Rare disease

A rare disorder: tumoral calcinosis and cirrhosis

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Summary

Tumoral calcinosis is a rare disease characterised by deposition of calcified mass near the joints. The pathogenesis of this disease is not exactly defined. A disorder of calcium and inorganic phosphate metabolism may play a role. Here, we report a case of 19-year-old girl who had both cryptogenic cirrhosis and idiopathic tumoral calcinosis. To our knowledge, there is few report of such concurrence.

BACKGROUND

Idiopathic tumoral calcinosis is a rare benign disorder characterised by the calcified soft tissue masses near the large joints, such as hips, shoulders, elbows and feet.^{1–3} The cause is not exactly known.⁴ However, genetic disorders, recurrent soft-tissue micro traumas and renal-failure are considered.³ An inborn error in vitamin D and inorganic phosphate metabolism is the most probable hypothesis in the pathogenesis of idiopathic tumoral calcinosis.^{5–11}

Idiopathic tumoral calcinosis should be diagnosed by excluding other possible disorders with similar calcified masses. Here we report a case of idiopathic tumoral calcinosis in a 19-year-old girl who was the known case of cryptogenic cirrhosis. We believe that, report of such cases may be helpful in early diagnosis of tumoral calcinosis which is a rare disorder with unknown causes.

Furthermore, correlation between tumoral calcinosis and cirrhosis has not been described in previous case-reports.

CASE PRESENTATION

A 19-year-old girl was admitted to the hospital because of a painful soft tissue mass over the right hip. She had the history of similar masses in other parts of body. The first mass was detected in lateral side of right foot when she was 5 years old that recurred after surgery. She had similar soft-tissue masses over the left foot, first right tarsometatarsal joint, suprapatellar space of left knee, left and right hips (figures 1 and 2). She underwent surgery for the mass of left hip when she was 12. The histological exam showed calcinosis. One month before admission, the right hip mass became painful. She was Persian-Iranian. There was no family history of the same disease.

She was a young woman in a good general condition. On abdominal examination, the spleen was palpated 5 cm below the left costal margin. Liver span was 8 cm. There was a 2×2 cm non tender mass over the first right metatarsophalangeal joint, and a non-tender mass in the left suprapatellar space caused limitation in flexion and extension of the ipsilateral knee joint. There was also a mass in the right hip and another 5×4 cm mass in the medial aspect of

the right thigh. Two infected fistulas on right hip and scars of past surgery, especially in the left hip were visible. The examination was otherwise normal.

INVESTIGATIONS

Blood cell count showed pancytopenia. The results of renal function tests,

blood sugar, uric acid and liver function tests including bilirubin, aminotransferases were normal. Prothrombin time was 17 s (12.7–15.4 s).

Corrected level of calcium was 2.32 mmol/l (2.2–2.6 mmol/l), inorganic phosphate was 1.81 mmol/l (0.81–1.4 mmol/l), 25-hydroxy vitaminD₃ was 15.45 nmol/l (34.9–200 nmol/l) and parathyroid hormone was 16 ng/l (8–51 ng/l). Serum albumin level was 35 g/l. Serum alkaline phosphatase and ferritin levels were 275 U/l (33–96) and 797.685 pmol/l (22.47–337.05), respectively. 1 mmol calcium (reference range: up to 7.5 mmol/day), 16.1 mmol phosphate (reference range: 12.9–42.0 mmol/day) were excreted in 24 collected urine sample. Her body weight was 50 kg.

Abdominal ultrasonography showed a cirrhotic liver, enlarged spleen (cephalocaudal diameter: 19 cm) and a small amount of ascites. In upper endoscopic study, two rows of F1, one row of F2 varicose veins and evidence of portal hypertensive gastropathy were seen. Doppler ultrasonography of abdominal veins verified the presence of portal hypertension. In the MRI of liver and biliary tree, there was no biliary abnormality or evidence of hepatic iron deposition. Normal transferrin saturation and result of liver MRI were against the diagnosis of haemochromatosis. Tests for antibodies to smooth muscle, liver microsomal, mitochondrial, neutrophil, cytoplasmic, nuclear antigens, hepatitis B and C virus were negative. Normal serum ceruloplasmin, urine copper and absence of Kayser–Fleischer rings were not in favour of Wilson's disease. It seemed that, she had cryptogenic cirrhosis. Percutaneous liver biopsy was not done, because there was fear of developing calcinosis in the biopsy site. She refused to undergo transjugular liver biopsy.

Results of bone marrow aspiration and biopsy (performed before admission to the hospital) were compatible

Figure 1 Anteroposterior and lateral view of right foot shows calcification around first tarsometatarsal joint.

with destruction of mature marrow elements peripherally. We guessed that, hypersplenism secondary to cirrhosis resulted in pancytopenia. Total colonoscopy was carried out to exclude the inflammatory bowel disease, underlying a probable sclerosing cholangitis. There was no gross or histological abnormality. Splenomegaly, umbilical and splenorenal collateral veins, severe varicose veins around the esophagus and calcified masses around the hip joints and right paravertebral muscle were found on abdominopelvic CT scan.

On MRI of pelvic area, right buttock, left femoral and posterior sacral soft-tissue masses with complex texture were demonstrated (figure 3A,B). Histological exam of samples from painful hip mass showed active phase of tumoural calcinosis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of tumoural calcinosis includes diseases and conditions associated with ectopic calcification such as primary and secondary hyperparathyroidism, sarcoidosis, renal-failure, calcinosis universalis, calcinosis circumscripta, chronic vitamin D intoxication, milk-alkali

syndrome, collagen vascular diseases and paraneoplastic syndromes. Hyperphosphataemia is the most common abnormality in tumoural calcinosis. Spontaneous soft-tissue calcification occurs when the concentration product of elevated serum phosphate along with serum calcium exceeds the safety threshold.

TREATMENT

As she had hyperphosphataemia, she was administered sevelamer, an oral phosphate binding agent.

OUTCOME AND FOLLOW-UP

The postoperative period was uneventful. She was followed up as an out-patient to reduce the complications of calcinosis and cirrhosis.

DISCUSSION

Idiopathic tumoural calcinosis is characterised by soft-tissue calcified masses around the large joints.¹⁻³ Statistically hip joint is the most common site being involved.^{12 13} It is not uncommon for the calcific masses to become secondarily infected.¹⁴

Figure 2 Pelvic x-ray shows cloudy calcified mass in paraspinal region and around both hip joints.

Figure 3 (A,B) Multiloculated heterogeneous collection with irregular border around the hip joint.

Pathogenesis of the disease is unclear, but an inherited error of inorganic phosphate and vitamin D metabolism is the most probable hypothesis.^{6–11} Hyperphosphataemia seen in some of the patients supports this theory.^{6–12} In this group, the disease develops earlier than 20 years of age. Such cases are familial with multiple lesions during disease course.^{12–15}

Renal function tests and levels of serum calcium, parathyroid hormone, alkaline phosphatase, inorganic phosphate and vitamin D are normal in tumoural calcinosis.

Sometimes the level of the latter two may be slightly elevated.¹⁶

The differential diagnosis of tumoural calcinosis includes primary hyperparathyroidism, chronic renal failure, calcinosis universalis, calcinosis circumscripta, chronic vitamin D intoxication, milk-alkali syndrome, collagen vascular diseases, sarcoidosis and paraneoplastic syndromes.^{6–9–16–20} They were excluded by history, physical examination and laboratory findings in our patient. The above mentioned diseases are usually associated with high-serum calcium level, while calcium level is normal in idiopathic tumoural calcinosis.^{13–21–23}

Our patient had cryptogenic cirrhosis. Some kinds of chronic liver diseases, especially biliary cirrhosis may be

associated with abnormalities in bone mineral metabolism. These patients develop osteomalacia and osteopenia due to vitamin D deficiency. Celiac disease may also cause chronic liver disease and concurrent vitamin D deficiency.^{24–26} The patient in this report had no evidence of mal-absorption disorders. To our knowledge, the association between tumoural calcinosis and cirrhosis has not been described in previous case reports.

The exact pathogenesis of tumoural calcinosis is not defined; so the disease treatment is mainly symptomatic. Diets restricted in calcium and phosphate along with phosphate binding antacids have been used in some cases.^{5 6 11–12} This modality may be successful in hyperphosphataemic patients.^{10 11} Complete surgical excision of the mass is the optimal treatment.^{5 6 12 14 27–28}

Recurrence is the rule after incomplete excision.^{12 27} In some cases, calcific mass may recur despite the complete surgical resections.^{11 23} We prescribed sevelamer to the patient and recommended her to be followed as an outpatient.

In conclusion, we believe that report of patients similar to our case may be of help in broadening our knowledge about this rare disease entity which leads to earlier diagnosis and treatment.

Learning points

- ▶ Idiopathic tumoural calcinosis is characterised by calcified masses in the soft-tissues around major joints.
- ▶ Idiopathic tumoural calcinosis may be misdiagnosed initially as the primary soft tissue tumour.
- ▶ Serum concentration of calcium, alkaline phosphatase and parathyroid hormone are frequently normal in these patients.
- ▶ The most common abnormal laboratory finding is hyperphosphataemia.
- ▶ Calcific masses recur after incomplete resection.

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Competing interests None.

Patient consent Obtained.

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