

Testicular Microlithiasis in a 2-Year-Old Boy With Pseudoxanthoma Elasticum

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Pseudoxanthoma elasticum (PXE) is a rare chromosomal disorder that results in mineralization of elastic fibers, especially in the skin, eye, and cardiovascular system. Recently, PXE has been associated with testicular microlithiasis (TM),¹ which itself might be associated with testicular malignancy.² Here we report on a 9-year-old boy with PXE who already had TM at 2 years. To our knowledge, this is the youngest patient with PXE in whom TM is documented.

Abbreviations

ABCC6, adenosine triphosphate-binding cassette subfamily C member 6; PXE, pseudoxanthoma elasticum; TM, testicular microlithiasis

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Case Report

A 9-year-old boy was referred for a left-sided undescended testis. Pseudoxanthoma elasticum was diagnosed because of skin abnormalities in the neck, in the armpits, around the umbilicus, and on the lower part of the abdomen (Figure 1). DNA analysis confirmed the diagnosis of PXE (PR1141X mutation in the adenosine triphosphate-binding cassette subfamily C member 6 [*ABCC6*] gene). His 13-year-old sister also had a diagnosis of PXE (same PR1141X mutation in the *ABCC6* gene) with similar skin abnormalities in the neck and armpits. In his 15-year-old brother, no indications for PXE were found. Both parents were identified as carriers of the PXE gene (PR1141X mutation). The boy had left-sided orchidopexy at 2 years for a congenital undescended testis. On examination after his referral at 9 years, the left testis again appeared to be undescended, and a diagnosis of a secondary acquired undescended testis was made.³

Sonography of both testicles at this age revealed extensive TM (>25 diffuse scattered foci per transducer) in both testes. Additionally, abnormalities were found in both eyes (peau d'orange aspect of the fundus) and cardiovascular system (thickness of the aortic flap). Abdominal sonography revealed no calcifications in the liver, spleen, or kidneys.

On reexamination, sonography of both testicles performed before orchidopexy at 2 years showed more than 25 diffuse scattered microliths in both testes (Figure 2).

Discussion

Pseudoxanthoma elasticum is a rare autosomal recessive disorder characterized by fragmentation and mineralization of elastin fibers, likely as a result of defects in muscle cells or fibro-

blasts.⁴ The disorder is usually suspected clinically because of its specific skin lesions, as in this patient. Pseudoxanthoma elasticum is associated with calcifications in the skin, eye, cardiovascular system, and internal organs.⁵ Recently, TM was found in all 12 studied patients with PXE, the youngest of which was 13 years.¹

Multiple small (<3-mm) deposits of hydroxyapatite are found in TM.⁶ Furthermore, TM also has characteristic sonographic findings of multiple hyperechoic nonshadowing foci.⁷ Its pathogenesis is unclear. Suggested sources of TM are seminiferous tubules as well as the layers outside these structures.¹ Because PXE mostly involves the basement membrane, this seems to favor the suggestion that the source of TM is there.⁸

Figure 1. A, Multiple papules and plaques on the left side of the neck as part of PXE. **B,** Details of the papules and plaques on the neck.

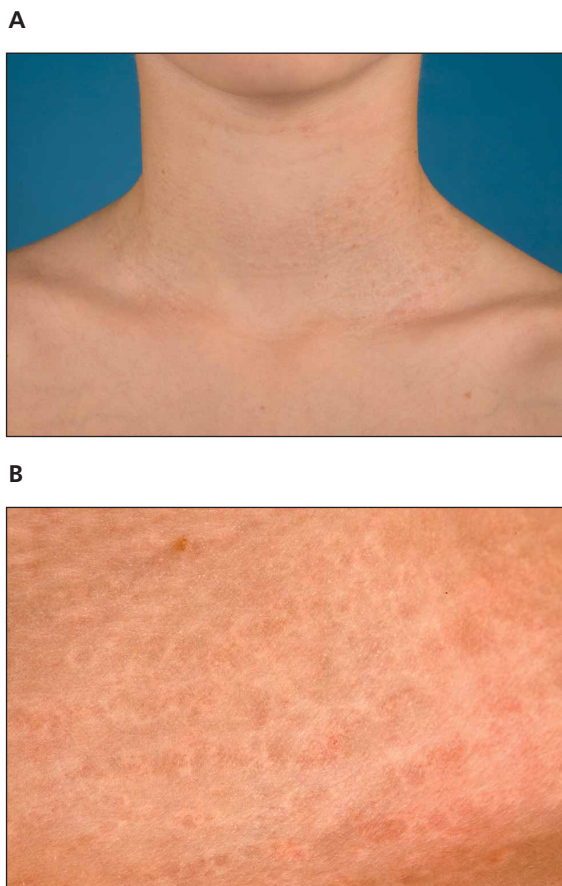
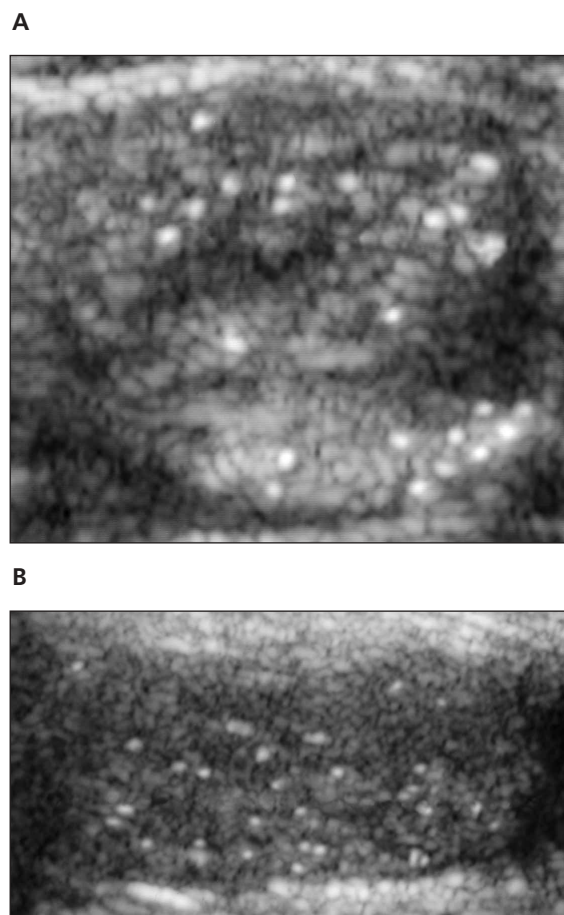


Figure 2. A, Transverse sonogram of the left testis showing more than 5 microliths per sonographic plane. The microliths are without acoustic shadowing and are scattered diffusely throughout the testicular parenchyma. **B,** Longitudinal sonogram of the left testis showing the same findings as in **A**.



Testicular microlithiasis is important because of its association with impaired spermatogenesis⁹ and increased risk of testicular cancer. In boys, TM is mostly associated with cryptorchidism and varicocele.¹⁰ Given TM's connection with testicular malignancy, patients with TM should perform regular self-examinations.¹¹ The age of onset of TM is largely unknown, but only a small number of cases have been reported in infancy. The age of onset of TM in PXE also remains unclear, but our case suggests that it might be at a very early age. As a result, it might be advisable to screen very young patients with TM for PXE.

References

1. Bercovitch RS, Januario JA, Terry SF, et al. Testicular microlithiasis in association with pseudoxanthoma elasticum. *Radiology* 2005; 237:550–554.
2. Derogee M, Bevers RFM, Prins HJ, Jonges TGN, Elbers FH, Boon TA. Testicular microlithiasis, a premalignant condition: prevalence, histopathologic findings, and relation to testicular tumor. *Urology* 2001; 57:1133–1137.
3. Surana R, Puri P. Iatrogenic ascent of the testis: an under-recognized complication of inguinal hernia operation in children. *Br J Urol* 1994; 73:580–581.
4. Gheduzzi D, Sammarco R, Quaglino D, et al. Extracutaneous ultrastructural alterations in pseudoxanthoma elasticum. *Ultrastruct Pathol* 2003; 27:375–384.
5. Sherer DW, Sapadin AN, Lebwohl MG. Pseudoxanthoma elasticum: an update. *Dermatology* 1999; 199:3–7.
6. De Jong BW, De Gouveia Brazao CA, Stoop H, et al. Raman spectroscopic analysis identifies testicular microlithiasis as intratubular hydroxyapatite. *J Urol* 2004; 171:92–96.
7. Höbarth K, Szabo N, Klingler HC, Kratzik C. Sonographic appearance of testicular microlithiasis. *Eur Urol* 1993; 24:251–255.
8. Wiedmer-Bridel J, Vogel A, Hedinger C. Elastic fibers in the tunica propria of the seminiferous tubules: light and electron microscopic investigations. *Virchows Arch B Cell Pathol* 1978; 27:267–277.
9. Thomas K, Wood SJ, Thompson AJ, Pilling D, Lewis-Jones DI. The incidence and significance of testicular microlithiasis in a subfertile population. *Br J Radiol* 2000; 73:494–497.
10. Domínguez Hinarejos C, Bonillo García MA, Sangüesa C, Serrano Durbá A, García Ibarra F. Intratesticular calcifications in childhood [in Spanish]. *Actas Urol Esp* 2007; 31:33–37.
11. Goede J, Hack WWM, Algra PR, Pierik FH. Testiculaire microlithiasis bij jongens. *Tijdschr Kindergeneeskde* 2008; 76:34–38.