Original Article
The outcome and analysis of different treatments for solitary plasmacytoma of bone

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Abstract: Solitary plasmacytoma of the bone (SPB) is a malignant proliferation of plasma cells that occurs within the axial skeleton and is characterized by destruction of the bone. SPB generally occurs in the pelvis, femur, humerus, and rib. Currently, radiation therapy remains the primary choice of treatment for SPB, as plasmacytoma is a radio-sensitive tumor. In this study, a total of 12 patients diagnosed with SPB were enrolled. Surgery was performed to all patients with SPB in combination with radiation therapy or chemotherapy, or both. The clinical outcomes were recorded and compared. Based on the follow-up data, no recurrence was observed in patients who received surgery and radiation therapy, or in those who received surgery with radiation therapy and chemotherapy. In conclusion, systematic therapy (surgery, radiation therapy, and chemotherapy) may be applied for the treatment of patients with SPB to obtain a better prognosis.

Keywords: Solitary plasmacytoma of bone, radiation therapy, chemotherapy

Introduction
Plasma cell neoplasm, or plasmacytoma, is a disorder of the plasma cells, involving the malignant proliferation of plasma cell in the soft tissue or axial skeleton [1, 2]. Currently, the International Myeloma Working Group (IMWG) defines plasmacytoma as having 3 distinct subgroups: solitary plasmacytoma of the bone (SPB), extramedullary plasmacytoma (EP), and multiple plasmacytomas [1]. All 3 types of plasmacytoma can occur in bones and soft tissues [1]. In patients with SPB, monoclonal plasma cells can accumulate locally in any part of the bone to form destructive lesions [3-5]. As the most common form of plasmacytoma, SPB is responsible for approximately 3-5% of all types of plasma cell malignancies [6, 7]. The criteria proposed by the IMWG for the diagnosis of SPB are as follows: the occurrence of a single bone lesion, normal bone marrow, little or no existence of paraprotein, no organ involvement, and a normal skeletal survey, except for the presence of the bone lesion [1].

A previous epidemiology study indicated the SPB is less prevalent in women (1:2 female to male ratio) with a median age of approximately 55 years at diagnosis [8]. In SPB, the most common symptom is pain in the affected bone, such as back pain due to the bone lesion occurring in spinal cord compression. Moreover, pathologic fractures, nerve involvement, or a combination of the above symptoms could also be present [7, 9]. Currently, radiotherapy remains the primary choice for treating SPB, as plasmacytoma is a radiosensitive tumor [3, 9]. The application of radiotherapy for the treatment of SPB can achieve promising local control of the tumor cells, as well as long term remission, or even cure SPB [10]. However, the determination of the prognostic factors for SPB is difficult owing to the limited number of available reports concerning SPB. For patients with SPB who receive radiotherapy, the development of multiple myeloma (MM) remains the primary problem, and it has been reported that the majority of patients could develop MM in 2-4 years after the diagnosis of SPB, especially in older patients [7, 11]. The prognosis for patients with SPB is consistently poor [11]. In addition, the application of chemotherapy in SPB was also controversial.

In this study, a total of 12 patients diagnosed with SPB from were enrolled. Surgical
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2010 and July 2014 were enrolled in this study. This study was conducted in accordance with the ethical guidelines of the local authority and the recommendations of the Declaration of Helsinki (Seoul revision, 2008). All participating patients were informed of the purpose of this study and signed a form of consent.

Of the 12 patients, 9 were men and 3 were women. The patients were aged between 41 and 65 years, with a median age of 54.5 years. The major clinical manifestations of patients were pain and limb numbness. Bone metastasis was observed in 3 patients. The average disease course ranged between 1 month and 2 years. During the following-up period, no deaths were reported.

Diagnosis and pathology analysis

The diagnosis of patients with SPB was conducted in accordance with the WHO classification system for hematologic malignancies, as recommended by National Comprehensive Cancer Network (NCCN). Radiologic examination, clinical manifestations, in addition to needle biopsy, were performed for diagnosis. All 12 cases were confirmed to be SPB.

Immunohistochemistry analysis

Immunohistochemistry analysis of samples from patients was conducted as previously described [12]. Sections were then incubated with the mouse anti-human CD38 monoclonal antibody (Abcam, Cambridge, MA, USA), mouse anti-human CD79a monoclonal antibody (Abcam) and mouse anti-human CD138 monoclonal antibody (Abcam) overnight at 4°C, and then washed with PBS 3 times, followed by incubation with mouse anti-rabbit horseradish peroxidase (HRP)-conjugated antibody (Sigma, St. Louis, MO, USA) with 1:500. The slides were visualized using a horseradish catalase DAB color kit (Sangon Biotech, Shanghai, China).

Therapy for patients

Surgical treatment was administered to all SPB patients with a combination with other methods in this study. Briefly, with the exception of 1 patient who received surgery only, 3 patients received a combination of surgery

Materials and methods

Ethics statement and general information

A total of 12 patients diagnosed with SPB who were admitted to the First Affiliated Hospital of Zhengzhou University between July

Figure 1. Representative Immunohistochemical picture of the tissue sample from SPB patients. A. Immunohistochemical analysis for CD38 of tumor sample; B. Immunohistochemical analysis for CD79a of tumor sample; C. Immunohistochemical analysis for CD318 of tumor sample.
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SPB is characterized by a single area of bone destruction [8]. SPB generally occurs in the pelvis, femur, humerus, and ribs [13]. In rare cases, SPB can also arise in the skull [13]. The majority of patients with SPB patients are aged above 50 years at the time of diagnosis, with a median age of 55 years. The clinical manifestations include pain and swelling due to the bone destruction, in addition to vertebral involvement due to spinal cord or nerve compression. In a number of patients, chronic inflammatory demyelinating polyneuropathy is also observed. For the accurate diagnosis of SPB, flow cytometry and molecular screening for gene recombination of immune globulin heavy chain or light chain could be conducted. Moreover, magnetic resonance imaging examination could provide more information with regard to the stage of SPB [5]. A combination of the methods mentioned above could provide accurate information in the diagnosis of SPB.

Currently, local radiation therapy remains the primary choice for the treatment of SPB because cancer cells are sensitive to X-rays [8, 14]. It was reported that superior control of cancer cells could be achieved if the radiation dose exceeded 40 Gy [15]. A number of researchers also recommended increasing the radiation dose up to between 50 Gy and 60 Gy [16, 17]. The 5-year control rates were 100% and radiation therapy, 3 received a combination of radiation therapy and chemotherapy in addition to surgery, and 5 received a combination of surgery and chemotherapy. The administered radiation therapy, with the exception of conventional radiation therapy, involved the administration of both 3D conformal radiation therapy and intensity-modulated radiation therapy. The radiation therapy dose ranged between 30 and 54 Gy. The chemotherapy regimens administered to patients were MP (melphalan + prednisone), VAD (vincristine + doxorubicin + dexamethasone), DCEP (dexamethasone + cyclophosphamide + etoposide + cisplatin), and BD (bortezomib + dexamethasone).

Results

Based on our immunohistochemistry analysis, it had been demonstrated that patients with confirmed SPB were all positive for CD79a and CD38 (Figure 1A and 1B). The majority of patients were positive for CD138 (Figure 1C), and certain patients were also positive for immunoglobulin κ chain and λ chain (data not shown).

During the hospitalization period, all patients were negative for serum myeloma protein (M protein or paraprotein) and urine Bence-Jones protein. There were 7 patients who also received a bone marrow biopsy. However, no abnormal results were observed from the bone marrow biopsy. The follow-up period for patients ranged between 2 months and 108 months (average, 27 months). With the exception of 1 patient who experienced recurrence and 2 who died, all patients survived and were recurrence free. The details of all patients are listed in Table 1.

Discussion

Table 1. The clinical data of 12 SPB patients

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age (Years)</th>
<th>Site</th>
<th>Therapy</th>
<th>Following-up duration (months)</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>65</td>
<td>C4</td>
<td>Surgery</td>
<td>108</td>
<td>Lost</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>62</td>
<td>T5 to T7</td>
<td>Surgery + Radiation + Chemo</td>
<td>35</td>
<td>Cured</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>57</td>
<td>L1</td>
<td>Surgery + Chemo</td>
<td>25</td>
<td>Lost</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>52</td>
<td>T4 and Vertebral Canal</td>
<td>Surgery + Radiation + Chemo</td>
<td>6</td>
<td>Cured</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>43</td>
<td>T1</td>
<td>Surgery + Chemo</td>
<td>3</td>
<td>Cured</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>65</td>
<td>Upper of the left humerus</td>
<td>Surgery + Chemo</td>
<td>60</td>
<td>Cured</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>48</td>
<td>Ribs in both side</td>
<td>Surgery + Chemo</td>
<td>5</td>
<td>Improved</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>45</td>
<td>T5</td>
<td>Surgery + Chemo</td>
<td>16</td>
<td>Local Recurrence after 6 months</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>60</td>
<td>Back of the right 5th ribs and T3 to T7</td>
<td>Surgery + Radiation + Chemo</td>
<td>48</td>
<td>Lost</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>42</td>
<td>L3 to L5</td>
<td>Chemo + Radio</td>
<td>2</td>
<td>Cured</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>60</td>
<td>Lumbar</td>
<td>Surgery + Chemo</td>
<td>10</td>
<td>Cured</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>41</td>
<td>Proximal end of the left femur</td>
<td>Surgery + Radio</td>
<td>6</td>
<td>Improved</td>
</tr>
</tbody>
</table>
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and 60% (P=0.04) for patients receiving radiation dosage of ≥40 Gy and <40 Gy, respectively [15]. By contrast, although there have been a limited number of reports demonstrating a low control rate with very high dosages (50 to 60 Gy), there was no evidence to suggest a dose-dependent relationship for radiation therapy in the treatment of SPB. In certain reports, no dose-dependent relationship was observed in patients who received a dose >35 Gy [13]. Mendenhall et al reported that the medium dosage (40 to 50 Gy) combined with surgery is the primary method to be applied for the treatment of patients with SPB, and the administration of chemotherapy did not improve the survival rate of patients [18].

In this study, there was 1 case of recurrence in a patient who received surgery and chemotherapy. However, no recurrence was observed during the follow-up period in patients who received surgery and radiation therapy, or patients who received a combination of surgery, radiation therapy, and chemotherapy. However, as there is no evidence regarding whether the application of chemotherapy could delay the progression of SPB to MM, the prognosis of SPB to MM is affected by several factors, including the dose of radiation therapy, the tumor size (≥5 cm), age of the patient, serum immune globulin level, cervical spondylosis, and SPB-related neuropathology [19-21]. In conclusion, systematic therapy (surgery, radiation therapy, and chemotherapy) may be applied for the treatment of patients with SPB if there was evidence to suggest the development of MM. However, the majority of enrolled patients in this study had a short follow-up period, and 3 patients died. A large-scale investigation is required to confirm our findings.

Disclosure of conflict of interest

None.

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References


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