RESIDENT ROUNDS: PART III

Nail-Patella Syndrome

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CASE REPORT

Clinical Presentation

A 35 year-old Caucasian female presented to clinic for a skin cancer screening examination. She had chronic gastrointestinal problems including reflux, bloating, constipation, and diarrhea. She had also experienced right arm numbness, especially with flexion, in addition to abnormal sensations in her feet and had difficulty standing in one position for long periods of time. Cold weather caused pain and color changes in her fingers. Additionally, she was on chronic vitamin D supplementation with a history of non-traumatic bone fracture. Calcium supplements were avoided given her gastrointestinal symptoms.

Her hypertension had been treated with an ACE inhibitor. She was a smoker and also has hyperlipidemia. Of note, she and her father have glaucoma and her paternal grandmother developed blindness at a young age however she does not know much additional family history.

On physical examination, she is unable to supinate her forearms and has a swan-neck appearance of multiple digits. Firm protrusions can be palpated along her bilateral lateral lower back. She has nail dysplasia involving her thumbnails and 2nd digits in addition to triangular lunulae involving most fingernails. Interestingly, her daughter has similar physical findings.

DISCUSSION

Nail patella syndrome (NPS) (also known as hereditary osteo-onychodysplasia, Turner-Keiser syndrome, Fong disease, and nail-patella-elbow syndrome) is an inherited, autosomal dominant disorder that affects the limbs, eyes, kidneys, and nails.[2,4] It is relatively rare with a prevalence of 1:50,000.[2] The syndrome was first described in the 19th century and is due to a mutation in LMX1B, a transcription factor important for regulating the development of nail, bone, and glomerular basement membrane.[6,4] This gene is also necessary for the normal functioning of renal glomerular podocytes as it maintains their actin cytoskeleton.[1]

This condition is not life threatening however it may cause functional impairments and morbidity related to bone abnormalities, impaired renal function, and glaucoma. The dermatologic findings include various nail dystrophies and have aesthetic implications. Nail involvement occurs in 98% of patients, is typically symmetrical and often more severe from 2nd to 5th fingernails. These patients may have triangular lunulae, severe nail dysplasia, and micronychia in addition to absence of the medial and distal aspects of the thumb and 2nd digit fingernails.[4]

> "Iliac horns are pathognomonic for nail-patella syndrome and contain cortex and medulla continuous with the iliac bone."

Iliac horns are pathognomonic for nail-patella syndrome and contain cortex and medulla continuous with the iliac bone. The gluteus medius muscle insertion site marks their location and from this point they protrude posterolaterally. They are frequently palpated during physical examination however should have no impact on the patients' gait.[3] The patellae may be hypoplastic or completely absent and patients may complain of knee pain. Dysplasia of the radial heads is also seen and may lead to the inability of forearm supination.[4] Not specific to NPS, swan neck deformities of the fingers may be present and are due to hyperextension at proximal interphalangeal joints in addition to flexion at distal interphalangeal joints.[2] Although patients with NPS may not have an increased risk of osteopenia or osteoporosis, they have been found to have decreased bone mineral density and increased prevalence of fractures, particularly involving long bones of prepubertal women.[7]

Renal involvement is present in up to 60% of patients with NPS. Like our patient, many develop hypertension. Although most

FIGURE 1. Pelvic radiograph demonstrates bilateral iliac horns.

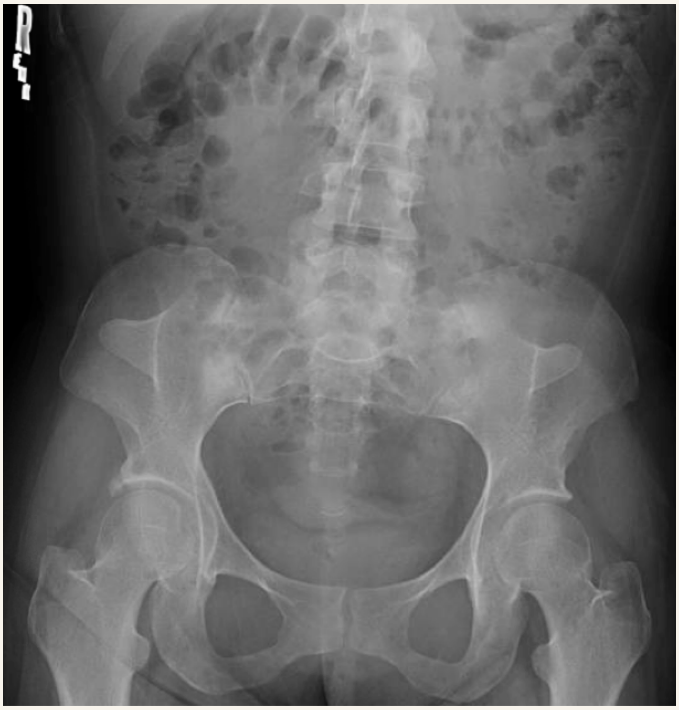
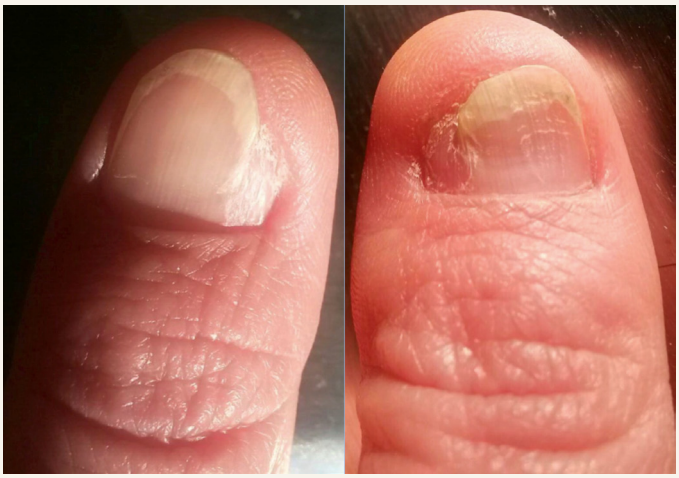


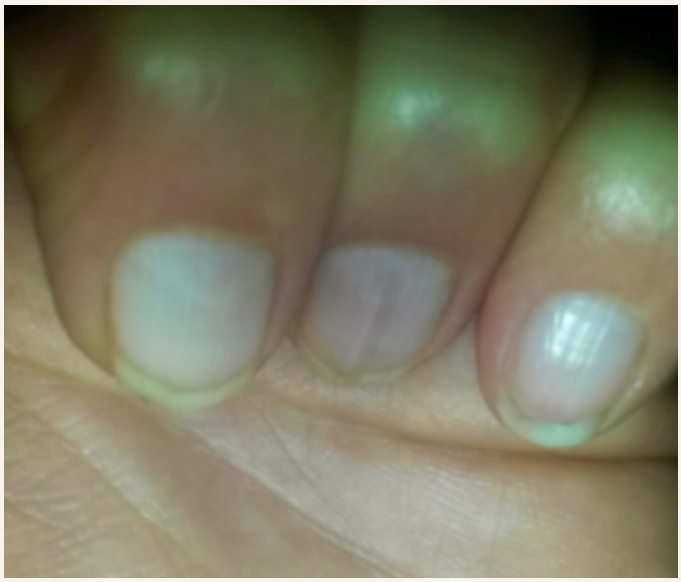
FIGURE 2. Dysplastic thumbnails.



have asymptomatic proteinuria or microscopic hematuria, less than 20% of patients progress to nephrotic syndrome and 10% develop renal failure necessitating dialysis or transplantation.[4]

In a murine model, the LMX1B gene is expressed in the developing structures important for aqueous drainage and production including the anterior segment, the trabecular meshwork and the ciliary body respectively. Compared to 1-2% of the general population 40 years or older, approximately 33% of NPS patients develop the most common type of glaucoma, open-angle. If untreated, patients may develop asymptomatic visual field loss and ultimately blindness.[5]

FIGURE 3. Triangular lunulae seen on 2nd, 3rd fingernails.



In conclusion, NPS is a relatively rare inherited disorder that affects bones, eyes, kidneys and nails. Although it usually does not impact lifespan, NPS may have significant implications regarding quality of life.

DISCLOSURES

The authors have no conflicts of interest to declare.

REFERENCES

1. Burghardt T, Kastner J, Suleiman H, et al. LMX1B is essential for the maintenance of differentiated podocytes in adult kidneys. *J Am Soc Nephrol.* 2013;24(11):1830-48. doi: 10.1681/ASN.2012080788. Epub 2013 Aug 29.
2. Chaturvedi S, Pulimodd A, Agarwal I. Quiz page December 2013: Hypoplastic nails, bowed elbows, and nephrotic syndrome. Nail-patella syndrome (hereditary osteo-onychodysplasia, Turner-Keiser syndrome, Fong disease). *Am J Kidney Dis.* 2013;62(6):A25-7. doi: 10.1053/j.ajkd.2013.05.027.
3. Goshen E, Schwartz A, Zilka LR, et al. Bilateral accessory iliac horns: pathognomonic findings in Nail-patella syndrome. Scintigraphic evidence on bone scan. *Clin Nucl Med.* 2000;25(6): 476-7.
4. Paller, Amy and Anthony Mancini. " Disorders of Hair and Nails." *Hurwitz Clinical Pediatric Dermatology.* Ed 4. Philadelphia: Elsevier, 2011. Pg 162. Print.
5. Park S, Jamshidi Y, Vaideanu D, et al. Genetic risk for primary open-angle glaucoma determined by LMX1B haplotypes. *Invest Ophthalmol Vis Sci.* 2009 Apr; 50(4):1522-30. doi: 10.1167/iovs.08-2483. Epub 2008 Oct 24.
6. Roeckerath W. Hereditary osteo-onychodysplasia. *Fortschr Geb Rontgenstr.* 1951;75(6):700-12.
7. Towers AL, Clay CA, Sereika SM, et al. Skeletal integrity in patients with nail patella syndrome. *J Clin Endocrinol Metab.* 2005; Apr;90(4):1961-5. Epub 2004 Dec 28.

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