

Agminated Papules on the Neck

Andrew Daugherty, MD; Jonathan S. Glass, MD; Timothy Sorrells, MD



A 24-year-old woman presented with a lesion on the neck of 3 months' duration. She noted occasional mild pruritus at the site but no other symptoms or similar lesions elsewhere. At the time of presentation, she was at 17 weeks of gestation without any complications. Her medical history was notable for hypertension, unspecified chest pain with a normal electrocardiogram, and 2 spontaneous abortions. She denied a personal or family history of notable cardiovascular or gastrointestinal tract diseases. Examination of the skin showed indurated 3- to 5-mm papules coalescing into a 3- to 4-cm plaque on the left posterolateral neck.

WHAT'S THE DIAGNOSIS?

- collagenous fibroma (desmoplastic fibroblastoma)
- cutaneous leiomyoma
- cutaneous sclerosis in sclerosing mesenteritis
- pseudoxanthoma elasticum
- xanthoma disseminatum

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From the Naval Medical Center Portsmouth, Virginia. Dr. Sorrells is from the Department of Pathology.

The authors report no conflict of interest.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the US Government.

Correspondence: Jonathan S. Glass, MD, Section of Dermatology, Dartmouth-Hitchcock Medical Center, 1 Medical Center Dr, Lebanon, NH 03756-0001 (glassjs@me.com).

THE DIAGNOSIS: Pseudoxanthoma Elasticum

Histopathology showed abnormal curled frayed elastic fibers in the mid dermis (Figure, A); von Kossa stain was positive for calcified and fragmented elastic fibers (Figure, B). Based on clinical and histologic findings, a diagnosis of pseudoxanthoma elasticum (PXE) was made.

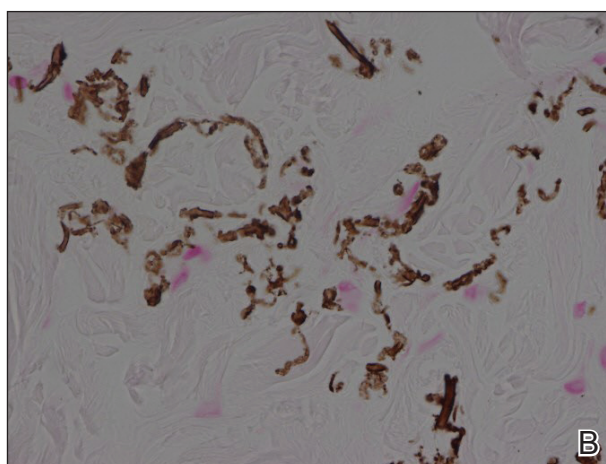
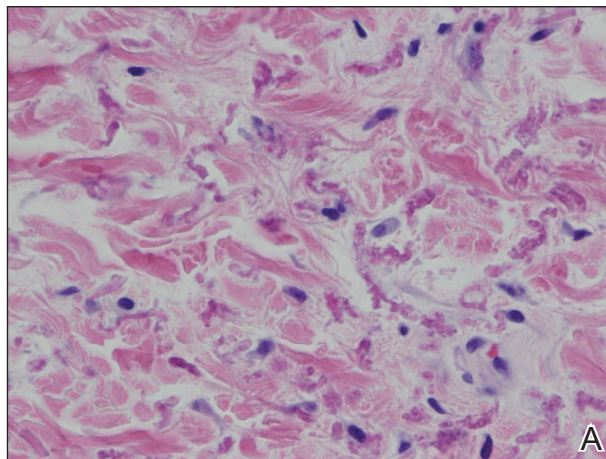
Pseudoxanthoma elasticum is a rare multisystem heterogeneous genetic disorder that causes abnormal mineralization and fragmentation of tissue elastin fibers. Clinically, accumulation of mineralized elastin fibers leads to soft tissue calcification and late-onset pathology in the dermis, retinal Bruch membrane, and medial layers of large- and medium-sized arterial walls.

Pseudoxanthoma elasticum is an autosomal-recessive disease associated with more than 300 loss mutations in the ATP-binding cassette subfamily C member 6 gene, *ABCC6*.^{1,2} However, PXE clinically is characterized by wide variability in clinical progression and outcome as well as phenotypic overlap with other disorders such as generalized arterial calcification of infancy. Pseudoxanthoma elasticum affects an estimated 1 in 25,000 to 100,000 individuals with a female preponderance (2:1 ratio).¹⁻³ Age of onset typically is in the second to third decades of life, with 80% of cases demonstrating skin manifestations before 20 years of age.^{2,3}

The first and most benign finding often is the appearance of small soft asymptomatic yellow papules with a plucked chicken skin-like appearance that occur on the flexural areas such as the neck, axilla, antecubital, popliteal, inguinal, and periumbilical areas. These papules may progress to irregularly shaped, yellowish plaques with a leathery appearance; mucous membranes, often the inner aspect of the lower lips, also may be involved. More severe abdominal striae also may affect some but not all women with PXE. Histologic examination demonstrates swollen, clumped, and fragmented elastin fibers with calcium deposits in the mid dermis. Elastin-specific stains such as orcein and calcium-specific stains such as the von Kossa stain aid in the diagnosis.

Vision impairment subsequently develops in 50% to 70% of patients, with severe vision loss in 3% to 8% of patients.^{4,5} Ophthalmologic examination identifies characteristic angioid streaks (ie, gray lines radiating from the optic disk) and subretinal hemorrhages caused by brittle new vessel formation.

Bleeding complications, especially from the gastrointestinal tract, caused by arterial wall fragility may affect 10% of PXE patients.⁵ Although bleeding complications also may affect the genitourinary system, the risk for fetal loss or adverse reproductive outcomes is considered



Histopathology revealed abnormal curled frayed elastic fibers in the mid dermis (A)(H&E, original magnification $\times 400$), and von Kossa stain was positive for calcified and fragmented elastic fibers (B)(original magnification $\times 400$).

low.⁶ More insidiously, progressive arterial calcification and peripheral arterial disease contribute to accelerated atherosclerosis, causing earlier presentations of claudication, angina pectoris, myocardial infarction, and hypertension by the third and fourth decades of life.

Management of PXE is limited. Primary care providers should be attentive to cardiovascular screening for coronary and peripheral arterial disease. Patients should receive regular eye examinations, and choroidal neovascularization should be aggressively treated with photocoagulation, photodynamic therapy, and vascular endothelial growth factor inhibitors.^{1,3}

Collagenous fibromas are slow-growing tumors but are histologically distinct, showing fibrous or myxoid

connective tissue arising within adipose tissue. Cutaneous leiomyomas may be solitary or grouped, often painful papules composed histologically of bundles of smooth muscle. Cutaneous sclerosis in sclerosing mesenteritis is a rare cutaneous manifestation of an internal disorder and presents as asymptomatic indurated subcutaneous nodules but histologically is distinctive, demonstrating sclerosis with fat necrosis. Xanthoma disseminatum is a rare form of histiocytosis that commonly presents as hundreds of small yellowish brown or reddish brown papules symmetrically distributed on the face, trunk, and intertriginous areas.

On follow-up within a year after initial presentation, our patient was found to have early subtle angioid streaks on ophthalmologic examination with no vision loss. A transthoracic echocardiogram was performed and showed no cardiac abnormalities. Her pregnancy was complicated by intrauterine growth retardation in the third trimester; however, the patient delivered a

healthy-appearing 2835-g neonate (10th percentile for gestational age) at 39 weeks of gestation via an uncomplicated cesarean delivery.

REFERENCES

1. Uitto J, Bercovitch L, Terry SF, et al. Pseudoxanthoma elasticum: progress in diagnostics and research towards treatment: summary of the 2010 PXE International Research Meeting. *Am J Med Genet A*. 2011;155A:1517-1526.
2. Li Q, Jiang Q, Pfindner E, et al. Pseudoxanthoma elasticum: clinical phenotypes, molecular genetics and putative pathomechanisms. *Exp Dermatol*. 2009;18:1-11.
3. Finger RP, Charbel Issa P, Ladewig MS, et al. Pseudoxanthoma elasticum: genetics, clinical manifestations and therapeutic approaches. *Surv Ophthalmol*. 2009;54:272-285.
4. Li Y, Cui Y, Zhao H, et al. Pseudoxanthoma elasticum: a review of 86 cases in China. *Intractable Rare Dis Res*. 2014;3:75-78.
5. Laube S, Moss C. Pseudoxanthoma elasticum. *Arch Dis Child*. 2005;90:754-756.
6. Bercovitch L, Leroux T, Terry S, et al. Pregnancy and obstetrical outcomes in pseudoxanthoma elasticum. *Br J Dermatol*. 2004; 151:1011-1018.