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Dural plasmacytoma as the initial presentation of multiple myeloma: A case report and review of the literature

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ABSTRACT

Dural plasmacytoma is a type of multiple myeloma of the central nervous system. Our patient presented with symptoms of headache. Imaging findings suspected glioblastoma, whereas pathological findings revealed mucosa-associated lymphoid tissue lymphoma associating with plasma cell differentiation. Further in-depth studies confirmed a diagnosis of dural plasmacytoma. This case indicates that morphological variations may occur in the extramedullary involvement of CD20-positive multiple myeloma. The multidisciplinary team contributes to the diagnosis of hematological diseases.

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Introduction

Extramedullary plasmacytoma is defined as the monoclonal proliferation of plasma cells most commonly in their disseminated form, namely, multiple myeloma. The incidence of extramedullary plasmacytoma is low at approximately 7%; however, it is more common in its recurrence, and it rarely involves the central nervous system (<1%), which is the focus of this paper.[1] Multiple myeloma of the central nervous system can involve the skull, pia mater, or brain parenchyma. In the absence of an existing diagnosis of multiple myeloma, these tumors are easily mistaken for meningiomas, metastases, or lymphomas. In the present report, the patient's initial imaging diagnosis was glioblastoma, followed by a diagnosis of mucosa-associated lymphoid tissue (MALT) lymphoma based on pathological findings and then a diagnosis of CD20-postive multiple myeloma based on additionalevidence.

Case presentation

A 61-year-old HIV-negative woman presented to the neurological clinic complaining of numbness in the right upper extremity for 4 months. A neurologic examination showed hyperalgesia of the right upper limb, indicative of positive bilateral Babinski signs. A head computed tomography (CT) scan without contrast revealed a left frontal-parietal soft tissue mass with localized bone thinning and destruction. A head magnetic resonance imaging (MRI) scan with contrast (Figure1 A) showed a skull mass with compression of the adjacent brain parenchyma, which raised the suspicion of a diagnosis of meningioma. The patient underwent a Simpson level 1 resection. The dura mater of the tumor, skull, and lesion was removed during surgery. MALT lymphoma with plasma cell-like differentiation was suspected given the immunohistochemical results as follows: CD20(+), CD38(+), CD138(+), Lambda (partially +), Bcl-2(+), CyclinD1(+), MUM1(+) IgG (partially +), Ki-67(20% +), CD79α(-), Kappa(-), IgG4(-), CD23(-), CD21(-), CD10(-), CD3(T lymphocyte +), and CD5 (T lymphocyte +).

We transferred the patient to our department of hematology for a systematic evaluation and observed multiple osteolytic lesions in the cranium, thoracic vertebrae, bilateral collarbone, ribs, lumbar vertebrae, pelvis, and bilateral upper femur. Fluorodeoxyglucose-positron emission tomography results showed a standardized uptake volume of 8.29 similar to that of enhanced lesions in the brain and bone (Figure 2) . A bone marrow smear showed 5.5% morphologically abnormal plasma cells, and this ratio included binuclear and multinucleate plasma cells. Bone marrow flow cytometry revealed 1.02% monoclonal plasma cells with results as follows: CD38(++), CD138(+), CD45 (dim+), CD19(-), CD56(-), CD20 (partially+), Kappa (-), and Lambda (+) (Figure 5). The results of the bone marrow biopsy were as follows: CD38(++), CD138(+), MUM1(+), CyclinD1(+), PAX (+), CD20 (+), Kappa (-), Lambda (+), and EBER (-), supporting a diagnosis of multiple myeloma. Fluorescence in situ hybridization (FISH)detection of bone marrow CD138(+) cells revealed del (13q14), t (11; 14) (q13; q32) (Figure 3A). The results of IgH FR2-JH rearrangement were positive. The 24-hour urine λ light chain quantization was 2.05 g. The results of serum protein immunofixation electrophoresis were positive for Lambda, and these findings were more consistent with the epidural invasion of multiple myeloma than MALT lymphoma. Therefore, we further performed FISH examination of intracranial tumor cells, and the results were consistent with those of bone marrow FISH (Figure 3B), thereby arriving at a diagnosis of multiple myeloma (Lambda) ISS II with del (13q), t (11; 14) and with epidural invasion. After the diagnosis of multiple myeloma, a regimen containing bortezomib, dexamethasone, cyclophosphamide, and thalidomide was administered. The disease status was assessed by strictly complete remission after 4 courses of chemotherapy (Figure1B). At the time of this writing, the patient has completed the eighth course of chemotherapy and is in a state of continuous remission.

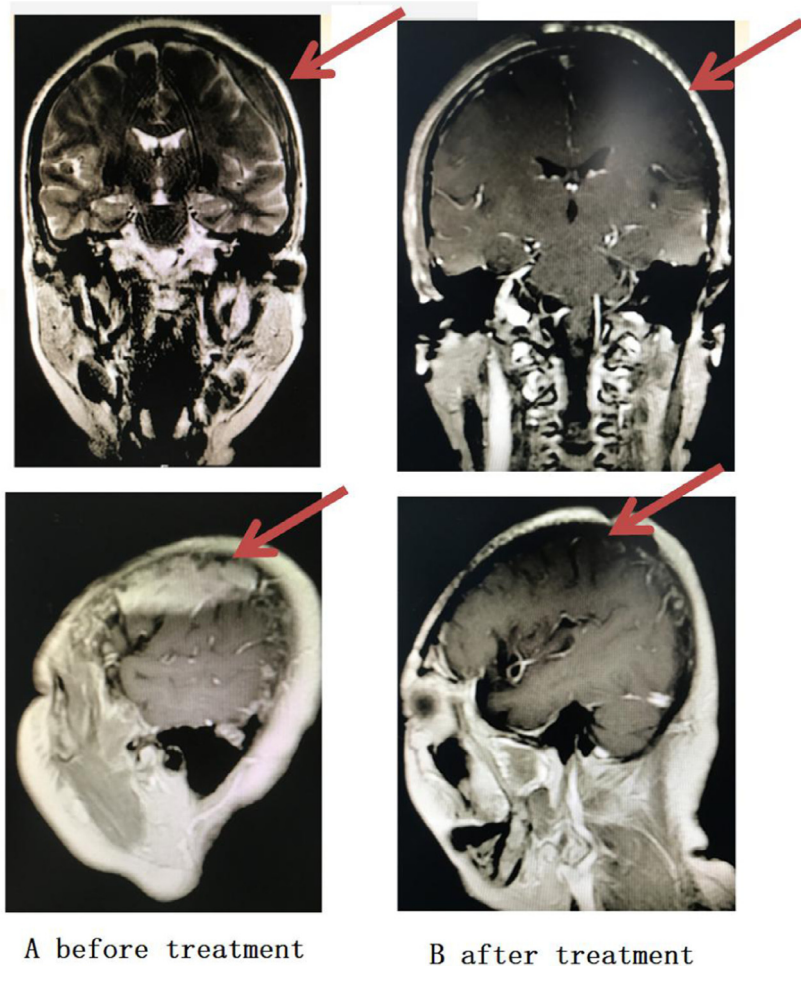

Fig. 1. (A) MRI results before treatment.Patchy hyperintensity can be seen in the skull laminae, and soft tissue signal invasion and epidural invasion can be seen in the left frontal parietal bone. The left frontal parietal mass showed obvious enhancement, and extensive abnormal enhancement was seen in the skull. The red arrows indicate abnormal MRI signals in the skull laminae. (**B)** The abnormal signal in the original left frontal parietal bone disappears after treatment.The red arrows representthe location of the tumor lesion.No abnormal enhanced signal was seen after the injection of contrast agent.

Discussion

Multiple myeloma is a malignant proliferative disease of plasma cells that occurs in the elderly and can cause a series of clinical manifestations such as bone destruction, anemia, renal insufficiency, infection, and hypocalcemia. Common neurological complications of multiple myeloma are spinal cord compression and peripheral neuropathy. Intracranial manifestations of multiple myeloma are very rare and represent <1% of multiple myeloma patients. The median age for diagnosis of multiple myeloma of the central nervous system is 56-58 years (range, 33-82 years), which is similar to multiple myeloma. There is no gender difference in the incidence ratio.[2] CNS infiltration can be identified at the time multiple myeloma is diagnosed or during its progression. However, it is more common in refractory disease or during a relapse. The median

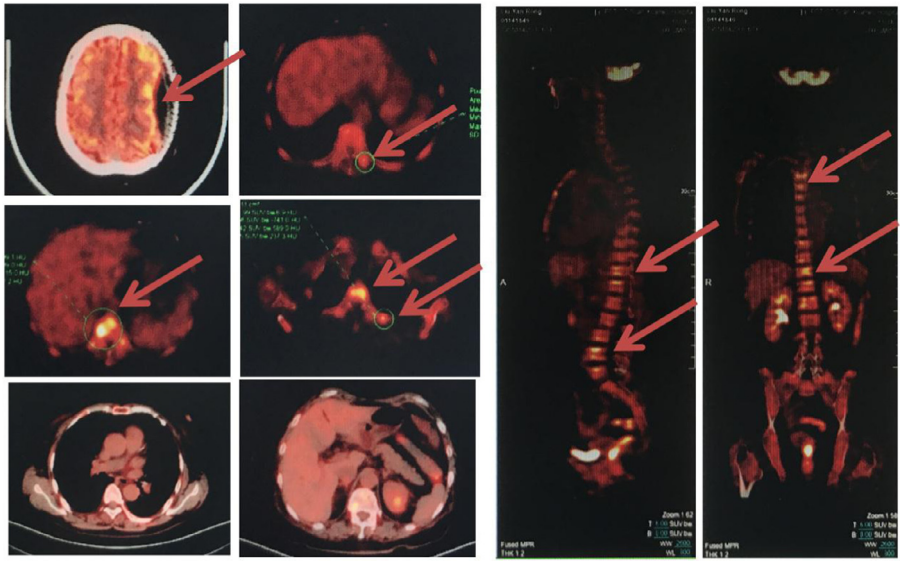

Fig. 2. Postoperative fluorodeoxyglucose positron emission tomography (FDG-PET) results:a standardized uptake volumeof 8.29 matched that of enhanced lesionsinthe brain and bone. The red arrows indicate abnormal locations of the brain and bones with high SUV value.

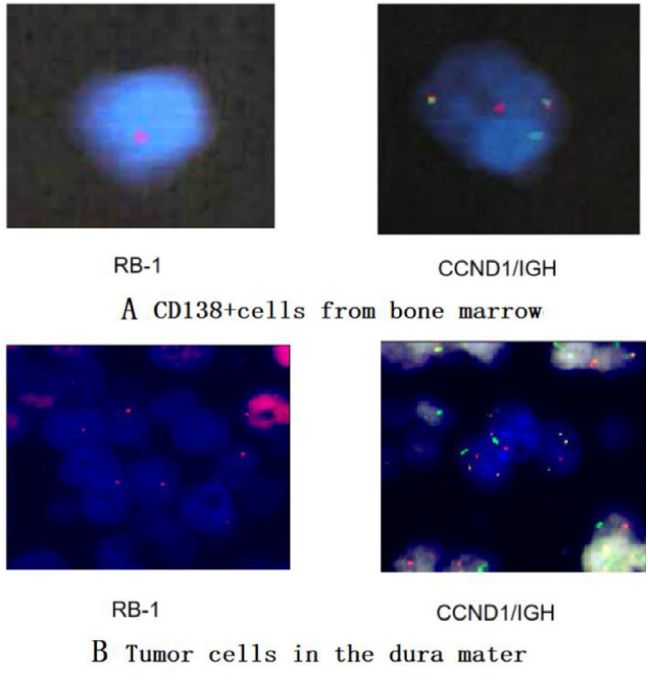

Fig. 3. FISH results show del(13q14) and t(11;14)(q13;q32) (**A)** CD138(+) bone marrow cells. (**B)** Tumor cells in the dura mater.

time from multiple myeloma diagnosis to the development of lesions in the CNS was 25 months. Multiple myeloma with concurrent CNS infiltration has a poor prognosis, with an overall survival of only 1-3 months, and the longest reported survival is 14 months.[3] The clinical manifestations of multiple myeloma involving the central nervous system are very extensive, with most lacking specific neurological symptoms and signs. The common symptoms at presentation were visual changes, headache, altered senses, radiculopathy, confusion, dizziness and seizures, cranial nerve palsy, and spinal cord symptoms such as limb sensory changes, motor loss, and urinary retention. A disproportionate number of patients had light chain disease (12/37 patients; 32%), with a lambda predominance (62%).[4]

The exact mechanism of CNS infiltration in multiple myeloma patients is unclear. Most researchers believe that there are 2 possible ways: (1) hematogenous dissemination and (2) direct infiltration and spread of adjacent plasmacytoma, although the former is more common in plasma cell leukemia (multiple myeloma of the central nervous system). The latter result comes from osteo-dural or primary dural multiple myeloma (OD-DMM).[5] Extramedullary tumor masses are most common in skull lesions, the skull base, nasal or sinus bone lesions. Both OD-MM and multiple myeloma of the CNS may cause parenchymal infiltration. According to imaging examination, the patient's diagnosis was more inclined to be the OD-MM type.

CT and MRI have certain auxiliary value in diagnosing multiple myeloma invading the CNS. One meta-analysis revealed that the most common imaging features of myeloma of the CNS are diffuse leptomeningeal enhancement in the brain (44%), followed by localized leptomeningeal involvement in the brain (30%) and intracerebral masses (20%).[6] Lesions involving the leptomeninges and skull concurrently are the imaging features of OD-MM. However, if the patient has a history of multiple myeloma, it is easy to diagnose multiple myeloma of the CNS by imaging. Otherwise, it cannot be easily diagnosed by CT or MRI alone. Because the intracranial lesions of multiple myeloma are often misdiagnosed as other malignant or benign diseases of the CNS by imaging,[7-11] biopsiesareneeded to confirm the diagnoses.

Pathological biopsy of an intracranial mass is the direct evidence for the diagnosis of myeloma of the CNS. However, pathological findings should be interpreted alongside clinical findings. The initial pathological examination of our patient was intracranial MALT lymphoma, which accounts for 3%-4% of lymphomas in the CNS. There is no systemic involvement, and the prognosis is good.[12] The pathological feature of our patient with MALT lymphoma was plasmacytic differentiation. However, it is difficult to distinguish between plasmacytoma and MALT lymphoma, which displays extensive plasma cell differentiation.[13-17] Furthermore, the growth pattern and histochemical staining of MALT lymphoma are variable, and there is no unique phenotype.[18] One study suggested that extramedullary plasmacytoma may represent a special type of MALT lymphoma that undergoes whole plasma cell differentiation.[19] However, the clinical manifestations of the 2 diseases are different, and the treatment regimen of multiple myeloma has a minor effect on MALT lymphoma.[14,16] The other pathological feature of this patient with B-cell lymphoma was CD20 expression. CD20 is a surface-specific antigenic marker for B lymphocytes. However, CD20 expression can be found in approximately 13%-32% of multiple myeloma patients.[20] CD20 expression is also associated with lymphoplasmacytic morphology and t (11; 14) in multiple myeloma patients.[21,22] Our multidisciplinary team combined clinical findings with pathological and imaging findings to ultimately diagnose this patient with multiple myeloma. Evaluations of bone marrow involvement; monoclonal λ light chain; del(13q14), t (11;14) (q13;q32); and lytic bone lesions were performed to exclude intracranial MALT lymphoma. The results of FISH support the similarity between tumor cells invading the dura mater and abnormal plasma cells in the bone marrow, although there were differences in cell morphology. This diagnosis was confirmed by the marked effectiveness of chemotherapy, which included bortezomib.

A previous study has reported that bortezomib is more effective than lenalidomide in multiple myeloma with del (13q14).[23] Other data have revealed that patients with multiple myeloma of the CNS respond well to bortezomib treatment. In an unvaried analysis, there was no statistical difference between lenalidomide and bortezomib in the treatment of multiple myeloma of the CNS.[4] Daluzumab alone or combined with bortezomib produced a lasting response in the

treatment of myeloma with no serious adverse events.[24] Although rituximab is effective in the treatment of malignant B-cell lymphoma, there is no consensus that rituximab is equally effective in patients with CD20-positive multiple myeloma.[25] It is currently believed that in the era of new drugs for multiple myeloma, the importance of hematopoietic stem cell transplantation still cannot be replaced. With regard to the poor prognosis of multiple myeloma of the central nervous system, the goal of current drug therapies is to provide patients with the opportunity to undergo hematopoietic stem cell transplantation to prolong survival.[26]

Conclusion

Multiple myeloma of the CNS usually occurs in the presence of obvious systemic diseases. Dural plasmacytoma can be CD20-positive, and it has morphological variations similar to those of intracranial MALT lymphoma. In-depth morphological examinations, such as FISH, are helpful in its diagnosis when the immunohistochemical examination of tumor cells is atypical or inconsistent with clinical features. Our case highlights the value of the multiple disciplinary teams in the diagnosis of hematological diseases, which sometimes requires more than pathological analysis.

Authors' contributions

Y-X.G wrote the manuscript. W-Y.K performed the surgeries. L-H.T. performed the pathological analyses.X-X.L and Z.h treatedthe patients. W-L.S contributed expertise, critically reviewed the manuscript, and approved the final version of the manuscript Dural plasmacytoma mimics CNS MALT lymphoma

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