Osseous Metaplasia in Renal Allograft

Osseous metaplasia (OM) is the presence of heterotopic bone tissue in the extraskeletal soft tissue. OM was described in many nontransplant organs like parotid, skin, lung, labyrinth, endometrium, and kidney.[1] OM is a rare finding in the renal allograft biopsy.

A 35-year-old male developed end-stage renal disease as a result of chronic interstitial nephritis. The patient underwent live donor renal transplantation and was on triple drug regimen of tacrolimus, mycophenolate mofetil, and steroids. Three years posttransplant, the patient developed acute pyelonephritis, which was treated with appropriate antibiotics, following which the graft function stabilized. Five months later, he again developed graft dysfunction, with serum creatinine of 2 mg/dl. Serum calcium was 9.3 mg/dl. The kidney was normal on ultrasonogram; no calcification was seen. A renal biopsy was performed. Light microscopy showed eleven glomeruli, 2 were globally sclerotic. All the viable glomeruli were of normal cellularity. The capillary loops were patent and no fibrin thrombus was noted in the lumen. Glomerular basement membrane appeared normal. Interstitial fibrosis involved 50% of the sampled cortex. Lymphocytic infiltration was seen in the fibrosed cortex. There was a focus in the renal cortex where woven bone formation was noticed [Figure 1]. The osteocytes located in the lacunae were appreciated under higher magnification. Focal mineralization was also observed [Figure 2]. There were no hematopoietic cells or adipocytes in the region of bone formation. The biopsy showed no features of rejection, including tubulitis, peritubular capillaritis, or vasculitis. C4d immunostaining was negative. On follow-up, his graft function is stable, with serum creatinine maintained at 2 mg/dl.

OM results from the differentiation of mesenchymal pluripotent cells into bone tissue. The heterotopic bone matrix can be mineralized and be associated with adipocytes and hematopoietic cells. The osseous differentiation, considered aberrant tissue repair, requires a suitable environment and osteogenic signals. Various experimental studies have described the occurrence of OM in association with ischemia and inflammation. OM can be associated with the presence of hematopoietic elements (myeloid metaplasia) as reported by Azhir *et al*.[2]

There are limited cases of OM reported in the renal allograft [Table 1]. Majority of them were detected following allograft nephrectomy.[1-4] The time taken for the appearance of OM varied between 6 months and 5 years. OM was observed during autopsy in one case.[5] All except our case had concomitant features of rejection. Chronic inflammation or ischemic changes were present in all the cases.[6] OM in our patient is likely to be the sequela of pyelonephritis. Similar to our patient, Bataille *et al.*[1] observed OM in association with recurrent pyelonephritis.[1] They hypothesized that OM resulted from chronic ischemia or inflammation following infection or as an immunologic process.

The calcification detected in the allograft by imaging studies could be due to nephrolithiasis, ectopic calcification, or OM.[1] Nephrolithiasis is located in renal pelvis. Ectopic calcification is the inappropriate biomineralization in soft tissues with deposition of calcium salts and can occur in uremic patients due to mineral imbalance. OM is different from ectopic calcification. Unlike OM, bone formation, osteocytes, or hematopoietic elements are absent in ectopic calcification.

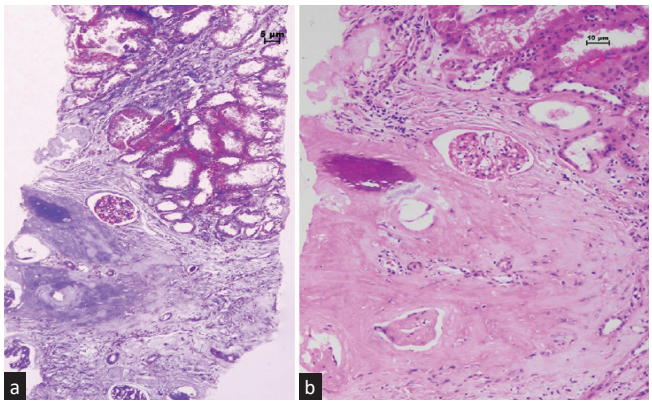

Figure 1: (a) Woven bone is seen in the renal parenchyma. The surrounding tissue shows fibrosis of the interstitium (Masson trichrome stain, 100×). (b) There is a focus of mineralization within the woven bone (hematoxylin and eosin stain, 200×).

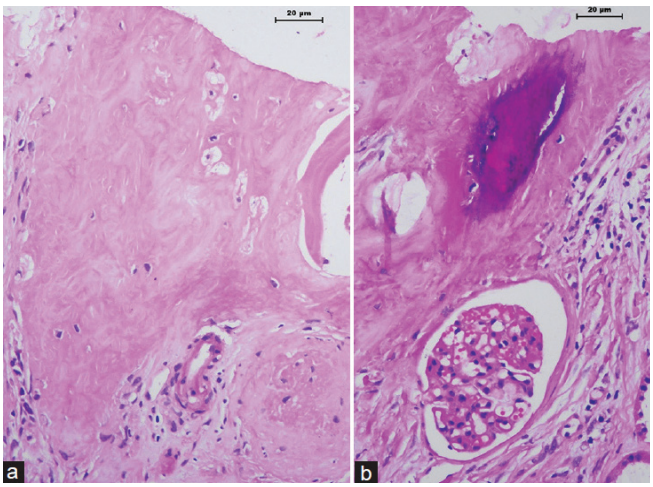

Figure 2: There are (a) osteocytes within lacunae and (b) a focus of mineralization (hematoxylin and eosin stain, 400×).

Table 1: Literature review of osseous metaplasia in the renal allograft[a]

Author	Age at Tx	Specimen type	Native kidney disease	Rejection	Type of donor	Location of osseous metaplasia
Current case	35	Allograft biopsy	Chronic interstitial nephritis	No rejection	Live	Renal cortex
Bataille *et al*.[1]	21	Graft nephrectomy	Interstitial nephritis	Chronic	Deceased	Renal cortex
Azhir *et al*.[2]	28	Graft nephrectomy	Diabetic Nephropathy	Acute on chronic	Live	Renal cortex and medulla
Tousignant *et al*.[3]	15	Graft nephrectomy	Renal dysplasia	Acute on chronic	Deceased	Renal cortex
Chan *et al*.[4]	43	Graft nephrectomy	IgA Nephropathy	Chronic	Deceased	Renal parenchyma
Makhoba *et al*.[5]	11	Autopsy	Unknown	Chronic	NA	Renal parenchyma
Sanders *et al*.[6]	22	Allograft biopsy	FSGS Collapsing variant	Acute on chronic	Deceased	Renal cortex

[a]Adapted from Sanders BP *et al*. *Exp Clin Transplant*. 2014;12(4):371-373. Tx = transplant, VUR = vesicoureteral reflux, FSGS = focal and segmental glomerulosclerosis, NA = Not Available

OM in the renal allograft is rare. Though not directly implicated in the graft dysfunction, its presence in the biopsy hints toward chronic injurious stimuli like inflammation, ischemia, or infection in the allograft.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

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Radiolucent Calculi in Kidneys on Intravenous Urography: Red Color on Dual-Energy Computed Tomography Clinches the Final Diagnosis

A 1-year-old girl, follow-up case of bilateral hydronephrosis, underwent intravenous urography (IVU) to assess the function and drainage. The plain spot [Figure 1a] of the IVU study showed no radiopaque calculus. Subsequently, in 1-h post-intravenous contrast injection, mild bilateral hydronephrosis was present with two radiolucent filling defects seen, one each in the right and left renal pelvis [Figure 1b] suggestive of radiolucent calculi. Low-dose dual-energy computed tomography (DECT) was subsequently done for further delineation and characterization to decide upon the management. It showed bilateral nephrolithiasis with mild hydronephrosis [Figure 1c and d]. On dual energy evaluation, bilateral renal calculi were red and found to have a uric acid composition [Figure 1e and 1f].

Radiolucent stones constitute only 10% of urolithiasis cases. These include uric acid, cysteine, and medication-induced (such as indinavir, triamterene, sulfonamides, and amorphous silica) calculi. DECT can help to differentiate uric acid stones from non-uric acid stones (such as calcium oxalate, calcium phosphate, struvite, cystine, and hydroxyapatite) due to their material decomposition ability.[1] Uric acid stones are color-coded red, while the non-uric acid stones are blue. This is important from a management point of view, as the uric acid calculi are