Literature Review

Percutaneous Vertebroplasty for Primary Non-Hodgkin's Lymphoma of the Thoracic Spine: Case Report and Review of the Literature

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Primary non-Hodgkin's lymphoma of the vertebra is rare in the spine of the elderly. The clinical presentation and radiological features are unspecific, which make it more difficult for diagnosis. We report a case of a 79-year-old woman complaining of serious backache without any injury. The magnetic resonance imaging (MRI) showed invasion of the fifth thoracic vertebra with the posterior vertebral body wall defect. There was a high suspicion that the patient had a metastatic tumor of the vertebra. A percutaneous vertebroplasty was performed under fluoroscopic guidance, which was used to treat the osteoporotic vertebral compression fracture, vertebral metastases, vertebral hemangioma, and multiple myeloma. The pain was rapidly and conspicuously relieved after the procedure. The visual analog scale (VAS) score decreased from 8 preoperatively to 2 postoperatively. The imaging examination postoperatively revealed a small amount cement leaking into the spinal canal, but there were no symptoms and no complications in our patient. During vertebroplasty, a biopsy was done by biopsy needle before injection of the cement (polymethyl methacrylate). The histopathological examination revealed a diffuse large B-cell lymphoma. No new evidence of any other lesion was found during a 6-month follow-up period. The patient was diagnosed with primary bone lymphoma finally. Due to the previous condition of the patient, R-miniCHOP chemotherapy was applied following the surgery in the department of hematology. Until the 9 months follow-up, the clinical result was still satisfactory.

Key words: Vertebroplasty, polymethyl methacrylate, biopsy, spine, lymphoma, large B-cell, diffuse

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Primary bone lymphoma (PBL) is an uncommon disease localized to the bone without evidence of lymphoma in lymph nodes or other tissues (1-3). Percutaneous vertebroplasty (PVP) is a minimally invasive technique in the treatment of metastatic lesion in bone, vertebral compression fractures (VCFs), and others (4-6). Until now, few studies concerning the technique applied in lymphoma of bone were reported, especially in primary lymphoma of bone. In the present study, we report a case of a 79-year-old woman who suffered from PBL in thoracic vertebra (T5). She received combined therapy with PVP and chemotherapy. Additionally, related reports of PBL are reviewed.

Case Report

We report a case of a 79-year-old woman who complained of a 3 month history of backache. The patient had no fever or night sweats, and denied any recent injury. Her past medical history included primary hypertension treated with telmisartan (Micardis) and type 2 diabetes treated with metformin. Physical examination demonstrated localized tenderness and percussion pain on the T5 spinous process with no restriction of the waist motion. Muscular tone of the lower limb was normal, and no hypoesthesia and asthenia of the lower limb was observed. There was no evidence of bladder or bowel dysfunction. Physiological reflexes were existent without any pathological ones.

Initially, the x-rays of the thoracic spine were obtained, which showed no obvious abnormality except for degenerative changes (Fig. 1). Then magnetic resonance imaging (MRI) was taken and it showed abnormal signal intensity in the T5 vertebra associated with a mild compression fracture, which presented as hypointensity on both T1-weighted (T1-W) images and on T2-weighted (T2-W) images. But hyperintensity was shown on Short TI Inversion Recovery (STIR) (Fig. 2). Although the posterior vertebral body wall was cracked and pressed on the dural sac slightly, there was no neurological deficit. However, routine laboratory evaluation on admission was unremarkable. Meanwhile, further diagnostic evaluation showed no abnormality, such as computed tomography (CT) scan of the lungs and abdomen. No evidence of primary tumor or metastatic tumor was found, so she was regarded as suffering from single-system or single-site disease. There was a high suspicion that the patient had a neoplastic lesion with the radiological feature of the lesion. At last, PVP was performed under the guidance of a C-arm x-ray machine in the prone position. The PVP was done using specialized instruments (Kyphon®, Inc, Medtronic, USA), consisting of an introducer stylet, cannula, blunt guide pin, precision drill, and bone filler device. The patient underwent PVP under local anesthesia (2% lidocaine and 1% rapivacaine, 1:1) by the unilateral pedicular approach. The tip of manual drill was then inserted through the working cannulas and placed inside the anterior 3/4 of the vertebral body on the lateral view, and located both sides to the midline on the anteroposterior view. A biopsy was done by biopsy needle before injection of the cement, and then the polymethylmethacrylate (PMMA) cement was injected slowly to fill the vertebra in a retrograde fashion from anterior to posterior under fluoroscopic control. The amount of cement filled

Fig. 1. *No obvious abnormality on the x-rays of the thoracic spine.*

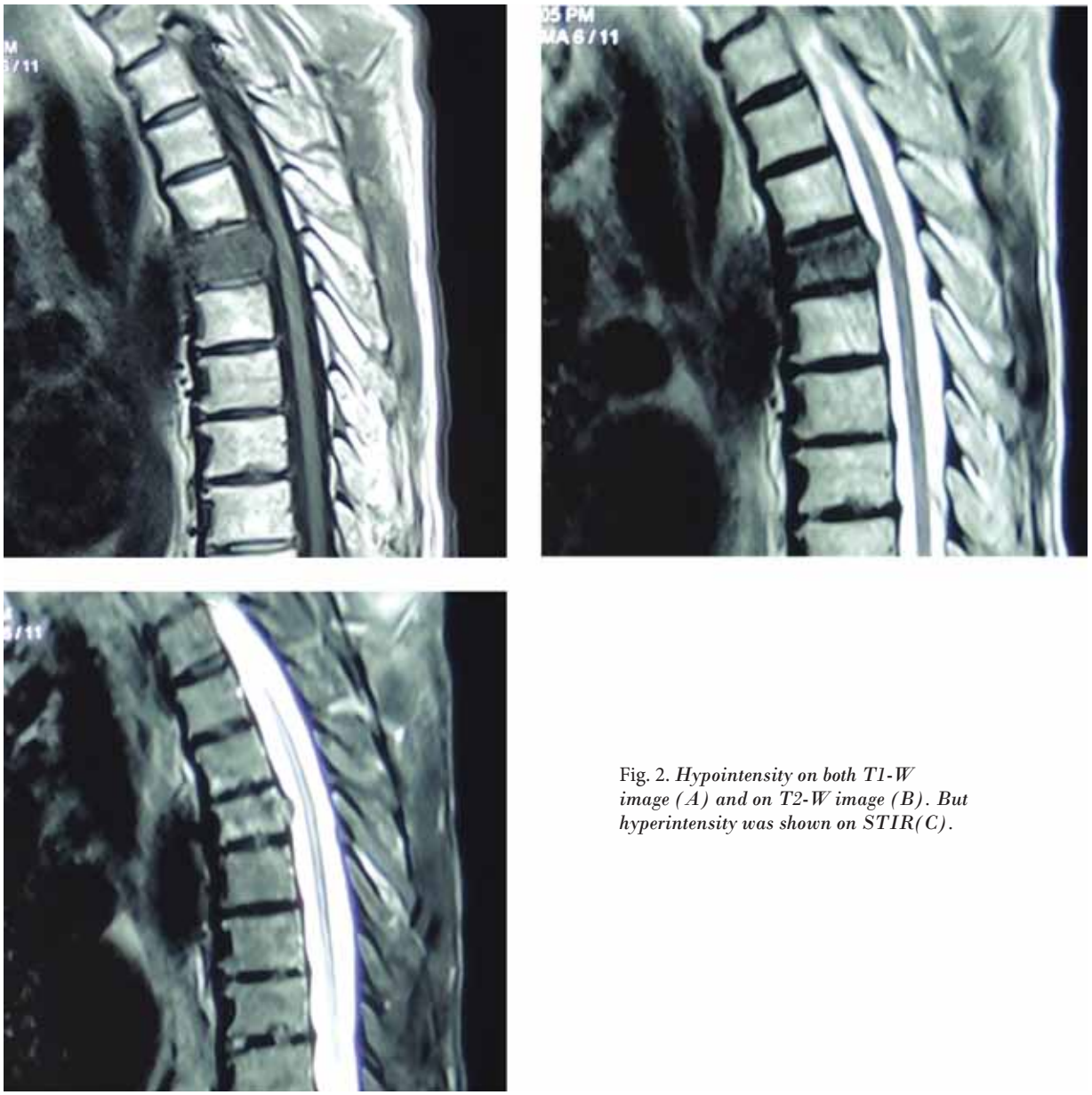

Fig. 2. *Hypointensity on both T1-W image (A) and on T2-W image (B). But hyperintensity was shown on STIR(C).*

in the vertebra was 3.0 mL. Blood loss during surgery was less than 10 mL. After the procedure, the backache resolved rapidly and conspicuously. The patient could sit freely and was allowed to walk 6 hours postoperatively. She was no longer taking any analgesic and the visual analogue scale (VAS) score decreased from 8 to 2. The plain radiographs and CT scan postoperatively revealed that the spread of cement was satisfactory in the vertebra, except for a small amount cement leaking into the spinal canal (Fig. 3). But the leakage did not cause any complaints and symptoms in the patient. No other complication was seen during operation and follow-up.

The histopathological examination of the sample revealed diffuse large B cell lymphoma. The immunochemistry showed: CD3(–), CD20(+), CD21(FDC–), Ki-67(80%+), CD10(–), Bcl-2(+), Bcl-6(+), Mum-1(+), CD5(+), CD56(–), Granzyme B(–), CyclinD1(–), c-myc(+), and EBER in situ hybridization (–). Two weeks after the

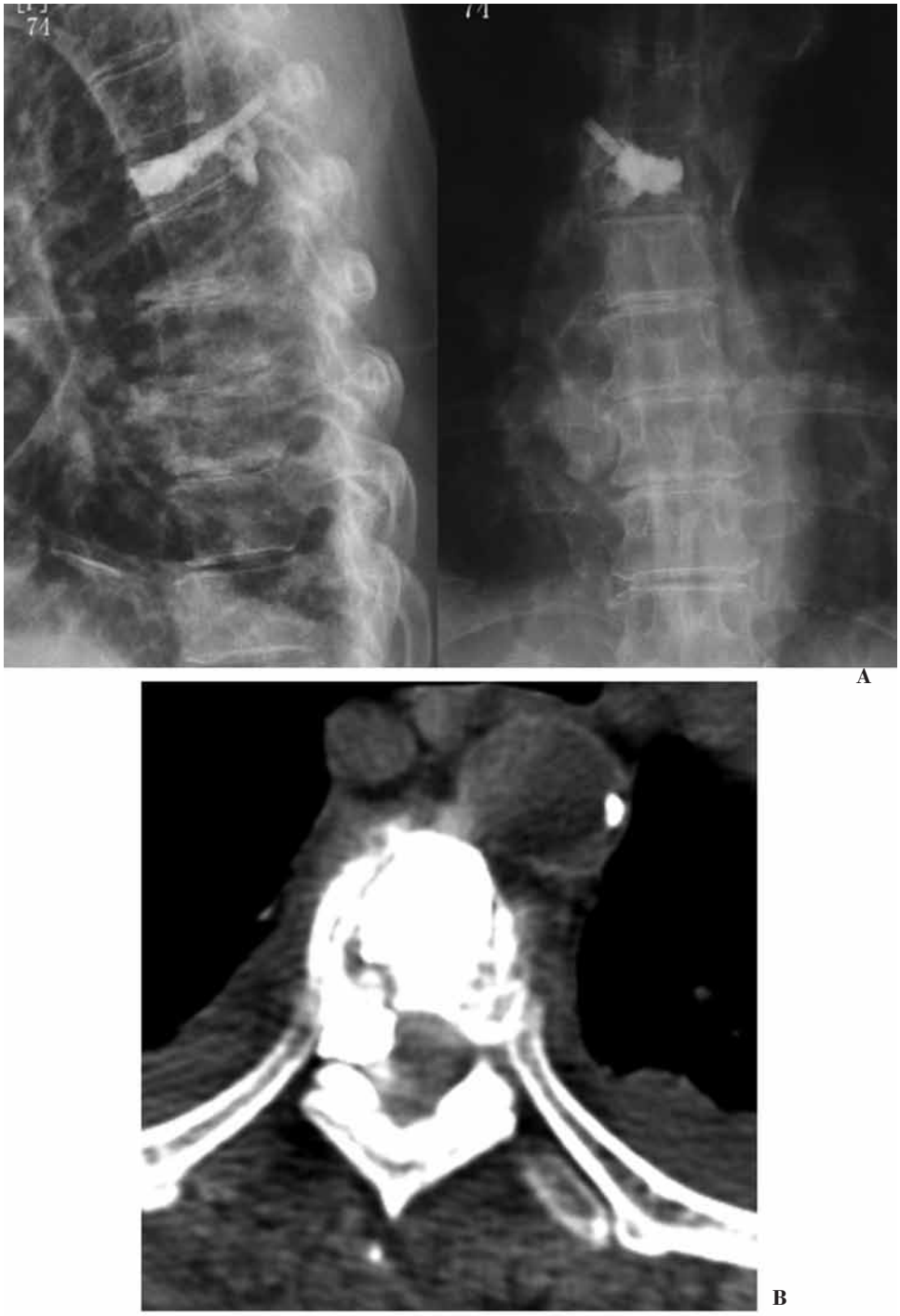

Fig. 3. *The plain radiographs (A) and CT scan (B) postoperatively revealed a small amount cement leaking into the spinal canal.*

PVP, she gradually received 3 chemotherapy cycles (R-miniCHOP) in the department of hematology. Meanwhile, the result of bone marrow aspiration in the ilium was normal. No new lesion was found during the 6-month follow-up period. To date, no neurological or other complaints were received and disease-free survival has reached nearly 9 months.

Discussion

Malignant lymphomas (ML) are a group of cancers in which cells of the lymphatic system (either B or T cells or their subtypes) become abnormal and start to grow uncontrollably. ML can be classified into Hodgkin's lymphoma (HD) and non-Hodgkin's lymphoma (NHL) by histopathology. PBL is defined as lymphoma localized to the bone without evidence of any other sites. The definition of PBL changed several times in the last decades. In the World Health Organization classification of neoplasms of the hematopoietic and lymphoid tissues published in 2008, PBL is characterized as an independent disease (7). Nowadays, the generally acknowledged definition of PBL is: 1) primary involvement site of the bone; 2) no evidence of extra-bone lesion; 3) no evidence of any other extra-bone lesion 6 months after bone lesion is diagnosed; and 4) the diagnosis is confirmed by both pathological morphology and immunohistochemistry (3,7).

PBL is one of the rarest primary bone malignancies. The exact incidence of PBL is still unclear, but it seems to account for approximately 5% of extranodal lymphomas, less than 1% of all NHL, and 3 – 7% of all malignant bone tumors (1,2). PBL was first defined as a distinct clinicopathological entity in 1939 by Parker and Jackson (8). It occurs in a wide spectrum of patients, commonly during 20 to 50 years of age with a slight preponderance in men (9). However, our case is an over 70-year-old woman, which was rarely reported in previous research. No racial or geographic predominance has been demonstrated (10). Every bone is a potential site for lymphoma development, but long bones and flat bones are the most commonly affected. PBL occurs most often in the diaphysis, whereas metaphysis or epiphysis involved often reflects progressive disease (11). Many studies found that the common places of PBL are the femur or pelvis, with other rare sites such as ribs, mandible, sternum, scapula, etc. (12-15). Primary vertebral lesion accounts only for 1.7% of all PBL, usually at the thoracic or lumbar levels (16). In our case, no evidence of lymphoma was found in lymph nodes or other tissues, so the patient was regarded as suffering from single-site (T5) only.

Although the clinical presentation depends on the location of the lesion, pain is the most frequent presenting symptom. The localized tenderness and percussion pain is detected easily by physical examination. When the vertebra is involved, back pain is the most common symptom. Some neurological deficits may be present, including hypoesthesia, paraparesis or paraplegia, bowel or bladder dysfunction, and others (17,18). Plain radiographs of PBL are usually non-specific which even underestimate the extent of the lesion. The CT scan can show the changes of bones and the soft tissues more clearly, which can display the boundaries of the lesion. MRI is a particularly useful imaging technique of choice due to its noninvasive nature and greater anatomic detail. In the areas of the lesion of lymphoma, abnormal signal intensity areas are visible on both T1-W and T2-W images with minimal contrast enhancement (19). STIR can also detect the abnormality in the bone marrow. MRI is more accurate in evaluating PBL, which could evaluate the extent of soft tissue extension, spine involvement, and spinal cord compression. Positron emission tomography (PET) scan is a test that can find a problem of bone days to months earlier than a regular x-ray or CT scan, which is great help for the accurate localization and staging of PBL (20). ^{18}F-flurorodeoxyglucose positron emission tomography (^{18}FDG-PET) CT scan (PET-CT) is a hybrid imaging technique that simultaneously provides functional and anatomical information, with a higher sensitivity and specificity in lymphoma patients (21,22). With the combined use of CT, MRI, and PET scan, a higher proportion of patients could be found (23). But some diseases need to be differentiated from PBL, such as metastatic carcinoma, Ewing's sarcoma, osteosarcoma, eosinophilic granuloma (skeletal), and chronic osteomyelitis (24).

The final diagnosis was established by histopathological examination of the sample obtained by surgical procedure. NHL are more common than HL in extranodal lymphomas, and diffuse large B cell lymphoma is the most common pathological type, accounting for about 80% of PBL (10,15,23). The pathological type in our patient is diffuse large B cell lymphoma also. Different strategies such as chemotherapy, local radiotherapy, surgery, and immunotherapy have been used to treat primary diffuse large B cell lymphoma of bone which is a separate entity usually displaying favorable clinical features and good prognosis (10). Some studies (25,26) suggest anthracycline-based chemotherapy followed by involved field radiotherapy as the first line treatment for patients with primary diffuse large B cell lymphoma

of the bone (Fig.4). The overall response rate is over 90% and the 5-year overall survival is 84%. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy is the first choice regimen. Our patient received 3 cycles of R-miniCHOP (low-dose CHOP) in the department of hematology, because this chemotherapy could offer a good compromise between efficacy and safety in elderly patients (27).

Destruction of vertebra caused by lymphoma can lead to local pain, decreased spinal stabilization, pathological fractures, kyphosis, and nerve or spinal cord compression syndromes. The goals of initial surgery in the

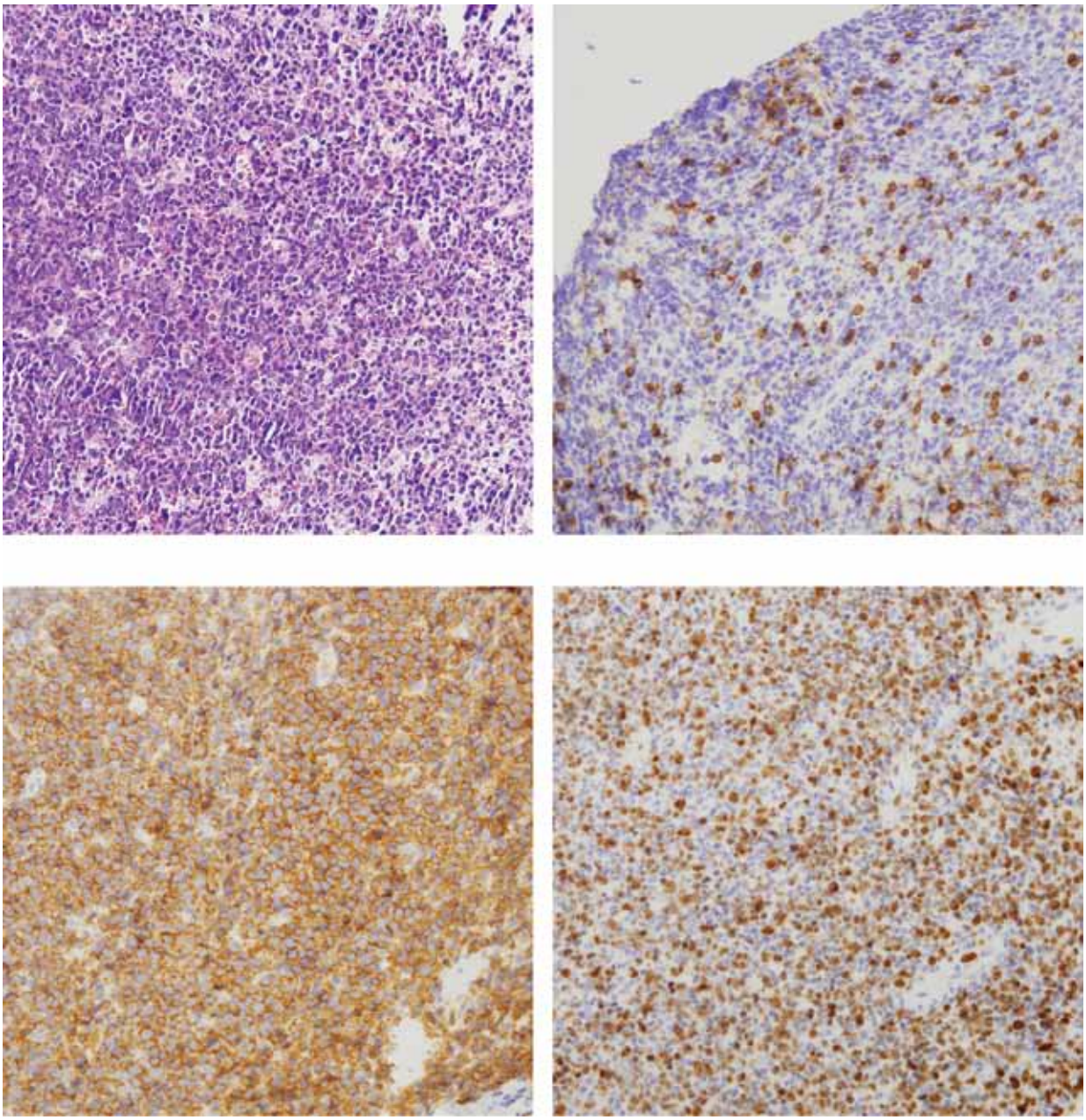

Fig. 4. *Diffuse infiltration of large B-cells. (A) Hematoxylin and eosin stained cells. Immunohistochemical analysi: (B) CD3(-), (C) CD20(+), (D) Ki-67 index 80%; (magnification, x 200).*

vertebra are usually to prevent further bone destruction and compression, to enable weight-bearing, to assist pain relief, and to obtain a better quality of life. Those patients with malignant tumors are often elderly, debilitated, or systemically ill from their malignant disease. Traditional open operation like corpectomy (17) is not the optimal selection for the patients due to the tremendous trauma and high risk, so it is only indicated for serious pathologic fractures causing spinal cord or nerve root compression. PVP is a minimally invasive procedure under x-ray guidance, which consists of percutaneous puncture and injection of PMMA into damaged vertebra. The lesion was filled with PMMA via a transpedicular or extrapedicular approach. PVP was first reported by Galibert et al (28) and appeared to offer an alternative treatment in patients with bone metastases or VCFs. PVP strengthens the vertebra weakened by the lesion and enhances the rigidity and intensity of the vertebra to allow early weight-bearing movement. It could effectively relieve pain and promote patients' rapid recovery (29,30). PVP has been generally accepted as a safe and effective treatment option for patients with vertebral hemangioma (28,31), osteoporotic vertebral compression fractures (4), vertebral metastases (6,32,33), multiple myeloma (5,34), and Langerhans cell histiocytosis (35). PBL has a favorable outcome in patients with diffuse large B cell lymphoma. It relieves the pain and improves the quality of life rapidly for these patients. However, there are few reports about PBL of the vertebra treated by PVP.

Cement leakage is one common complication of PVP related to spinal metastases. Especially, the posterior wall defect could increase the risk of cement leakage and subsequently induce spinal cord or nerve root compression. Therefore, posterior wall defect was regarded as a contraindication to PVP by some previous studies (36,37). However, with the development of the technique, this surgical procedure for patients with posterior wall deficiency was not only effective but safe (33,38). The process of injection of PMMA should be monitored under fluoroscopy carefully to prevent the leakage as much as possible (5). With fluoroscopic guidance, the injection of PMMA is not stopped until it near the posterior wall of the vertebral body when PVP is performed. At the same time, appropriate cement injection and increased cement viscosity should decrease the risk of cement leakage (39,40). Although the risk of cement leakage is relatively higher in the patients with spine metastases treated by PVP, especially with severe posterior wall defects, there were no clinical symptoms such as spinal cord or nerve root compression and no other complications in most of them (6,33).

VAS score was decreased obviously after the procedure in our patient. Pain relief was the primary aim of the surgical intervention. However, the mechanism of pain relief remains unclear. Many studies (5,29,41-46) speculated that it may be due to 1) PMMA improving the strength and rigidity of the vertebra, with prevention and treatment of pathologic fractures; 2) reconstructing the stabilization of vertebra by PMMA immediately, reducing the irritation to vertebral nerves; 3) the damage the nerve endings by hyperthermia generated during cement consolidation or cytotoxicity of cement; and 4) killing part of tumor cells, and reducing tumor burden by hyperthermia and cytotoxicity. The overall outcome of PBL is usually good with a 5-year survival ranging from 62% to 88% (3,13,22,26). The overall outcome of PBL is usually good, some studies (25,26) reported the overall response rate is over 90% and the 5-year overall survival is 84% for patients with primary bone diffuse large B cell lymphoma. During 9 months of follow-up with our patient, there were no complaints and no new lesions. But the long-term effect still needs to be further observed in the future.

Conclusion

Primary bone lymphomas arising from the spine are rare, especially in the elderly. Diagnosis of this disease may be challenging due to its low incidence and unspecific clinical and radiological features. When severe pain occurs, early PVP is indicated, which could relieve pain quickly and allow early weight-bearing movements.. A biopsy that is good to clarify diagnosis could be done during the operation. The patient with primary bone diffuse large B cell lymphoma could receive combined therapy and have a good prognosis.

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