

TUMORAL CALCINOSIS IN CHRONIC RENAL FAILURE : TWO CASE REPORTS

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SUMMARY: Two cases of tumoral calcinosis occurring in patients with chronic renal failure on hemodialysis are described. The aetiology of tumoral calcinosis is described with particular reference to the patients presented. The metastatic calcification occurring in these two cases is most likely related to hyperphosphataemia and secondary hyperparathyroidism possibly aggravated by vitamin D therapy. Treatment was with withdrawal of vitamin D therapy, parathyroidectomy and stricter control of serum phosphate levels.

Key Words : Tumoral calcinosis, metastatic calcification, hyperparathyroidism, hyperphosphataemia, vitamin D.

INTRODUCTION

Metastatic soft tissue calcification is a well known complication of chronic renal failure. Vascular calcification is commonly seen in chronic hemodialysis patients with calcification of the soft tissues observed less frequently (1). The factor most commonly associated with soft tissue calcification is reported to be hyperparathyroidism, a frequently encountered feature of chronic renal failure. Sporadic cases of soft tissue calcification without accompanying hyperparathyroidism have been reported in the literature (1). Metastatic calcification in hyperparathyroidism may include tumoral calcinosis. This is periarticular calcification predominantly located around the large joints and sometimes manifested clinically as a palpable tumor like mass (1). We present

two cases of soft tissue calcification with associated hyperparathyroidism who had been dialyzed at other centers prior to referral to our clinic.

CASE 1

S. U., a 45 year old female presented in 1986 with signs and symptoms of chronic renal failure. Following renal and rectal biopsies, a diagnosis of amyloidosis was made and she was prescribed colchicine 0.5 mg tds. Despite therapy her renal function rapidly deteriorated and she required hemodialysis one month later. The patient was maintained on hemodialysis 4 hours three times weekly, and at the end of the second year started to complain of painful swellings over both hands. Shortly afterwards she developed a similar swelling over her left elbow by another on the left side of her neck.

At this stage the patient was referred to our outpatient clinic for evaluation. On physical examination the

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patient was sallow in complexion. A hard, fixed, non tender mass measuring 4 x 4 cm was present on the left side of her neck on the superior aspect of sternocleidomastoid muscle. Fluctuant or hard swellings of both hands were also noted. These were located over the metacarpophalangeal joints with some of them extending to the distal interphalangeal joints and markedly restricting the movement of her fingers (Figure 1). There was a 5 x 5 cm fixed, hard tender mass present on the posterior aspect of her left elbow (Figure 2) and a similar mass measuring 5 x 6 cm on the anterolateral aspect of the right shoulder (Figure 3). The movement of her elbow was unaffected, whilst the shoulder could be elevated up to 135 degrees. X-rays of the affected joints revealed soft tissue calcification in the involved areas. The swelling of the hands were aspirated and a dense white viscous material that became a coarse powder on drying was obtained. Analysis of the aspirate revealed it to contain calcium phosphate. Routine testing revealed the following : BUN 69 mg/dl, serum creatinine 6.7 mg/dl, serum Ca^{2+} 10.2 mg/L, PO_4 7.5 mg/dl, alkaline phosphatase 249 IU/L, and parathormone 126 ng/ml. At referral the patient was taking colchicine, aluminium hydroxide and 1-alpha cholecalciferol irregularly. We discontinued the vitamin D replacement therapy and stressed the importance of regular phosphate binding therapy with aluminium hydroxide. Ultrasound examination of the parathyroid glands revealed only parathyroid enlarge-

ment. In view of the clinical findings a putative diagnosis of secondary hyperparathyroidism with hyperplasia of the parathyroid gland was made, and a subtotal parathyroidectomy was performed. Postoperatively the swellings on her hands gradually decreased and movements of the fingers improved. Unfortunately the patient died due to sepsis three months later.

CASE 2

S. Ç. was a 57 year old gentleman with signs and symptoms of chronic renal failure developing following longstanding pyelonephritis due to urolithiasis. He was maintained on hemodialysis 4 hours three times per week. At the end of his second year on hemodialysis he presented to us complaining of painless swelling over both knees and ankles. He described a local increase in the temperature of the swellings at first, their consistency being rubbery to begin with but later hard. X ray findings were consistent with soft tissue calcification, and again a white aspirate found by analysis to contain calcium phosphate was recovered. Serum calcium and phosphate levels were 8.6 and 11.0 mg/dl respectively, the serum alkaline phosphatase 119 IU/L and the serum parathormone level 178 ng/ml. As in the first case the patient was taking aluminium hydroxide and a vitamin D preparation (1,25-dihydroxycholecalciferol) on an irregular basis, and again the vitamin D was discontinued and regular aluminium hydroxide therapy continued. Ultrasound examination

Figure 1: X ray of hands showing soft tissue calcification effecting mainly the right third digit and second left digit.



Figure 2: Postero-anterior and lateral X rays of the left elbow showing tumoral calcification in the posterior aspect.



of the parathyroid gland revealed diffuse enlargement. A diagnosis of secondary hyperparathyroidism due to diffuse hyperplasia was made and a subtotal parathyroidectomy performed. At surgery only 3 of the glands could be identified and excised, the fourth not being found, and despite radiographic and radio-isotopic investigations the fourth gland remained unidentified. Postoperatively there was marked clinical improvement with serum phosphate, calcium, and parathormone levels dropping to 6 mg/dl, 9.5 mg/dl and 0.17 ng/ml respectively. The patient died the following year following an acute myocardial infarction.

DISCUSSION

Although calcification of periarticular tissues is frequent in chronic hemodialysis patients tumoral calcinosis is reported to be rare (1). Despite various investigations the aetiology of soft tissue calcification is still not well understood. An elevated calcium x phosphate product it thought to be the most important cause of extra-skeletal calcification although secondary hyperparathyroidism, adynamic bone disease, hypermagnesemia vitamin D, and vitamin K overload, aluminium intoxication, metabolic alkalosis, and tissue injury may also play a part (1,2).

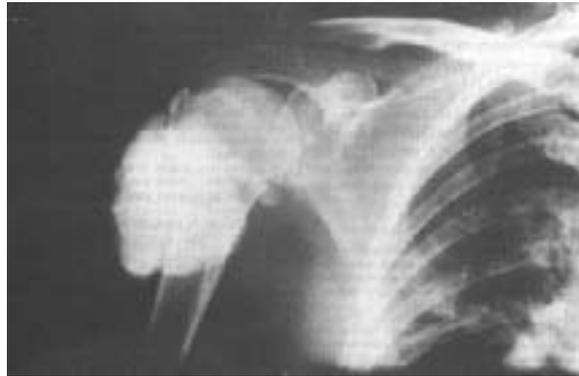
The calciumxphosphate products in our patients at admission were 76 and 95 mg^2/dl^2 respectively, and each exceeded the value of 65-75 mg^2/dl^2 which has been reported to be associated with soft tissue calcifi-

cation (3). It must be noted however that the relationship between soft tissue calcification and calcium phosphate product is not straightforward, a number of studies finding no relationship between the two (4,5), but with others demonstrating an effect (6).

Secondary hyperparathyroidism with subsequent hypercalcaemia has been reported to play an important role in the aetiology of tumoral calcinosis. Parathyroid enlargement was demonstrated in both our patients with concomitant elevation in serum parathormone levels in each of them. Elevated serum 1,25 dihydroxycholecalciferol level due to either excessive intake or produced by granulomas such as sarcoid (7), may lead to rapid development of tumoral calcinosis in dialysis patients especially if serum phosphate levels are also elevated (8). We were unable to measure the 1,25 dihydroxycholecalciferol levels in our patients although levels were unlikely to have been raised both patients being incompilant and only taking their medication irregularly. Similarly patients had not taken their phosphate binding agents as instructed and this may explain in part the high serum phosphate levels recorded and the subsequent hyperparathyroidism.

It is perhaps fortunate that these patients with uncontrolled hyperphosphataemia did not regularly take vitamin D replacement therapy since this is contraindicated under these circumstances, the resulting high calcium phosphate product predisposing to soft tissue calcification.

Figure 3: X ray of the right shoulder showing pronounced soft tissue calcification over the anterior and lateral aspects of the humerus.



Adynamic bone disease has been proposed to predispose to tumoral calcinosis (1). Here osteomalacia is characterized by an osteoid mineralisation rate which is slower than the osteoid formation rate. Adynamic bone disease is common in patients with aluminium osteodystrophy on hemodialysis (9) but has also been described in continuous peritoneal dialysis patients who were not overloaded (10). Presently the incidence in patients exposed to heavy loads of aluminium is unknown although Zins *et. al.* saw ten patients with tumoral calcinosis between 1974 and 1984 and searched for aluminium overload in eight patients with a positive result in all of these (11). Eisenberg *et. al.* have postulated that a high dialysate calcium concentration during dialysis may predispose patients with adynamic osteomalacia to extra-osseous calcification (1) although neither patient had been dialyzed against a high calcium dialysate.

Aluminium intoxication may also exert an effect by other mechanisms such as changing the equilibrium between free and bound calcium in tissues in the direction of the bound form (2), or by increasing collagen cross linking and predisposing to dystrophic or metastatic calcification (12).

Robert *et. al.* have hypothesized that vitamin K excess favors the occurrence of extra-skeletal calcium deposits in hemodialysis patients; possibly by inducing the formation of Gla-proteins distinct from bone Gla-protein (13).

The cause of the calcification observed in our patients was probably uncontrolled hyperphosphataemia with consequent hyperparathyroidism. This may well have been compounded by simultaneous prescription of vitamin D preparations even though the patients may not have taken them as prescribed. We were unable to quantitate aluminium levels in our patients and can therefore make no comment regarding their aluminium status.

Following referral to our unit the importance of good phosphate control was explained to each patient, regular phosphate binding therapy instigated, vitamin D therapy stopped and parathyroidectomy performed. In one patient therapy was successful with complete resolution of symptoms whilst in the other marked clinical improvement was seen although the continuance of mild symptoms may have been related to the fact that one parathyroid gland could not be localized and removed.

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