently OCT angiography (OCTA), enable non-invasive observation of neovascular flow patterns.³ An

essential self-monitoring tool for identifying early central visual abnormalities is still the Amsler grid.

Anti-VEGF injections administered intravitreally are presently regarded as the standard of care for treating CNV caused by Angioid streaks, replacing laser photocoagulation and photodynamic therapy, both of which have high recurrence rates.¹ Aflibercept, ranibizumab, and bevacizumab have all shown promise in stabilizing or enhancing visual acuity; early initiation of treatment yields the greatest outcomes.⁶ However, considering that CNV in these patients is chronic and recurrent, long-term treatment would be necessary.⁷

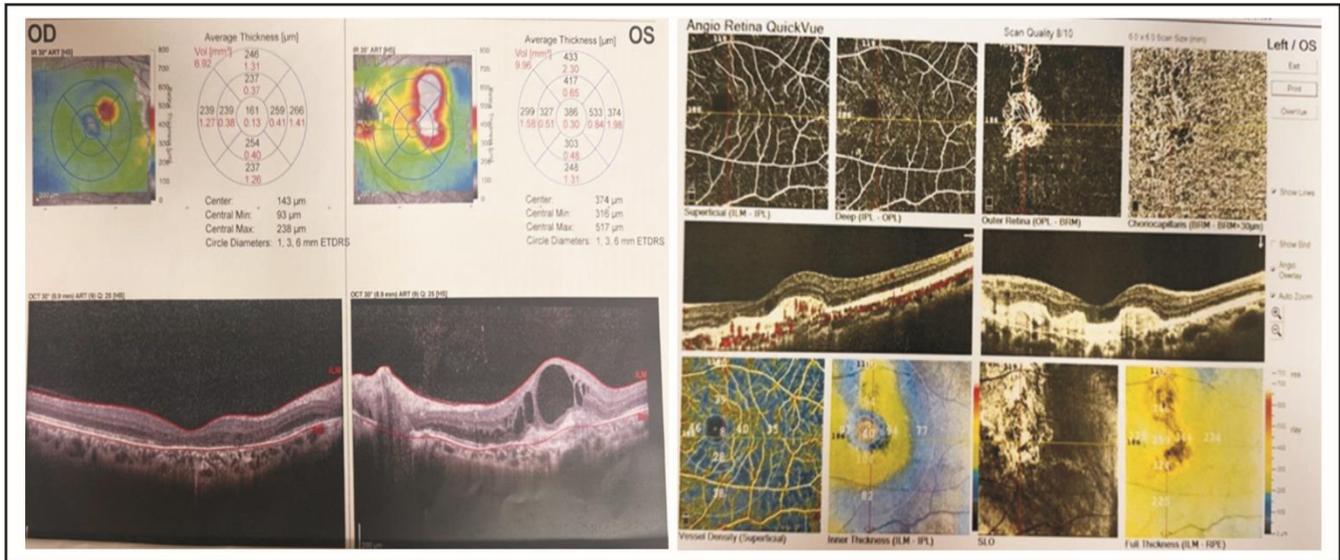


Figure 2: OCT and OCTA of Left eye showing active CNV.

Counseling and patient education are crucial aspects of management. In order to reduce trauma-related ruptures, patients should be counseled to wear protective eyewear, refrain from high-risk activities, undergo routine Amsler grid testing, and continue lifelong monitoring. Early detection and treatment of CNV are crucial, as outcomes are significantly better when intervention occurs before disciform scarring develops.^{6,7}

This report describes a middle-aged female with Angioid streaks secondary to pseudoxanthoma elasticum, with CNV managed successfully using intravitreal anti-VEGF therapy.

Case Presentation

Written informed consent for publication was obtained from the patient, and the case received approval from the Institutional Ethical Review Board. This report conforms to the ethical tenets of the Declaration of Helsinki and its later updates. A 45-year-old married female, mother of three, presented to the ophthalmology outpatient department in November 2024 with complaints of gradual, painless decrease in vision in the right eye for three months, followed by sudden painless loss of vision in the left eye for two weeks. There was no history of flashes, floaters, trauma, or curtain-like vision loss and she did not seek any eye consultation for right eye. Her past medical and ocular history was unremarkable and non-contributory. Ocular examination showed reduced visual acuity in both eyes (Counting fingers in the left

eye and 6/24 in the right eye). Fundus examination of both eyes showed classic Angioid streaks radiating from the optic disc. The right eye demonstrated a fibrotic disciform scar with hyperpigmentation at the macula, consistent with end-stage Choroidal neovascularization and poor visual potential (Figure 1). The left eye revealed metamorphopsia and central scotoma on Amsler grid testing. Left eye fundus image showed greyish to greenish Choroidal neovascularization in the macular area with subretinal hemorrhage along the superotemporal vascular arcade in the macular area (Figure 1). FFA showed hyperfluorescence due to staining of the disciform scar in right eye and increasing hyperfluorescence in size and intensity in the left eye, consistent with leakage from an active CNV. Angioid streaks appear as linear hyperfluorescent streaks on FFA (Figure 1).

Optical coherence tomography (OCT) of the left eye revealed a maximum central macular thickness of 517 µm with intraretinal edema and hemorrhage secondary to active CNV, while the right eye confirmed the presence of a fibrotic scar. OCT angiography (OCTA) further demonstrated neovascular activity in the left eye within the avascular zone on en-face images, along with corresponding blood flow signals on cross-sectional (B-scan) views (Figure 2).

On general physical examination, the patient was of average build, with stable vitals and no systemic abnormalities of joint hypermobility or skin elasticity (Figure 3). Dermatological examination revealed

yellowish papules coalescing into plaques distributed along the lateral surface of the neck, giving a “plucked chicken skin” appearance, along with redundant skin folds in the axillae, features highly suggestive of PXE (Figure 3).

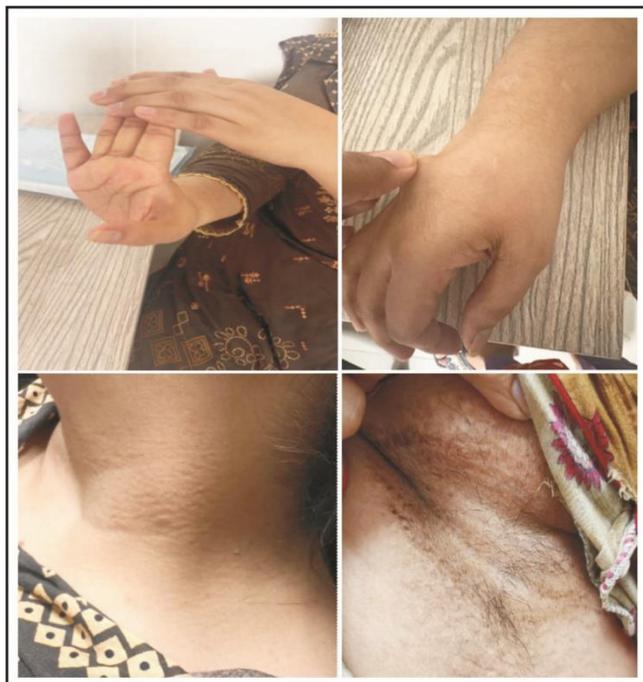


Figure 3: Systemic examination of Joints and Skin (Top). Plucked chicken appearance along with redundant skin folds in axillae (Bottom).

Systemic workup was performed to exclude other associations of Angioid streaks. Serum calcium, alkaline phosphatase, and ESR were within normal limits, effectively ruling out Paget’s disease. Screening

for hemoglobinopathies and Ehlers–Danlos syndrome was negative. A skin punch biopsy from the neck demonstrated fragmentation and calcification of mid-dermal elastic fibers, confirming the diagnosis of pseudoxanthoma elasticum (Figure 4).

To assess potential cardiovascular involvement linked to pseudoxanthoma elasticum, a consultation with a cardiologist was sought. There was no indication of vascular abnormalities, left ventricular dysfunction, or valvular calcification on the electrocardiogram (ECG) or transthoracic echocardiography (ECHO), which were both within normal ranges.

As the right eye had a permanent disciform scar, no intervention was undertaken. Three monthly intravitreal injections of Ranibizumab 0.5 mg/0.05 ml

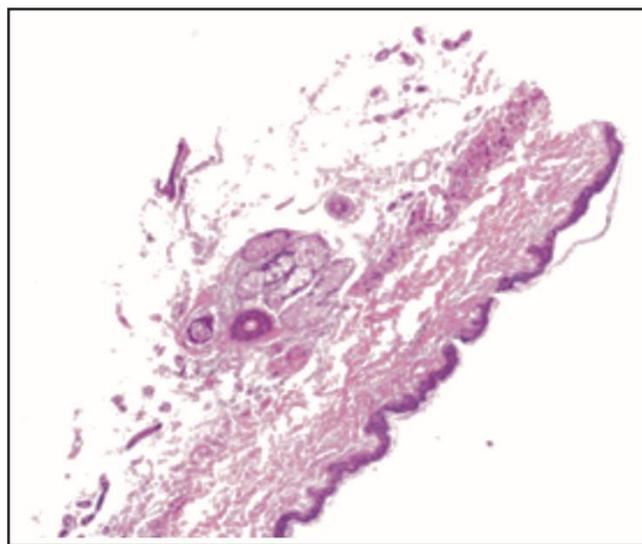


Figure 4: Histopathology sections showing fragmentation of mid-dermal elastic fibres.

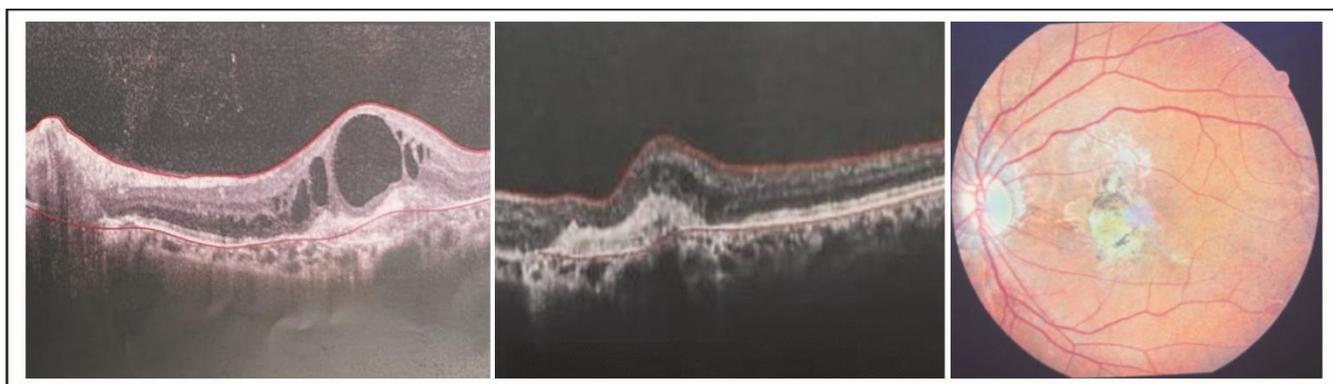


Figure 5: Left image showing Pre-treatment OCT. Central image showing Post-treatment OCT of CNV of Left eye. Right image showing Post-treatment Fundus photograph of left eye with resolution of hemorrhage and CNV with scarring.

(Patizra) were given in left eye. Following treatment, the central macular thickness decreased from 517 μm to 210 μm , and best-corrected visual acuity improved from 6/60 to 6/12 (Figure 5). The patient was counseled regarding lifelong monitoring, use of protective eyewear to prevent trauma-related rupture, and regular self-assessment with the Amsler grid.

DISCUSSION

Angioid streaks are structural breaks in Bruch's membrane that predispose to hemorrhage, rupture, and CNV formation. CNV is the most frequent cause of visual loss, with bilateral involvement in most cases over time.³

Pseudoxanthoma elasticum, confirmed in our patient, is an autosomal recessive connective tissue disorder caused by ABCC6 gene mutations leading to reduced inorganic pyrophosphate and abnormal calcification of elastic fibers.⁵ Cutaneous features include yellow papules in flexural areas, often coalescing into plaques and giving a cobblestone or "plucked chicken" appearance.⁵ While the skin changes are often cosmetic, PXE carries systemic risks such as gastrointestinal hemorrhage, claudication, hypertension, angina, and occasionally life-threatening cerebrovascular or coronary events. Histopathology shows elastorrhexis with calcified mid-dermal elastic fibers.⁵

Clinically substantial cardiovascular involvement of PXE has been linked to peripheral arterial disease, decreased diastolic function, and an elevated risk of myocardial infarction or ischemic stroke.^{4,5} Therefore, multidisciplinary care that includes cardiologists, dermatology, and ophthalmologists is crucial. Genetic counseling should also be made available to patients.

The most severe side effect of PXE with Angioid streaks in the eyes is CNV. Recent developments in multimodal imaging have improved the follow-up and diagnostic precision of Angioid streaks and related CNV.^{3,8} OCT angiography (OCTA) provides non-invasive viewing of neovascular networks and disease activity, although FFA and OCT continue to be the gold standards for detecting leakage and measuring retinal alterations. Early detection and more accurate treatment response monitoring are made possible by these modalities.⁸ The stage of CNV at presentation determines the prognosis; eyes with early, active membranes recover significantly in vision with prompt anti-VEGF medication, while late stage disciform

scars cause irreversible loss of vision.⁷

Anti-VEGF treatment has changed results by improving anatomical and functional characteristics and postponing the development of scarring.^{1,6} Long-term monitoring is essential though, as recurrence is frequent. While the eye with a pre-existing disciform scar had a dismal prognosis, our patient's better-seeing eye showed good anatomical and visual healing after receiving ranibizumab.

To detect recurrences early, patients should be advised to wear protective eyewear, prevent ocular stress, and undergo routine Amsler grid testing. Potential disease-modifying treatments for pseudoxanthoma elasticum are supported by recent clinical studies.^{9,10} In order to lessen ectopic calcification and enhance ocular and cutaneous symptoms, oral inorganic pyrophosphate supplementation is being assessed in the PROPHECI study (NCT04868578).⁹ Likewise, in ABCC6-deficient mice, ENPP1 enzyme replacement treatment (INZ-701) has demonstrated encouraging preclinical and early clinical outcomes, including elevated plasma pyrophosphate levels and decreased tissue calcification.¹⁰ These new treatments give hope for changing the trajectory of Angioid streaks caused by PXE, which are now treated only with supportive measures.

CONCLUSION

Angioid streaks present a risk for developing a vision-threatening Choroidal neovascularization. While end-stage disciform scars cannot be reversed, prompt anti-VEGF medication may be able to restore vision in patients with active CNV. For the best care, systemic screening, patient counseling, and lifetime follow-up are essential.

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Patient's Consent: Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

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