

Case Report

Effectiveness of Intravenous Bisphosphonate in Treatment of Giant Cell Tumor: A Case Report and Review of the Literature

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Giant cell tumor is a benign locally aggressive tumor. The standard treatment is en bloc resection followed by major reconstructive surgery, or extended curettage conjunction with bone grafting or the use of bone cement implantations. Surgical treatment of giant cell tumor at the sacrum is associated with high morbidity, and local recurrence. The authors present a case of giant cell tumor at the sacrum treated with intravenous 4 mg zoledronate every 4 weeks for seven courses followed with curettage and cement implantation. At two years follow-up, the patient had no pain, no neurological deficit, and no local recurrence. The patient's gait was normal. From the present study, the authors demonstrate the effectiveness of zoledronate for treatment of giant cell tumor at the sacrum. It can reduce the morbidity from major surgery.

Keywords: Giant cell tumor, Bisphosphonate, Zoledronate, Sacrum

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Giant cell tumor of the bone is a benign locally aggressive neoplasm characterized by extensive bone destruction, and high rates of local recurrence⁽¹⁻⁴⁾. It is rare in the vertebral bodies, but the sacrum is the most common site of giant cell tumor in the axial skeleton⁽⁵⁻⁷⁾. Generally, the treatment of giant cell tumor is en bloc resection followed by major reconstructive surgery, or extended curettage conjunction with bone grafting or the use of bone cement implantation⁽⁷⁻⁹⁾. The surgery causes high morbidity to the patients. Some studies reported the roles of bisphosphonates cause apoptosis of giant cell tumor, and reduce the local recurrence in giant cell tumor⁽¹⁰⁻¹³⁾. The authors present the case that was treated with intravenous bisphosphonates in the patient who had extensive giant cell tumor at the sacrum.

Material and Method

A 32 year-old woman presented with a 2-months history of pain at the buttock radiated to

right lower extremity. There was no history of trauma. Physical examination revealed marked tenderness at the right sacral region. She had weakness of flexion, and extension of the right big toe grade 4/5 on manual testing. Plain film of the pelvis showed an expansile osteolytic lesion with ill-defined margin at right ala of the sacrum (Fig. 1). CT scan revealed osteolytic lesion at the right sacral area with an inhomogeneous soft tissue mass. An open incisional biopsy of the sacrum was performed. Histological diagnosis of the lesion was giant cell tumor (Fig. 2). The authors treated the patient with intravenous 4 mg zoledronate every 4 weeks for seven courses (Fig. 3). The curettage and bone cement implantation was performed at the fifth month (after the fourth dose of intravenous zoledronate) of the treatment (Fig. 4). The patient was followed for two years in terms of local recurrence, metastasis, and functional outcome.

Results

At two years follow-up, the patient had no pain, and no neurological deficit. The patient's gait was normal. The patient could do normal activity. Plain radiographs, and CT scan showed increasing bone

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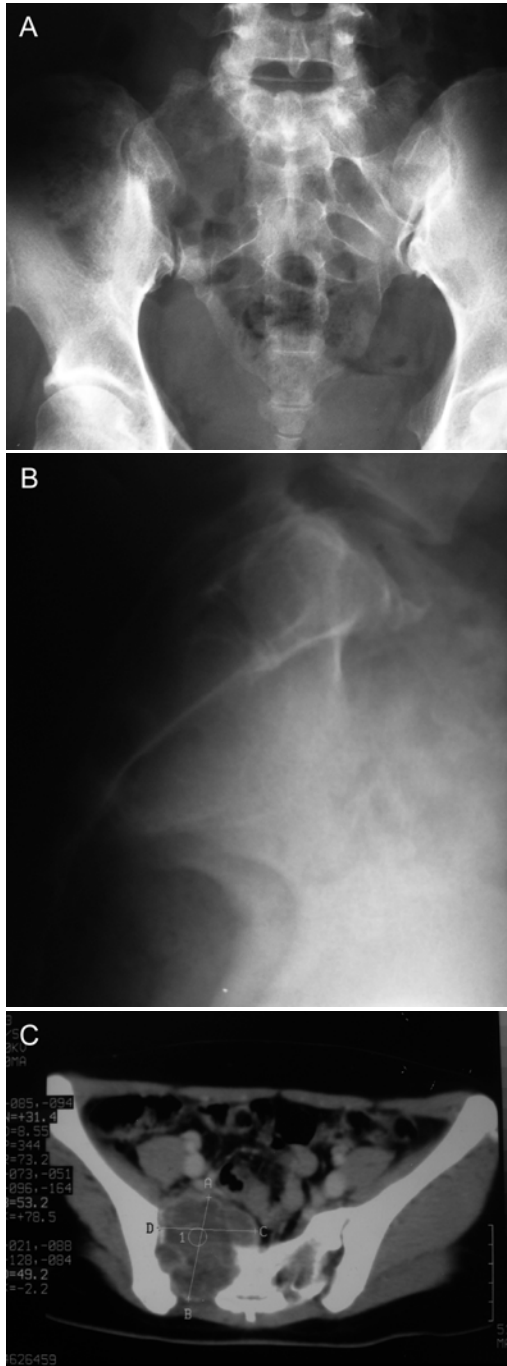


Fig. 1 Giant cell tumor at the right sacrum. (A) an antero-posterior (AP) radiograph of patient showed an osteolytic lesion in the lateral part of the right upper sacrum. (B) lateral plain radiographs of sacrum revealed soft tissue mass at anterior aspect of sacrum. (C) CT scans demonstrated the extent of soft tissue projection, and osteolytic lesion at the right sacrum

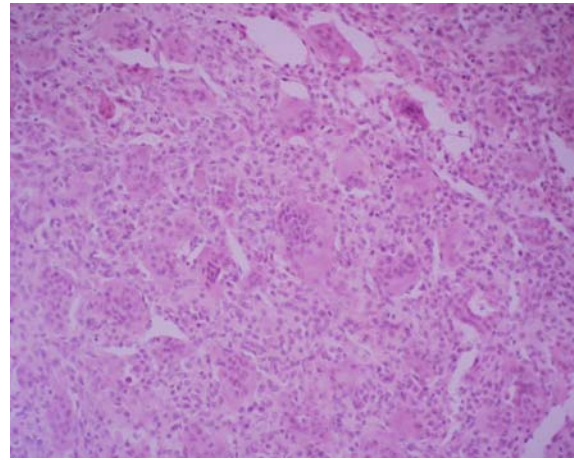


Fig. 2 Histopathology of giant cell tumor. At medium magnification, the tumor consists of histiocytoid cells among which many osteoclast-like giant cells are distributed in uniform manner

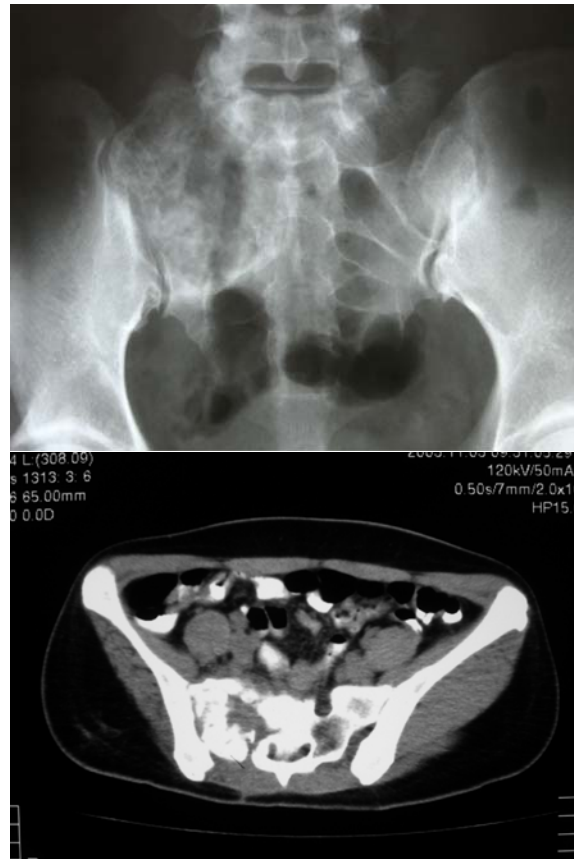


Fig. 3 Radiographs of the sacrum. The radiograph showed sclerosis at the lesion after received intravenous zoledronic acid 4 mg every 4 weeks for 4 courses



Fig. 4 A, B, and C. The lesion was curetted, and the defect was filled with bone cement

density around the lesion. Histological examination from specimens curetted at the fifth month after receiving zoledronate showed no residual giant cell tumor.

Discussion

Surgical treatment of giant cell tumor at the sacrum is associated with high morbidity, and local recurrence. The present study is the first clinical report for the treatment giant cell tumor at the sacrum with bisphosphonates following to intralesional curettage. The outcome of the treatment was satisfactory in terms of local recurrence and functional outcome. There have been a few studies using bisphosphonates for treatment of giant cell tumor of the extremity. Tse et al demonstrated the effectiveness of bisphosphonates to reduce the local recurrence rate for giant cell tumor at the extremity⁽¹⁴⁾. In the bisphosphonates treated group, one of 24 patients developed local recurrence, while in the control group, six of 20 patients developed local recurrence. The local recurrence rate was statistically significantly different between the two groups, Log Rank test $p = 0.056$. Cheng et al showed the results that pamidronate significantly induced apoptosis in both osteoclast-like giant cells and stromal tumor cells, *in vivo*⁽¹²⁾. The local recurrence rate occurred in four of six cases with pamidronate treatment, and in one of 12 cases with pamidronate treatment. The follow-up periods ranged from one to four years. Cheng's study did not mention the location of the giant cell tumor. Study of Chang et al revealed the efficacy of bisphosphonates (zoledronate) to induce apoptosis in giant cell tumor culture in a dose-dependent response⁽¹⁵⁾. Zoledronate binds to the bone. It inhibits osteoclastogenesis, and osteoclastic bone resorption. The action of the zoledronate targets directly the osteolytic process that may reduce the local recurrence, and avoid extensive surgical procedures. From the present study, the authors demonstrate the effectiveness of zoledronate for treatment giant cell tumor at the sacrum. It can reduce the morbidity from major reconstructive surgery. It is helpful for the treatment of giant cell tumor at the sacrum.

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รายงานการรักษาผู้ป่วยเนื้องอกกระดูกชนิด giant cell tumor ที่ตำแหน่งกระดูกสันหลังส่วน sacrum ด้วยการให้ยา zoledronic acid ในรูปแบบฉีดเข้าหลอดเลือด

ไอพาร อภรณ์ชยานนท์, ธนินนิตย์ สิริพันธ์

เนื้องอกชนิด giant cell tumor เป็นเนื้องอกที่มีการทำลายกระดูกมาก และมีโอกาสเกิดการกลับเป็นซ้ำสูง การรักษามาตรฐานในปัจจุบันคือการผ่าตัดซึ่งมีอยู่หลายวิธีขึ้นอยู่กับตำแหน่งของรอยโรค ระยะของโรค (stage of disease) การผ่าตัดสามารถทำได้ทั้งวิธี intralesional curettage and adjuvant treatment เพื่อเอาเนื้องอกออก ร่วมกับการใส่ bone grafting หรือวิธีการผ่าตัดแบบผ่าตัดเอาก่อนออกทั้งหมด (en bloc resection) ซึ่งการรักษา โดยการผ่าตัดเอาเนื้องอกออกที่บริเวณกระดูกก้นกบก่อให้เกิดอันตราย หรือ ความพิการต่อบริเวณที่ผ่าตัด และการเกิดซ้ำของเนื้องอกค่อนข้างสูง ทางคณะผู้ประพันธ์จึงเสนอวิธีการรักษาเนื้องอกชนิด giant cell tumor ที่กระดูก บริเวณก้นกบ (sacrum) ด้วยวิธีการให้ยากลุ่ม bisphosphonates ในรูปแบบฉีดเข้าหลอดเลือด คือ zoledronate ในปริมาณ 4 มิลลิกรัมทุก 4 สัปดาห์ ทั้งหมด 7 ครั้ง ในการติดตามผู้ป่วยเป็นระยะเวลานาน 2 ปี ผู้ป่วยไม่มีอาการปวด สามารถเดินได้ปกติ และไม่พบการกลับมาเป็นอีกของเนื้องอก (local recurrence)