

# CJASN

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**On the Cover**

*What's the diagnosis?*

A 26-year-old African American woman with steroid-dependent nephrotic syndrome diagnosed at age five was admitted for shortness of breath, orthopnea, and paroxysmal nocturnal dyspnea. Three prior kidney biopsies, performed for relapses and suspicion of alternative diagnoses, were consistent with minimal change disease. She had received appropriate, lengthy courses of corticosteroid and calcineurin inhibitor therapy. On current presentation, blood pressure was 163/82; there were bilateral rales with 3+ pedal edema. Serum chemistries and kidney function were normal. There was 8.3 grams of protein per gram creatinine. The patient's kidneys were 11 cm bilaterally. A fourth biopsy was performed to assess the degree of fibrosis and disease activity prior to adjusting therapy.

**Image Description:**

Kidney biopsy revealed two of 18 glomeruli had small areas of segmental sclerosis. Interstitial fibrosis was mild except for very focal tubular atrophy (<5%); however, 2 separate fibrotic foci showed metaplastic trabecular (or "spongy") bone formation. It is characterized by connecting matrix trabeculae that vary from eosinophilic to basophilic (red to purple) with the degree of calcification. Within the trabeculae are scattered cells termed osteocytes. The trabeculae surround potential marrow spaces for extramedullary hematopoiesis, not seen in this case. Podocyte foot processes were approximately 80% effaced with segmental microvillus change. The patient received two doses of intravenous rituximab at 375 mg/m<sup>2</sup>, two weeks apart, along with 16 weeks of corticosteroids. At one-year follow-up, her disease remains in remission with low-dose maintenance corticosteroid therapy.

**Teaching Points:**

Osseous metaplasia is heterotopic bone formation that uncommonly occurs in visceral organs. It has been reported with primary kidney cancer, presumably due to factors such as ischemia, necrosis, and inflammation. Chronic inflammation or immunosuppressive therapy may have contributed to OM formation in this case, yet the exact etiology is unknown. This is the first reported case in the native kidney of a patient without kidney malignancy.

Ectopic calcification must be distinguished from osseous metaplasia. Histologically, ectopic calcification lacks the supporting tissue structure described above for bone and can consist of various calcium phosphate salts including hydroxyapatite as well as calcium oxalates and octacalcium phosphate as seen in kidney stones. Osseous metaplasia is not seen in radiographic studies, unlike ectopic calcification. Osseous metaplasia is asymptomatic and standard of care is expectant management with treatment of underlying disorders.

**Figure 1 | (A)** Glomerulus with perihilar sclerosis with hyalinosis. (Hematoxylin and eosin stain. Bar = 20 μm) **(b)** Histological findings from kidney biopsy. **(B)** Focal metaplastic bone formation partially surrounding a normal-appearing glomerulus. (Hematoxylin and eosin stain. Bar = 50 μm).

(Images and text provided by Vignesh Ramachandran B.S.<sup>1,3</sup>, Jingyin Yan M.D.<sup>1,2,3</sup>, Saed H. Shawar M.D.<sup>2,3</sup>, William F. Glass II M.D.<sup>4</sup>, and Rajeev Raghavan M.D.<sup>1,2,3</sup>)

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