CASE REPORT

Brown tumours of the tibia and second metacarpal bone in a woman with severe vitamin D deficiency

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SUMMARY

Brown tumours caused by vitamin D deficiency are rare. Most cases are caused by primary hyperparathyroidism, and are rarely caused by secondary hyperparathyroidism in cases of renal failure. We present a case of Brown tumours of the tibia and second metacarpal bone in a 50-year-old woman who had a low dietary intake of vitamin D and had worn a veil for most of her adult life. The Brown tumours were caused by vitamin D deficiency and secondary hyperparathyroidism. The patient improved on treatment with vitamin D3 and calcium supplements. This is a rare case and the first, to our knowledge, with a Brown tumour of the tibia caused by vitamin D deficiency due to decreased dietary intake and decreased exposure to sunlight. The course of treatment and investigations of the patient are described.

BACKGROUND

Brown tumours are known to occur in primary hyperparathyroidism and also in secondary hyperparathyroidism caused by renal failure. Brown tumours caused by vitamin D deficiency have rarely been reported.^{1–6} The differential diagnosis of Brown tumours include giant cell tumours, which was the initial diagnosis in our patient. Depending on the histopathology alone, it is difficult to differentiate between the two. When the histopathology was revised taking into consideration the history, clinical findings, laboratory investigations and radiological findings, the diagnosis of a Brown tumour was performed and treated appropriately. Vitamin D deficiency is very common in middle eastern countries, especially among females, due to low sunlight exposure^{7,8} and low consumption of foods-containing vitamin D.⁸ Prevention of vitamin D deficiency by instituting public health measures such as encouragement of moderate sunlight exposure has been shown to be effective in Arab populations.⁹ We describe the course of treatment, and radiographic and laboratory findings of a patient with a long history of decreased sunlight exposure leading to severe vitamin D deficiency and Brown tumours of the bone.

CASE PRESENTATION

A 50-year-old woman presented to us in April 2013, with a history of painful swellings in the right hand and leg, of 3 months duration. The patient stated that she had started having severe pain in the upper and lower limbs for the last year, with difficulty in standing and walking; this was followed by the appearance of tender swellings in

the right hand and leg; she required a cane to walk. The patient gave a long history of decreased exposure to the sun as she wore a veil and did not have any direct exposure to sunlight in her home, she also had low vitamin D content in her diet. There was no history suggestive of malabsorption. The patient initially saw an orthopaedic surgeon.

INVESTIGATIONS

Radiographs of the hand and leg showed an expansile osteolytic lesion in the right second metacarpal bone and a cortical osteolytic expansile lesion in the middle aspect of the right tibial diaphysis (figure 1A, B). A bone biopsy was performed from the right tibia, which showed uneven distribution of the giant cells in a highly vascular stroma. No evidence of mitosis, necrosis or atypia was seen. A diagnosis of giant cell tumour was performed. The patient was then referred to an oncologist, who ordered an intact parathyroid hormone level (iPTH), which came back high at 677 pg/mL. Laboratory analysis (haemoglobin, white blood cell and platelet count, and calcium levels) and CT scan of the neck were all reported as normal. Parathyroid scintigraphy was not carried out as it was not readily available at that time. The patient was then referred to an endocrinologist for further work up. At the patient's first visit, there were tender swellings in the right hand and leg (figure 2A, B); the pathology slides were reviewed with another pathologist and after reviewing all the data (clinical, biochemical, radiological and histopathological), the case was diagnosed as Brown tumours

Figure 1 (A) Multiple expansile osteolytic lesions noted in the second metacarpal bone, proximal phalanges of index and ring fingers with another small non-expansile lesion noted in the third metacarpal bone; no cortical destruction or soft tissue component could be seen. (B) Cortical osteolytic expansile lesion noted in the mid aspect of the right tibial diaphysis bulging in the surrounding soft tissue.

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Figure 2 Visible swelling in the hand at the site of the Brown tumour in the right second metacarpal bone and in the leg at the site of the Brown tumour in the right tibia (A and B).

(figure 3). The protein-bound calcium was normal and the 25 (OH) vitamin D was undetectable <3.0 ng/mL (30–40 ng/mL). The biochemical profile corresponded with normocalcaemic hyperparathyroidism. Bone density test was ordered but the patient was not able to have it performed due to the cost. To further confirm that the hyperparathyroidism was secondary to vitamin D deficiency, a 24 h urine collection for calcium was carried out, which also came back as low (table 1).

DIFFERENTIAL DIAGNOSIS

- Brown tumours occur in patients with primary, secondary or tertiary hyperparathyroidism resulting from excess osteoclast activity, and consist of collections of osteoclasts intermixed with fibrous tissue and poorly mineralised woven bone. They can occur throughout the skeleton and usually affect the diaphysis of the bone.
- Giant cell tumours: The most commonly affected sites are the epiphyses of the long bones; approximately one-half of all cases affect the distal femur or proximal tibia. Most cases are solitary. On plain X-rays, these tumours appear as expansile eccentrically-placed lytic areas. The lesions normally involve the epiphysis and the adjacent metaphysis, and there is frequent extension to the subchondral plate, sometimes with joint involvement. Matrix calcification and reactive periosteal new bone formation are typically absent.¹⁰
- Aneurysmal bone cysts tend to occur in adolescents, in females more than in males; they usually affect the posterior

Figure 3 Histopathology report on the biopsy taken from the right tibial lesion (H&E stain), which shows uneven distribution of the giant cells in a highly vascular stroma. No evidence of mitosis, necrosis or atypia was seen.

element of the spine or the metaphysis of the distal femur, proximal tibia or proximal humerus, and on radiological examination, show aggressive, expansile, lytic lesions with an eggshell sclerotic rim.¹⁰

- Reparative granulomas or central giant cell granulomas occur in a younger age group, in females more than males, and tend to affect the jaw.¹¹
- Fibrous dysplasia most commonly occurs in teenagers, more often in males than in females. It usually affects the proximal femur, tibia, ribs and skull. On radiological examination it appears as a lytic lesion with a ground glass appearance.¹⁰

In our patient the characteristics of the lesions on radiological and histological examination and the association with an elevated parathyroid hormone level made a Brown tumour the most likely diagnosis. The normal creatinine level was against secondary or tertiary hyperparathyroidism caused by renal failure. The normal calcium, low vitamin D level and low 24 h urinary calcium excretion, made vitamin D deficiency and secondary hyperthyroidism a more likely diagnosis than primary hyperparathyroidism.

TREATMENT

The patient was diagnosed as having secondary hyperparathyroidism due to vitamin D deficiency causing Brown tumours of the bone. The patient was started on vitamin D3 drops 45 000 IU (V D3 solution, Razi Labs, Aleppo, Syria) weekly and calcium 500 mg daily, and was asked to follow-up in 6 weeks.

OUTCOME AND FOLLOW-UP

The patient came back stating that her range of movement was much better but that the upper and lower limb masses were still tender. The vitamin D level had improved to the normal range (table 1) with a normal calcium level and a much lower PTH. The patient was instructed to continue the same treatment but to increase the pharmacological calcium intake to 1000 mg daily. The patient came back 3 months later feeling much better; she was now walking without a cane and the bony swellings were less tender, she did not tolerate the 1000 mg of calcium daily due to epigastric pain so she continued to take 500 mg daily. The patient continued to follow-up over a period of 16 months, the course of her laboratory work can be seen in table 1. Showing a marked decrease in the alkaline phosphatase and normalisation of the vitamin D levels, the calcium levels also remained within the normal range. X-rays taken after 16 months of treatment showed increased density of lesions in the second metacarpal and tibial bone (figure 4 A, B). The iPTH level remained slightly elevated throughout her treatment and finally normalised after 16 months of treatment. She is still receiving vitamin D3 45 000 units monthly (this has been reduced from weekly) and calcium 500 mg daily.

DISCUSSION

Brown tumours of the bone are known to occur mainly in cases of primary hyperparathyroidism and in cases of secondary hyperparathyroidism secondary to renal failure.¹² It has also been reported rarely in patients with malabsorption¹³ and after bariatric surgery.¹⁴ Brown tumours due to vitamin D deficiency caused by decreased sun exposure and decreased dietary intake are rare, with only a few cases reported in the literature.^{1–6} Our patient improved markedly on pharmacological supplement with vitamin D and calcium. She did not receive any calcitriol or intramuscular vitamin D therapy, as reported in other cases. We did not give intramuscular vitamin D for fear that she might develop hypercalcaemia if she had an underlying primary hyperparathyroidism that

Table 1 Laboratory results for the patient

Laboratory	24/3/13 Patient was seen by oncologist	13/4/13 First endocrine visit	3/6/13 First follow-up visit after 6 weeks of treatment	11/9/13 Second follow-up visit after 5 months of treatment	14/8/14 Laboratory work after 16 months of treatment
Serum intact parathyroid hormone (15–68.3 pg/mL)	677		87.38	104.6	50
Serum albumin (3.2–5.0 gm/dL)	4.4				
Serum vitamin D (30–40 ng/mL)		<3.0	31.96	31.27	46.3
Serum alkaline phosphatase (40–150 U/L)			220	133	83
Serum calcium (8.8–10 mg/dL)	8.8	8.2	8.7	8.9	9.8
Serum phosphate (87–1.45 mmol/L)					1.24
Serum magnesium (0.66–1.07 mmol/L)					0.77
Serum creatine (0.55–1.02 mg/dL)	0.8		0.9	0.88	0.95
Urine calcium (150–300 mg/24 h)		121.5			

Figure 4 There is marked sclerosis mainly in the second metacarpal bone and that of the tibial expansile lesion (A and B); (After 16 months of treatment).

was not obvious due to vitamin D deficiency, and since she improved markedly over the first 6 weeks, we did not consider any other form of vitamin D replacement. The patient was followed for symptoms of vitamin D hypervitaminosis, such as anorexia, nausea, constipation or fatigue, but she denied any similar symptoms so she was kept on weekly vitamin D 45 000 IU for 16 months. The clinical and laboratory course of the patient showed marked improvement and she is still on replacement therapy. The parathyroid level finally normalised after 16 months of treatment. A study has shown that it may take years for Brown tumours to resolve completely.¹⁵

Our patient had most likely had long-standing osteoporosis due to the vitamin D deficiency in addition to the Brown tumours. Studies have shown an increased risk of osteopaenia, osteoporosis and hip fractures in patients with vitamin D deficiency.^{16–18} The patient has shown marked improvement in her symptoms with no more bone pain and a reduction in the size of the bony swellings. The radiographic findings have improved but have not normalised completely. We will continue to treat the patient with vitamin D3 and calcium supplements. The patient has not shown any evidence of having primary hyperparathyroidism, as her calcium levels have remained normal throughout the period of her treatment and her PTH level also normalised, so most likely her condition was caused by long standing vitamin D deficiency and

secondary hyperparathyroidism. Maintaining adequate vitamin D status is important in preventing many conditions. Patients should receive education regarding the importance of vitamin D and adequate sun exposure on health, and how to achieve adequate vitamin D intake.

Learning points

- ▶ Brown tumours can be histologically mistaken for giant cell tumours, aneurysmal bone cysts, giant cell reparative granulomas and fibrous dysplasia, and correlation with the clinical features is important in reaching the diagnosis.
- ▶ Brown tumours may rarely occur due to vitamin D deficiency, this should be kept in mind if the patient has normocalcaemic hyperparathyroidism and a history suggestive of osteoporosis.
- ▶ People who are at risk of vitamin D and/or calcium deficiency, such as those with decreased sunlight exposure and/or poor intake of food-containing vitamin D or calcium, must have vitamin D and calcium supplements in their diet, which can be effective in treating many conditions including Brown tumours.

Contributors BAA-S saw the patient and wrote the script. SAA-I assisted in writing the script. AMS wrote the pathology report and prepared the histopathology slide. DHA-F reviewed the X-rays and wrote the radiology reports.

Competing interests None declared.

Patient consent Obtained.

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