Management of brown tumor of spine with primary hyperparathyroidism: A case report and literature review

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Abstract

Rationale: Brown tumor (BT) is a rare benign lesion in skeletal system. It is especially rare secondary to primary hyperparathyroidism (HPT). The differential diagnosis can be misleading due to its diversified clinical characteristics. Final diagnosis mainly relies on excessive elevated parathyroid hormone and biopsy. Treatments include surgical interventions and drugs. Only 19 articles (total 22 cases) reported BT of spine caused by primary HPT.

Patient concerns: A 50-year-old woman was admitted to our hospital complaining left elbow and thoracodorsal pain with the lower limbs weakness.

Diagnoses: Multifocal BT.

Interventions: The patient received intramuscular injection of Micalecalc and incense of Calcitonin (Salmon) Nasal Spray to decrease serum calcium level. Surgery was performed later to excise the ectopia parathyroidoma.

Outcomes: At 1-year follow-up, the patient was able to lead an independent life in her full capacity, even though she occasionally complained mild weakness of lower limbs.

Lessons: BT of spine with HPT is rarely seen in the clinical practice. Treating the primary parathyroid diseases can be effective. For patients with vertebral fractures and neural deficits, immediately surgical intervention will be necessary to prevent the worse of neurological function.

Abbreviations: BT = brown tumor, CT = computed tomography, MRI = magnetic resonance imaging, PHT = primary hyperparathyroidism, PTH = parathyroid hormone, SHT = secondary hyperparathyroidism.

Keywords: brown tumor, case report, primary hyperparathyroidism, spine

1. Introduction

Brown tumor (BT) is a rare benign lesion in skeletal system due to the endocrine disorder. It occurs secondary to either primary hyperparathyroidism (PHT) or secondary hyperparathyroidism (SHT). Elevated parathyroid hormone (PTH) level results in the abnormal bone remodeling which brings about unusual reactive bone lesion.

2. Case presentation

A 50-year-old woman was admitted to our hospital complaining left elbow and thoracodorsal pain with the lower limbs weakness for over 1 month. The patient suffered right femoral neck fracture when falling down, and received fracture reduction with internal fixation. Later she was diagnosed as right humerus pathologic fracture and received lesion clearing and plate fixation surgery. The subsequent pathologic report failed to provide the definite diagnosis. Muscle strength of the upper extremities was 3/5 (left) and the lower was 3/5 (left) and 2/5 (right). Hypotonia were observed in both upper and lower limbs especially lower limbs. Computed tomography (CT) and thoracic magnetic resonance
imaging (MRI) showed mass lesion involving the T9 vertebral with expansive growth but not compressing the spinal cord. Positron emission tomography (PET)-CT revealed multifocal lesions with high $^{18}$F-fluorodeoxyglucose ($^{18}$FDG) uptake (Fig. 1A–C). PTH was measured as high at 1811 pg/mL (normal, 15–65 pg/mL); serum calcium level was high at 2.61 mmol/L (normal, 2.1–2.55 mmol/L); hemoglobin was low to 45 g/L (normal, 110–155 g/L); erythrocyte sedimentation rate was high at 94 mm/h; osteocalcin was >300 (normal, 11–43 ng/mL).

After admission, blood transfusion was conducted immediately because of severe anemia. A biopsy was performed at the left tibia by confirming the pathologic diagnosis of BT (Fig. 1D). Since the lesion in the spine did not cause obvious unstable fracture or compression of spinal cord, the patient did not receive spine surgery but was transferred to the endocrinology department for decreasing serum calcium level. The patient received intramuscular surgery but was transferred to the endocrinology department for compression of spinal cord, the patient did not receive spine lesion in the spine did not cause obvious unstable fracture or

3. Discussion

PHT, as one of the endocrine disorders, can be diagnosed and treated effectively at an early stage. $^{11,13}$ BT secondary to PHT is rare in skeletal system and it can be misleading because of its biological behavior mimicking multiple metastatic tumors.

3.1. Literature review

Pubmed, Embase, and Web of Science database were selected for searching studies reporting clinical outcomes of BT of spine caused by PHT. Studies were searched within selected database according to the following algorithm: (PHT) AND (BT) AND (spine). Animal, in vitro, biochemical, non-English language articles were excluded. The potential eligible articles were reviewed rigorously by 2 reviewers independently. Data were collected and recorded including the following items: sex, age, affected spinal level, symptoms, treatment, primary disease, and postoperative outcome.

Based on the inclusion and exclusion criteria, after screening the title and abstract of articles, full text of the 32 written-in-English articles were obtained for further reviewing (Fig. 2). Eight animal researches were excluded. And 5 were excluded because it’s with SHT or not involving spine. The rest 19 studies were included for final analysis. $^{1,4,7,9,12,14–25}$ Table 1 shows the detailed features, managements, and outcomes of enrolled patients. Total 22 cases of BT of spine caused by primary hyperparathyroidism (PHPT) were published in literature: 13 females and 9 males. The patients’ age ranged from 16 to 69 with a mean age of 44.7. Thoracic spine (35%) was observed to be the most commonly involved part of the spine, followed by lumbar (27%), cervical (9%), and sacral (4.5%) regions. There was no significant difference in involving parts including vertebral body, pedicle, and posterior elements. Most of the patients presented with paraparesis due to compression of spine. Pain was also common among these patients followed by sphincter dysfunction and numbness. The main reason causing PHPT was parathyroid adenoma, whereas only 2 cases were due to carcinoma. Half of the patients underwent both spine surgery and parathyroidectomy. Six patients (27%) underwent spine surgery only and 4 patients (18%) underwent parathyroidectomy only. Neurological function was improved in almost all the patients after operation.

3.2. Clinical characteristics

Few cases progresses as BT and manifested with skeletal-related symptoms. The clinical manifestations of BT vary due to the different lesion locations. $^{14,26}$ Typical symptoms include pain, pathologic fracture, and spinal cord compression with related neurologic deficits when it occurs in spine. Although some patients are asymptomatic and part of them manifested with hypercalcemia, hypophosphatemia, elevated in PTH, and

Figure 1. The radiologic and pathologic findings. A, The previous reconstruction surgery for the humerus pathologic fracture. B, The transverse computed tomography (CT) image of the lesion in the spine. C, The PET-CT image showed multifocal abnormal signal. D, The HE-staining finding of the biopsy (100 X).
decrease in bone mineral density. In more severe cases, pathologic fracture, decrease in muscle strength, loss of sensation, and even paralysis can be observed due to compression of the spinal cord.\[1,7,17\] In our case, pathological fracture occurred in the right femur and humerus. Thoracodorsal pain and weakness of lower limbs are also found due to thoracic spine lesion. In published cases, thoracic spine was the most predilection site of spine. More than half of the cases presented with thoracic lesions according to our statistic. The pathogenesis could be that long-term substantial PTH gave rise to the imbalance of bone formation and resorption, further resulting in changes in microarchitecture which may increase the risk of bone fractures and other clinical symptoms.\[2,27–30\]

Radiographically, abnormal osteoclast activity affects both cortical and trabecular microstructure and the appearance of BT can be complicated. On x-ray, solitary, or multiple expansile lesions with sharp outlines can be seen.\[31\] Sclerotic margins, invading tissue, and sclerotic rim are rare.\[32\] CT scan reveals expansile lytic lesions, with various bone erosion and cortical attenuation. The lesions are relatively well demarcated.\[17\] On MRI, BTs show hypointense on T1-weighted images, hypointense or hyperintense on T2-weighted images. The cyst of the lesion is characterized by watery signal. The enhanced scanning is obviously strengthened, and intratumoral hemorrhages lead to fluid-fluid level appearance. Spinal MRI can show compression fractures of vertebra and intraspinal soft tissue masses with neural compression.\[13\] PET/CT can also be sensitive in detecting BTs.\[34\]

### 3.3. Diagnose

Diagnosis of BTs depends on clinical, biochemical, and radiological presentation. When BT occurs as a single lesion involving spine, the differential diagnosis should include true giant cell tumor, giant cell reparative granuloma, and aneurysmal bone cyst.\[13\] For BT involving multiple lesions, it can mimic metastases tumors or multiple myeloma.\[4,36\] As for imageological characteristics, giant cell tumor, metastases, or myeloma may have a similar appearance, which contains soft tissue mass with local bone erosion and expansion and shows contrast enhancement. The elevated level of PTH and presence of severe hyperparathyroidism in BTs may be helpful to make diagnosis.\[16,24,7,38\] Final diagnosis mainly depends on histological findings as neither cellular atypia nor mitotic figures are observed in BT. Biopsy is helpful in some situations so that proper treatments can be made according to histological findings. It is interesting in our case that the patients presented with multiple lesions. We performed biopsy at the left tibia on account of surgical risks and the report indicated BT. With the guidance of biopsy, we finally detected the ectopia parathyroidoma by chest CT.

### 3.4. Treatment

For BT with HPT, managing the cause of HPT is the primary treatment.\[15,39\] Parathyroid adenoma is one of the most common diseases leading to HPT, whereas other diseases may include parathyroid carcinoma and hyperplasia.\[12,40\] Surgical interventions including removing the offending parathyroid mass can be effective. Parathyroid surgery rapidly decreases the excessive amount of PTH and thus achieving complete regression of the lesions with remineralization. Medical treatment may also be used together. Normalizing serum calcium level should be the goal to stabilize the microenvironment of bone. Bisphosphonates are also recommended for treatments.\[4\] As for spine lesions, the treatments vary according to the situation. The pathological fractures need surgical intervention. After mass excision, spinal instrumentation and fusion are indicated to maintain stability.\[17\]
Table 1
Characteristics of eligible patients with brown tumor caused by PHPT in the reported studies.

| Authors (year)          | Sex | Age | Segment | Vertebral body | Pedicle | Posterior elements | Local pain | Radicular pain | Numbness | Paraparesis | Sphincter dysfunction | Spine surgery | Parathyroidectomy | Reason of PHPT | NF | Recurrence |
|-------------------------|-----|-----|---------|---------------|---------|--------------------|------------|---------------|----------|-------------|----------------------|---------------|---------------------|---------------|----|------------|
| Shaw and Davies (1968)  | F   | 58  | T10     | N             | Y       | N                  | N          | N             | N        | Y           | Y                    | Y             | Y                   | Adenoma        | Imp.| Unknown   |
| Shuangshouli et al (1972) | M   | 32  | L4      | N             | N       | Y                  | N          | Y             | N        | N           | Y                    | Y             | Y                   | Adenoma        | Imp.| Unknown   |
| Sundaram and Schloz (1977) | F   | 63  | T10     | Y             | Y       | N                  | N          | N             | N        | Y           | Y                    | Y             | Y                   | Adenocarcinoma | Imp.| Unknown   |
| Su et al (1977)         | F   | 64  | T10     | –             | –       | –                  | N          | N             | N        | Y           | Y                    | Y             | Y                   | Adenoma        | Imp.| Unknown   |
| Ganesh et al (1981)     | M   | 40  | T2      | Y             | Y       | N                  | N          | N             | Y        | N           | Y                    | N             | N                   | Adenoma        | Imp.| Unknown   |
| Yokota et al (1989)     | F   | 58  | T5      | N             | Y       | N                  | N          | N             | Y        | Y           | Y                    | N             | N                   | Adenoma        | Imp.| Unknown   |
| Dries et al (1990)      | F   | 54  | T9      | N             | Y       | N                  | N          | N             | Y        | N           | Y                    | N             | N                   | Unknown        | Imp.| Unknown   |
| Kashefi et al (1990)    | F   | 51  | T6–7    | Y             | N       | N                  | N          | N             | Y        | N           | Y                    | N             | N                   | Adenoma        | Imp.| Unknown   |
| Sarda et al (1993)      | F   | 23  | T3–4    | Y             | N       | N                  | N          | N             | Y        | N           | Y                    | N             | N                   | Adenoma        | Imp.| Unknown   |
| Motaleanu et al (1994)  | M   | 57  | L4–5    | N             | N       | Y                  | Y          | Y             | N        | N           | Y                    | N             | N                   | Unknown        | Imp.| N          |
| Mustonen et al (2002)   | M   | 28  | L2      | N             | N       | Y                  | Y          | Y             | N        | N           | N                    | Y             | N                   | Adenoma        | Imp.| Unknown   |
| Haddad et al (2007)     | F   | 26  | T2–4    | Y             | N       | Y                  | N          | N             | Y        | Y           | Y                    | N             | N                   | Adenoma        | Imp.| N          |
| Khalil et al (2007)     | M   | 69  | T2      | Y             | Y       | N                  | Y          | Y             | N        | N           | Y                    | N             | N                   | Adenoma        | Imp.| N          |
| Altan et al (2007)      | F   | 44  | S2      | N             | N       | Y                  | Y          | Y             | N        | N           | Y                    | N             | N                   | Adenoma        | Imp.| N          |
| Hoss et al (2008)       | F   | 23  | Sacrum  | –             | –       | –                  | N          | Y             | N        | N           | N                    | N             | N                   | Adenoma        | Imp.| Unknown   |
| Lee et al (2013)        | M   | 65  | L2      | Y             | N       | Y                  | Y          | Y             | N        | N           | Y                    | N             | N                   | Unknown        | Unknown| Unknown   |
| Khalatbari and Moharamzad (2014) | M,E  | 16  | L2      | N             | Y       | Y                  | N          | N             | N        | N           | Y                    | Y             | Y                   | Adenoma        | Imp.| N          |
| Moharamzad (2014)       | F   | 46  | L3      | N             | N       | Y                  | Y          | N             | N        | Y           | Y                    | N             | N                   | Adenoma        | Imp.| N          |
| F                   | 52  | C6    | N       | Y             | Y       | Y                  | Y          | N             | N        | N           | Y                    | N             | N                   | Adenoma        | Imp.| N          |
| M                   | 36  | T7    | Y       | Y             | Y       | N                  | N          | N             | Y        | Y           | Y                    | Y             | Y                   | Adenoma        | Imp.| N          |
| Sonmez et al (2015)     | M   | 50  | T9      | N             | Y       | N                  | N          | N             | N        | Y           | Y                    | Y             | Y                   | Adenoma        | Imp.| N          |
| Aftawrith et al (2019)  | F   | 26  | C2      | Y             | N       | Y                  | Y          | N             | N        | N           | Y                    | N             | N                   | Adenoma        | Imp.| N          |

C = cervical, F = female, Imp = improved, L = lumbal, M = male, N = no, NF = neurological function, PHPT = Primary hyperthyroidism, S = sacrum, T = thoracic, Y = yes.
Surgical decompression should be taken immediately on occasion of spinal cord compression to preserve neural function. On the basis of published literatures, decompressive surgery at an early stage can be effective to improve life quality apparently in relieving pain and paralysis. In the literature, most patients underwent both spine surgery and parathyroidectomy. The outcome is, however, similar without significant difference between patients who underwent parathyroid adenoma resection with/without spine surgery. In our case, the lesion in the spine did not cause unstable fracture or spinal cord compression. The patient did not receive spine surgery but was immediately transferred to the endocrinology department and underwent ectopia parathyroidoma excision only. Finally, the patient obtained improvements of neurological function and led an independent life.

In conclusion, BT of spine with HPT is rarely seen in the clinical practice. However, owing to its character of mimicking metastatic malignant tumor, it can be misleading in the differential diagnosis of spinal cord compression. The diagnosis mainly relies on excessive elevated PTH and biopsy. Once the differential diagnosis of spinal cord compression is established, treating the primary parathyroid diseases can be effective in regressing the tumor progression. In some severe cases including vertebral fractures and neural deficits, immediately surgical intervention will be necessary to prevent the worsening of neurological function.

Acknowledgments

The authors are thankful to the patient for her consent to the report.

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