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Uremic tumoral calcinosis, report of a rare case at King Chulalongkorn Memorial Hospital

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Uremic tumoral calcinosis is primarily found in patients with chronic kidney disease (CKD) or end-stage renal disease (ESRD). Its clinical and radiologic presentations are highly characteristic. We herein report a case of a 33-year-old Thai male with ESRD and tertiary hyperparathyroidism. He presented with multiple cystic nodules on the right shoulder, hands, and feet without causing joint destruction for 2 years. The plain radiographs of the right shoulder and hands showed the pathognomonic "sedimentation sign". The patient underwent subtotal parathyroidectomy, as a result, the masses significantly decreased in size 3 months later. This case should increase the awareness among dermatologists and internists in the diagnosis and management of this rare disorder.

Keywords: *Chronic kidney disease, hyperparathyroidism, sedimentation sign, uremic tumoral calcinosis.*

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ชันทิ์ กำรรัตน์, น้้ำผึ้ง น้้ำการุณอรุณโรจน, ภาวินิ์ ฤกษ์นิมิตร. รายงานผู้ป่วยโรคไตเรื้อรังที่มีภาวะแคลเซียมสะสมในผิวหนังที่โรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2557 พ.ย. - ธ.ค.; 58(6): 621 - 7

Uremic tumoralcalcinosis เป็นภาวะที่มีก้อนหินปูนผิดปกติ ซึ่งพบได้ในผู้ป่วยโรคไตเรื้อรังและไตวายเรื้อรังระยะสุดท้าย แม้พบอุบัติการณ์ที่ค่อนข้างต่ำ แต่มีลักษณะทางคลินิกและรังสีวิทยาที่จำเพาะ โดยอาการแสดงจะตรวจพบก้อนที่ค่อนข้างนิ่มคล้ายถุงน้ำ มักขึ้นบริเวณรอบข้อต่อของผู้ป่วย แต่จะไม่ทำให้การเคลื่อนไหวของข้อนั้นผิดปกติไป ภายในก้อนบรรจุด้วยของเหลว มีลักษณะเป็นน้ำสีขาวอมเหลือง ส่วนลักษณะทางรังสีวิทยาเห็นเป็นระดับของของเหลวแยกกันอยู่ในแต่ละช่อง ล้อมรอบบริเวณข้อแต่ไม่มีการทำลายของข้อ ยังไม่เป็นที่ทราบสาเหตุของภาวะนี้แน่ชัด แต่ปัจจัยเสี่ยงที่สำคัญคือ ภาวะแคลเซียมฟอสเฟตในเลือดสูงผิดปกติ ซึ่งอาจพบร่วมกับภาวะฮอร์โมนพาราไธรอยด์สูงชนิดทุติยภูมิหรือตติยภูมิได้ พบการพยากรณ์โรคค่อนข้างดี ก้อนหินปูนสามารถหายเองได้ โดยเฉพาะเมื่อทำการรักษาให้ระดับแคลเซียมและฟอสเฟตในเลือดกลับมาเป็นปกติ ในที่นี้ได้รายงานกรณีศึกษาผู้ป่วยที่มีภาวะไตวายเรื้อรังและภาวะฮอร์โมนพาราไธรอยด์สูงชนิดตติยภูมิ ที่มีอาการแสดงและลักษณะทางรังสีที่เฉพาะกับภาวะนี้ และก้อนหินปูนมีขนาดเล็กถึงได้เองหลังการรักษาด้วยการผ่าตัดต่อมพาราไธรอยด์

คำสำคัญ : โรคไตเรื้อรัง, ภาวะฮอร์โมนพาราไธรอยด์สูง, การตกตะกอน, ภาวะแคลเซียมสะสมในผิวหนัง.

The cutaneous signs in patients with kidney diseases can be classified into two groups: the first group mainly manifests in patients with acute kidney injury such as edema and uremic frost; the second is usually associated with chronic kidney disease (CKD). Each condition reflexes different pathogenesis and prognosis in the patients. Tumoral calcinosis (TC) is another typical skin sign found in patients with end-stage renal disease (ESRD). It has an excellent prognosis depends upon the control of serum calcium and phosphate.

Case Report

A 33-year-old Thai male from Bangkok presented with progressive multiple painless subcutaneous nodules and masses on his right shoulder, both hands and feet for 2 years. The masses progressively enlarged without causing limitation on range of motion of the involved joints. He denied any previous trauma in those areas. He also had end-

stage renal disease with undefined etiology and was on regular hemodialysis three times a week for 5 years. He has been diagnosed as having hypercalcemia and hyperphosphatemia with tertiary hyperparathyroidism for 6 months. His general physical examination showed mildly pale conjunctivae. Other systems were within normal limits. His skin examination revealed multiple subcutaneous nodules and masses, firm in consistency, without surface changes on the right shoulder, both hands, and feet (Figures 1 A and 1 B).

Further laboratory investigations showed serum calcium of 11.7 mg/dl, albumin of 4.3 g/dl, phosphate of 8.5 mg/dl, and intact parathyroid hormone of 2,425 pg/ml (normal value 15 - 65 pg/ml). Tc-99m sestamibi and Tc-99m pertechnetate disclosed an enlargement of three parathyroid glands. In addition, plain radiographs of the right shoulder and the right hand showed masses with multiple pockets of calcium-fluid levels, so-called: "the sedimentation sign" (Figures 2 A and 2 B).

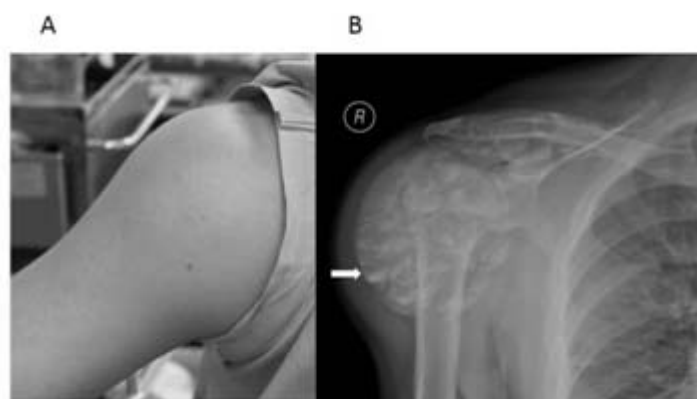


Figure 1. A: a firm subcutaneous nodule without surface changes on the patient's right shoulder;
B: Plain radiograph of right shoulder in anteroposterior projection shows mild lobulated soft tissue mass overlying right proximal humerus and right distal clavicle, measured about 14.0 x 10.4 cm. This mass shows multiple pockets of calcium-fluid levels, representing sedimentation sign (arrow). The inferior layer represents calcium while the superior layer represents fluid.



Figure 2. A: a firm nodule on the patient's right hand; B: Plain radiograph of right hand in anteroposterior projection shows multiple lobulated periarticular soft tissue masses on radial side of right 2nd MCP and 3rd DIP joints and nearby distal phalanges of 1st, 2nd, and 5th fingers. The largest one was located at radial side of the 2nd MCP joint with sedimentation sign (thick arrow), measured about 2.8 × 4.0 cm. There is also subperiosteal resorption on radial side of the 2nd and 3rd middle phalanges (thin arrow) with terminal tuft resorption of all digits.

Skin biopsy from his right hand revealed a dome-shaped lesion within the dermis. Large aggregations of homogenous amorphous basophilic material consistent with calcium were identified in the deep dermis. Von Kossa stain, which is used to demonstrate calcium, was also positive (Figure 3). Furthermore, upon obtaining the skin specimen with a 4-mm punch biopsy, milky discharge was observed

(Figure 4).

The diagnosis of uremic TC associated with tertiary hyperparathyroidism was then made based on the typical clinical and radiological findings.

Four months later, after subtotal parathyroidectomy was performed, his nodules and masses progressively decreased in size. Some nearly disappeared without any joint complications.

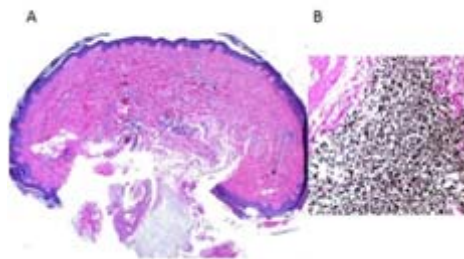


Figure 3. Photomicrographs showing A: a dome-shaped lesion of normal epidermis. Within the dermis, there is a vascular proliferation with perivascular lymphohistiocytic infiltrate. Large aggregations of homogenous amorphous basophilic material consistent with calcium are identified in the deep dermis (haematoxylin and eosin; original magnification × 20); B: positive Von Kossa stain that stains calcium black (Von Kossa; original magnification × 100).



Figure 4. Tumoral calcinosis nodule of the patient containing yellowish chalky material called “milk of calcium” which is a typical characteristic of the condition.

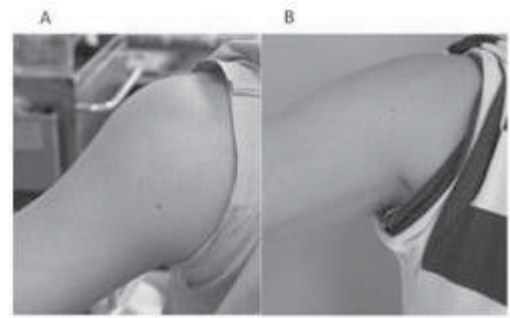


Figure 5. A: before treatment; B: four months after subtotal parathyroidectomy, the size of the subcutaneous nodule has dramatically decreased.

Discussion

TC is a form of calcinosis cutis, classified as either metastatic or idiopathic type upon the presence of abnormal metabolic activity. It is categorized according to the pathogenesis into primary and secondary TC; however, the clinical findings are similar in all groups. ⁽¹⁾

Uremic TC is a form of secondary TC which rarely occurs in patients with CKD or ESRD. The prevalence varies from 0.5 - 7%. ⁽²⁾ The pathogenesis is unclear, but Slavin RE *et al.* ⁽³⁾ proposed that a concurrence of a reaction to multiple repetitive injuries in periarticular soft tissue and an abnormal calcium and phosphate metabolism may contribute to the pathogenesis of this rare disorder.

Most important risk factors found in patients with uremic TC are an elevation of calcium-phosphate product and hyperphosphatemia. Secondary and tertiary hyperparathyroidism, sometimes, are associated with uremic TC. Aluminium intoxication, hypermagnesemia, hypervitaminosis K, hypervitaminosis D, and metabolic alkalosis have been reported as being precipitating factors. ⁽⁴⁾

The clinical manifestations are slowly progressive subcutaneous nodules and soft tissue masses with firm consistency. They are usually asymptomatic but can cause pressure effect if their sizes are big enough. These nodules commonly involve the periarticular and trauma-related areas including hips, shoulders, elbows, knees, hands, and feet. Those masses contain yellowish chalky material called “milk of calcium” which is another typical characteristic of TC. ⁽⁵⁾

Radiologic findings of TC are pathognomonic. They are multilobulated calcified cystic masses, usually located adjacent to trauma-related area without evidence of joint or bone involvement. Each lobule, sometimes, shows fluid level called “sedimentation sign” (Figure 1 B), representing the sediment of the chalky material. This sign can be identified by plain film, ultrasonography, and MRI. ⁽⁶⁾

Histopathological study also correlates with the radiologic findings. The gross specimen illustrates a well-defined mass with amorphous lobulated appearance with chalky-white fluid. In section, multiple calcified foci surrounded by foreign body reaction at the rim of cysts can be demonstrated. ⁽⁷⁾

The aim of the treatment is to control serum phosphate and calcium levels. Phosphate depletion therapy includes low phosphate diet, phosphate binder medications, and to increase renal phosphate excretion by acetazolamide. Nocturnal hemodialysis⁽⁸⁾ and hemodialysis with low calcium dialysate are reported to be helpful.⁽⁹⁾ In case of secondary and tertiary hyperparathyroidism, which is recalcitrant to medical treatments, subtotal or total parathyroidectomy may be indicated.

Our patient also presents with tertiary hyperparathyroidism, defined as a state of excessive secretion of parathyroid hormone after longstanding secondary hyperparathyroidism. This condition usually manifests as hypercalcemic hyperparathyroidism and occurs as a complication of CKD. Four-gland hyperplasia of parathyroid tissue is frequently observed. However, triple adenoma as seen in our patients is also possible.⁽¹⁰⁾

Despite the effort with medical treatments to lower serum calcium and phosphate in our patient, normalization of the levels could not be achieved. Finally, the patient underwent subtotal parathyroidectomy. At 4-month follow up, the size of the subcutaneous nodules was decreased dramatically (Figure 5). Resolution of TC a few months after operation has also been reported in the literature.⁽¹¹⁾

In summary, we herein report a case of secondary TC in a patient with ESRD and tertiary hyperparathyroidism. The patient presents with classic cutaneous lesions and pathognomonic x-ray findings. The condition rarely occurs. This should increase the awareness among dermatologists and internists in the diagnosis and management of this rare disorder.

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