

METASTATIC CALCIFICATION IN CHRONIC RENAL FAILURE

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ABSTRACT

Metastatic calcification is the deposition of calcium salts in previously healthy tissues, usually as a result of abnormalities of calcium and phosphorous metabolism. The pulmonary parenchyma is most susceptible to calcification. Such condition may be caused by both benign and malignant diseases, most commonly metastatic pulmonary calcification is seen in patients with chronic renal failure who are on hemodialysis. In autopsies, 60–80% of patients with CRF reportedly present MPC.¹ We report two cases with chronic renal failure and metastatic calcifications, both patients were hypertensive and were on dialysis. A 46 yrs old female suffering from chronic renal failure, is on dialysis for 2 years. Another patient 48 yrs old was a known case of chronic renal failure. She is on dialysis for 6 years.

Key words: Chronic renal failure; Metastatic calcification; Vascular calcification

Case 1

We present a case of 46 yrs old female suffering from chronic renal failure, on dialysis for 2 years, came with the complaint of fever for 5 months and mild cough. There was no hemoptysis, chest pain or shortness of breath. Patient was hypertensive but there was no history of diabetes mellitus, drug allergies or dust exposure. Chest radiography showed thickened pleural plaques in right hemithorax at periphery and at apex. coarse fibrosis was seen in both lungs more marked on right side. Bronchiectatic changes were seen in both upper lobes and in right lower lobe. Small thick walled cavities were also seen in both upper lobe. Cardiac transverse diameter was increased with C:T ratio of 156 : 250 but pulmonary vascularity was normal. Hila and mediastinum were normal, Costophrenic angles and rib cage was normal. No previous x-ray was available for comparison. Subsequently CT scan Chest was done in which axial images were obtained after contrast injection with re-constructive coronal images. There was evidence of extensive nodular calcific densities noted in both lungs with predominant

involvement of the upper zones. There was also dense pleural thickening noted along the posterior margins extending from the apical region inferiorly up to the basal region. Pleural calcification was also noted in the left apical region posteriorly. Findings were secondary to metastatic calcification secondary to renal failure/hemodialysis. There were also discrete small areas of calcification noted in the paraspinal muscles and also in the anterior chest wall. These are also secondary to chronic renal failure. No acute infiltrates, mass or consolidation seen in either lung. No evidence of hilar or mediastinal lymphadenopathy. No evidence of pleural effusion. The vascular and bony structures were normal. With the advent of CT and HRCT, it is becoming increasingly easy to make an antemortem diagnosis of metastatic pulmonary calcification, thereby obviating the need for open lung biopsy.⁵

Case 2

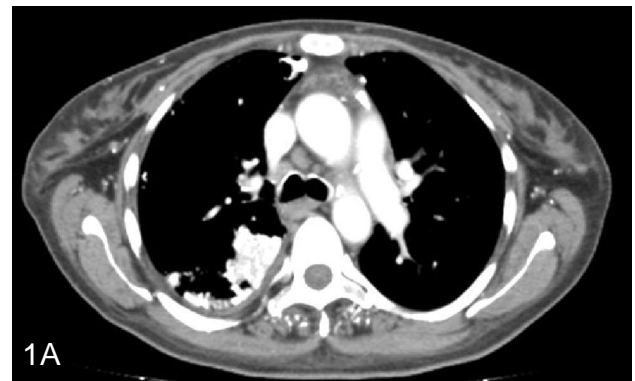
Another patient presented to us with the complains of painless subcutaneous swelling around left elbow joint,

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at the lower abdomen, around both shoulders and hands. She also complained of non-healing ulcers on toes of right foot. Skin is erythematous and indurated. Patient was a known case of hypertension and chronic renal failure. She is on dialysis for 6 years. On laboratory investigations serum calcium was 8.0 mg/dl (Normal 8.4-10.1 mg/dl), serum phosphorus was 10.0 mg/dl (Normal 2.5 - 4.5 mg/dl). CBC was normal.

On chest x-ray, Chest radiography showed thickened pleural plaques in right hemithorax. Left upper, mid and lower zone infiltration was also noted. Cardiac transverse diameter was increased. Hila and mediastinum were normal, Costophrenic angles and rib cage was normal. Extensive, moderately well defined, calcific masses were noted within the soft tissues around both shoulder joints and scapular regions, more towards right side. Moreover another large calcified mass was also noted on x ray pelvis. The mass was extending downward into the soft tissues of pelvis and perineum.

On CT angiogram, there was evidence of extensive vascular calcification, seen involving the splenic artery, celiac axis, hepatic artery, and superior mesenteric artery. Calcification is also noted in bilateral internal iliac arteries in distal course and uterine arteries. There was also evidence of interrupted areas of mural calcification in bilateral anterior tibial and common peroneal arteries. There are segmental areas of narrowing in both anterior tibial and common peroneal arteries. Aorta, both common iliac, external iliac, common femoral, superficial femoral, profunda femoris and popliteal arteries were patent without evidence of any narrowing or occlusion. Both kidneys were small and atrophic consistent with chronic renal failure. Confluent calcific nodular masses are noted in anterior abdominal wall, extending into pelvis down into the perineum and in the subcutaneous tissues of left thigh. There was evidence of multilevel bone resorption involving body, left inferior ramus of pubic bone and left acetabulum. Resorption was also noted along both sacroiliac joint more on ileal side. Visualized spine demonstrates altered density with areas of osteosclerosis, giving an appearance of Ruggers spine. Visualized lung fields demonstrate pleural calcification on right side. All these findings were due to chronic renal failure with superimposed secondary hyperparathyroidism.



1A

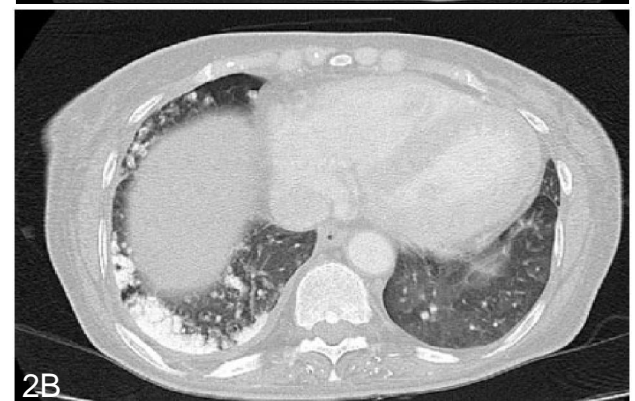


1B

Figure 1A-B: CT Scan Chest with contrast, mediastinal windows, Axial images : Dense pleural thickening noted along the posterior margins extending from apical region inferiorly up to the basal region. Small areas of calcification are also present in paraspinal muscles and anterior chest wall.



2A



2B

Figure 2A-B: CT Scan Chest, Lung windows, Axial Images: Nodular calcific densities noted in both lungs, predominantly in upper zones.

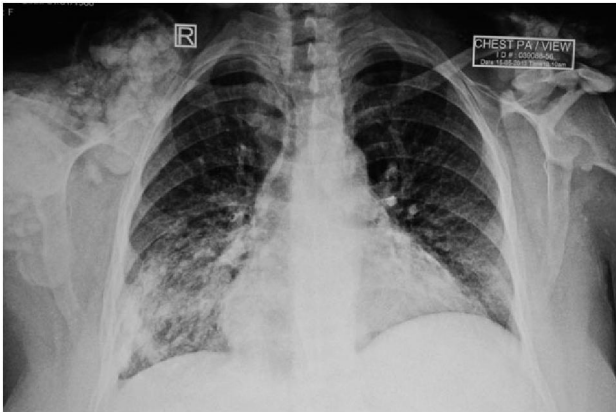


Figure 3 : Chest Xray PA view ,Thickened pleural plaques in right hemithorax, predominantly in right lower zones. Nodular calcific masses are present extensively involving soft tissues of both shoulders. Changes are more marked towards right side.

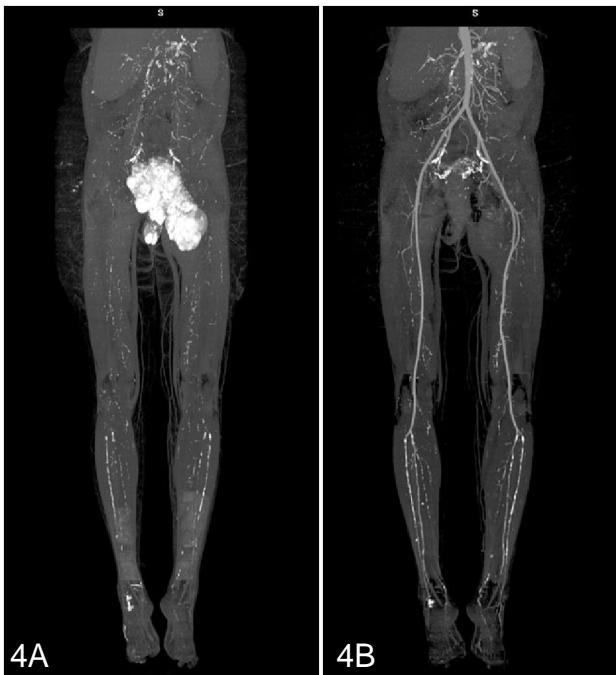


Figure 4A-B: CT Angiogram, reconstructed images : extensive calcification, seen involving the splenic artery, celiac axis, hepatic artery, and superior mesenteric artery. Calcification is also noted in bilateral internal iliac arteries, uterine arteries, bilateral anterior tibial and common peroneal arteries. There are segmental areas of narrowing in both anterior tibial and common peroneal arteries. Aorta, both common iliac, external iliac, common femoral, superficial femoral, profunda femoris and popliteal arteries are patent without evidence of any narrowing or occlusion. In addition, confluent calcific nodular masses are noted in pelvis, extending into perineum and in the subcutaneous tissues of left thigh.

Discussion

Ectopic calcification is divided into two groups, according to the physiopathological mechanism, as dystrophic calcification - deposition of calcium salts in

previously injured tissues, and metastatic calcification-deposition of calcium salts in previously healthy tissues.¹ Typically, extensive microvascular calcification and occlusion/thrombosis leads to violaceous skin lesions, which progress to nonhealing ulcers and sepsis. Secondary infection of skin lesions is common, often leading to sepsis and death. The lower extremities are predominantly involved (roughly 90% of patients) lesions distal to the knees or elbows). In early stages of the disease, calciphylaxis lesions can resemble those seen in vasculitis, SLE, cryoglobulinemia, scleroderma/CREST syndrome, DIC, cholesterol emboli, or bacterial endocarditis. Calciphylaxis should be distinguished from the acral ulcerations or gangrene that accompany atherosclerotic peripheral vascular disease, resulting in distal necrosis and gangrene. Preserved peripheral pulses favor the diagnosis of calciphylaxis.² Calcification is an almost ubiquitous pathological process in patients with end stage renal disease (ESRD). It can result in range of pathologies including calcific uremic arteriopathy, extraosseous soft tissue calcification and solid organ calcification. However vascular and valvular calcification is the most common and perhaps the most clinically significant manifestation. Vascular calcification is the most common type of extra-osseous calcification in end-stage renal disease (ESRD), manifesting as both medial and intimal calcification of large arteries. It is highly prevalent, progressive and is associated with reduced arterial elasticity and increased mortality. Risk factors for calcification in ESRD include age, duration of dialysis, diabetes mellitus, most probably an elevated calcium phosphorus product (Ca x P) level, the dose of calcium-containing phosphate binders and the induction of systemic inflammatory response.³

Patients with CKD show vascular calcification almost in all localizations, from high-caliber arteries, such as aorta, where the prevalence is extremely high, to medium and small size vessels, including coronary arteries. Also, calcification of the cardiac valves represents a high risk for cardiovascular dysfunction.⁴ Other organs such as stomach, kidneys and heart can also be affected by calcification; but the pulmonary parenchyma is the most susceptible tissue.¹ Metastatic pulmonary calcification commonly occurs in conditions that produce an elevated calcium-phosphate product and result in the deposition of calcium salts in the alveolar and vessel walls of normal lungs. The overall incidence of metastatic pulmonary calcification is low.⁵ However, this condition is a common complication of

chronic renal failure. It occurs in 50% or more of renal patients with metastatic soft tissue calcification.⁶ Multifocal patterns of pulmonary parenchymal calcification may also be associated with infection (especially histoplasmosis and tuberculosis), silicosis, diffuse parenchymal amyloidosis, alveolar proteinosis, idiopathic pulmonary hemosiderosis, and alveolar microlithiasis, haemosiderosis secondary to mitral stenosis and fat embolism associated with adult respiratory distress syndrome.⁷ Chronic kidney disease requiring hemodialysis is the condition most frequently associated with metastatic pulmonary calcifications.⁷ Even when seen on chest radiograph, diffuse calcification is often mistaken for other process such as pulmonary edema, because it appears as non discrete infiltrates. Similarly, localized pulmonary calcification often is confused with infection, pneumonia or malignancy.⁸ CT, especially HRCT, is much more sensitive than chest radiography in detecting small amounts of calcification and is increasingly used in the diagnosis of MPC,¹⁰ thereby obviating the need for open lung biopsy.⁹ The combination of pulmonary and vascular calcification is characteristic of metastatic pulmonary calcification.⁷

The most sensitive technique for detecting calcifications appears to be technetium-99m-methylene diphosphonate (99mTc-MDP) scintigraphy, which also has the advantage of being capable of detecting calcification in other organs.¹⁰ Because pulmonary calcification is often misinterpreted as pneumonia or pulmonary edema both on the chest radiograph and CT scan, bone scintigraphy with the bone-avid radiotracer 99mTc-MDP helps sort equivocal cases.⁹

Conclusion

Over all incidence of metastatic calcification is low, however high prevalence of metastatic calcification is known in the setting of patients with end stage chronic kidney disease and patient who are on hemodialysis. Vascular calcification is the most common type of extra-osseous calcification in end-stage renal disease, manifesting as both medial and intimal calcification of large arteries. Organs such as stomach, kidneys and heart can also be affected by calcification but the pulmonary parenchyma is the most susceptible tissue.¹ HRCT is the efficient method for detecting MPC but as findings on HRCT may be difficult to distinguish from other parenchymal process, 99 Tc- MDP bone scintigraphy may be useful to detect pulmonary as well as other organs calcification.

Conflict of Interest: None

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