Case Report

Visual impairment as the initial presentation in multiple myeloma: a case report and literature review

Zhijian Xu[1#], Song Yang[2#], Lina Zhu[1], Xing Wan[1], Hu Xu[1], Huahui Chen[1], Lude Wang[3], Minfeng Tong[1], Qi Tu[1]

[1]Department of Neurosurgery, Jinhua Hospital Affiliated to Zhejiang University, Jinhua, China; [2]Department of Neurosurgery, Jiaozhou Branch, East Hospital Affiliated to Tongji University, Qingdao, China; [3]Central Laboratory, Jinhua Hospital Affiliated to Zhejiang University, Jinhua, China

Contributions: (I) Conception and design: Z Xu, Q Tu, M Tong; (II) Administrative support: L Zhu, X Wan, H Xu, L Wang; (III) Provision of study materials or patients: X Wan, H Xu; (IV) Collection and assembly of data: H Chen, L Wang; (V) Data analysis and interpretation: S Yang, L Zhu, X Wan; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work as co-first authors.

Correspondence to: Dr. Qi Tu, MD; Dr. Minfeng Tong, MD. Department of Neurosurgery, Jinhua Hospital Affiliated to Zhejiang University, 365 Renmin East Road, Jinhua 321000, China. Email: neurotuqi@sina.com; tmfhyj@sina.com.

Background: Multiple myeloma (MM) is a type of blood cancer, which rarely infiltrates the central nervous system (CNS) and lacks specific neurological symptoms. The prognosis is often poor, as the disease progresses rapidly. Herein, we present a rare case of MM with CNS involvement.

Case Description: A 53-year-old man was admitted to the Neurosurgery Department, Jinhua Hospital Affiliated to Zhejiang University with initial symptoms of "blurred vision for 3 months accompanied by numbness on the right side of the face for 7 days". Enhanced cranial magnetic resonance imaging revealed a tumor deep in the right temporal bone. During exploratory surgery, the "fleshy" mass was completely removed. Postoperative pathology confirmed a diagnosis of "plasmacytoma with intermediate features". The patient received multiple systematic chemotherapy treatments after surgery in the department of hematology of Jinhua Hospital Affiliated to Zhejiang University. During a 10-month follow-up period, the patient's neurological symptoms improved, and his general condition was considered good.

Conclusions: This report summarizes the clinical features, diagnosis, treatment, and prognosis of a patient with MM involving the CNS and examines the relevant literature. This case may serve as a reference for future clinical treatment and diagnosis. Further research on the pathophysiology of such cases is warranted.

Keywords: Multiple myeloma (MM); central nervous system tumor invasion (CNS tumor invasion); neurological deficiencies; prognosis; case report

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Introduction

Multiple myeloma (MM) is a cancer characterized by the monoclonal proliferation of plasma cells in the bone marrow with extensive infiltration. It typically remains localized in the bone marrow; however, extramedullary infiltration, when it happens, is more common in the liver, spleen, lymph nodes, and kidneys (1). The incidence of extramedullary plasmacytoma is relatively low (approximately 7%), but it has a high rate of recurrence, and clinical infiltration of the central nervous system (CNS) is rare (less than 1%). Consequently, in clinical practice, these tumors are often misdiagnosed as meningiomas, metastatic tumors, or lymphomas. Limited literature is available, consisting mainly of individual case reports or small retrospective studies. Patients with intracranial infiltration often have a very poor prognosis (2-4), highlighting the importance of early diagnosis. This case report and retrospective review aims to contribute to our understanding and accurate

diagnosis of MM with CNS involvement (CNSMM). We present this case in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-511/rc).

Case presentation

A 53-year-old man was admitted to Jinhua Hospital Affiliated to Zhejiang University (Jinhua, China) on February 11, 2023, due to "blurred vision for 3 months accompanied by numbness on the right side of the face for 7 days". Physical examination revealed that the right eye had limited outward movement; however, direct and indirect light reflexes were present. Muscle strength, movement, and sensation were normal in all limbs. Laboratory tests indicated the following: white blood cell count 12.53×10^9/L, red blood cell count 4.70×10^{12}/L, hemoglobin 141 g/L, platelet count 179×10^9/L; myeloma index series: blood immunoglobulin G (IgG) 31.40 g/L, IgA 1.92 g/L, IgM 0.58 g/L, κ type light chain 1.88 g/L, λ type light chain 6.55 g/L, β2-microglobulin 2.82 mg/L; urine κ type light chain 5.73 g/L, Urine λ type light chain 57.46 g/L; serum immunofixation electrophoresis: IgG, λ monoclonal bands were visible; urine immunofixation electrophoresis: λ monoclonal band was visible, suggesting proliferation of monoclonal plasma cells. Blood biochemistry: creatinine 70.00 μmol/L, uric acid 402.00 μmol/L, calcium 2.34 mmol/L, lactate dehydrogenase (LDH) 153 U/L. Bone marrow (iliac bone) examination, bone marrow image: plasma cell system is abnormally proliferated, and proto-juvenile plasma accounts for 10.0%. The cells were round, oval, or irregularly shaped, with dark blue cytoplasm, vacuoles, coarse nuclear chromatin, and vague nucleoli, consistent with MM bone marrow picture; Bone marrow pathology: increased number of proto-juvenile plasma cells, and MM was considered. Enhanced cranial magnetic resonance imaging (MRI) showed a mass-like, long T1- and mixed T2-signal shadow in the right temporal bone, with slightly unclear boundaries measuring approximately 3.5 cm × 2.1 cm. Diffusion-weighted imaging showed high signal intensity, and post-enhancement showed significant uneven enhancement. Perfusion-weighted imaging revealed high perfusion (*Figure 1*). On February 21, 2023, the tumor was resected from the skull base via endoscope-assisted surgery following routine preoperative preparation. Postoperative pathology revealed no brain malignancy (plasmablastic lymphoma). Immunohistochemistry showed the following: CD138 (–), CD38 (–), CD56 (–), CD19 (–), CD79a (+), CD10 (–), Bc1-2 (–), Bcl-6 (+), Ki-67 (+): 95%, MUM1 (+), kappa (+), lambda (+) (kappa expression greater than that of lambda), cyclin D1 (–), κ light chain (–), λ light chain (+++) (*Figures 2,3*). Immunofixation electrophoresis of the urine showed λ-type light chain at 57.46 mg/L. Postoperative physical examination revealed improvement in the numbness of the right side of the face.

On March 8, 2023, after the patient became stable postoperatively, he was transferred to the hematology department for further treatment. Routine examination of the bone marrow revealed an abnormal proliferation of plasma cells, with 10.0% immature plasma cells. On March 10, 2023, bone marrow immunotyping showed monoclonal proliferation of plasma cells, accounting for approximately 2.03% of nucleated cells (*Figure 4*); chromosomal analysis and florescence *in situ* hybridization were negative. A whole-body positron emission tomography and computed tomography (PET-CT) scan performed the same day showed the following after cranial base plasma cell tumor resection: (I) multiple skeletal bone density reductions with increased FDG (fludeoxyglucose) metabolism, suggesting a plasma cell tumor; and (II) postoperative changes in the cranial base with increased local FDG metabolism. According to the 2020 Revised Chinese Multiple Myeloma Diagnosis and Treatment Guidelines, the diagnosis of IgG-λ type MM was confirmed (5) with Durie-Salmon stage IIIA and International Staging System stage II. Treatment using the twice-weekly induction with ixazomib-lenalidomide-

Highlight box

Key findings

- This is a rare case reported in the literature with visual impairment as the initial manifestation of multiple myeloma (MM). Using a personalized surgical approach, the patient's neurological function was maximally preserved.

What is known and what is new?

- MM, as a malignant hematologic disease, rarely infiltrates the central nervous system. It is even rarer for MM to be combined with specific neurologic symptoms.
- Firstly, visual impairment as the first symptom of MM is rare. Furthermore, to preserve the patient's neurological function as much as possible, a transnasal anterior auricular approach was chosen. This case provides a diagnostic and treatment experience for neurosurgeons.

What is the implication, and what should change now?

- Research and reporting of MM in which neurologic function is the first symptom is necessary. Improving neurosurgeons' knowledge of multiple myelopathies will optimize patient treatment planning.

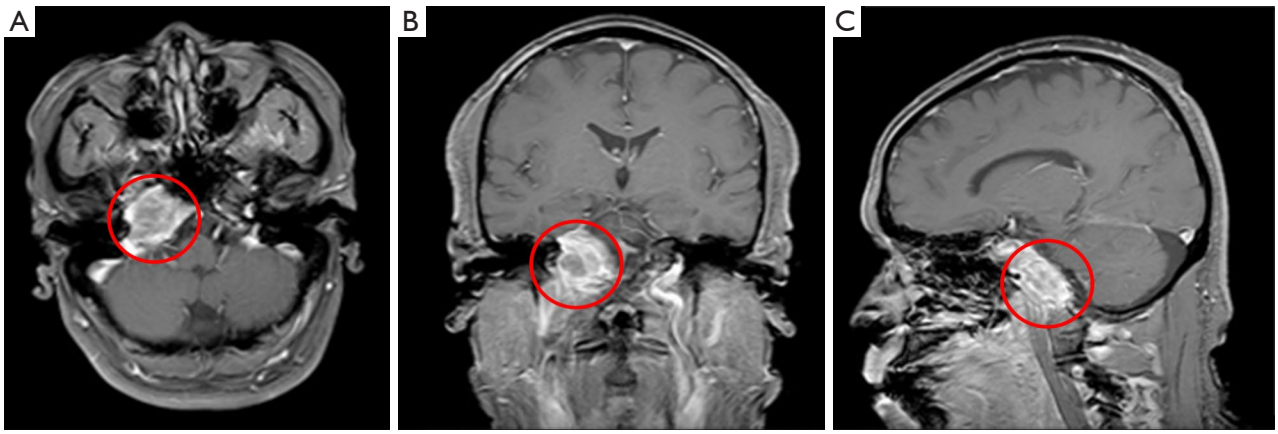

Figure 1 The patient's enhanced cranial MRI upon admission (February 14, 2023) shows a slightly indistinct border mass in the right temporal bone measuring approximately 3.5 cm × 2.1 cm. (A) Axial, (B) coronal, and (C) sagittal views of enhancement after contrast administration is significantly uneven and involves the left cavernous sinus, sphenoid sinus, and slope. The location of the tumor operative zone is circled in red in the figure. MRI, magnetic resonance image.

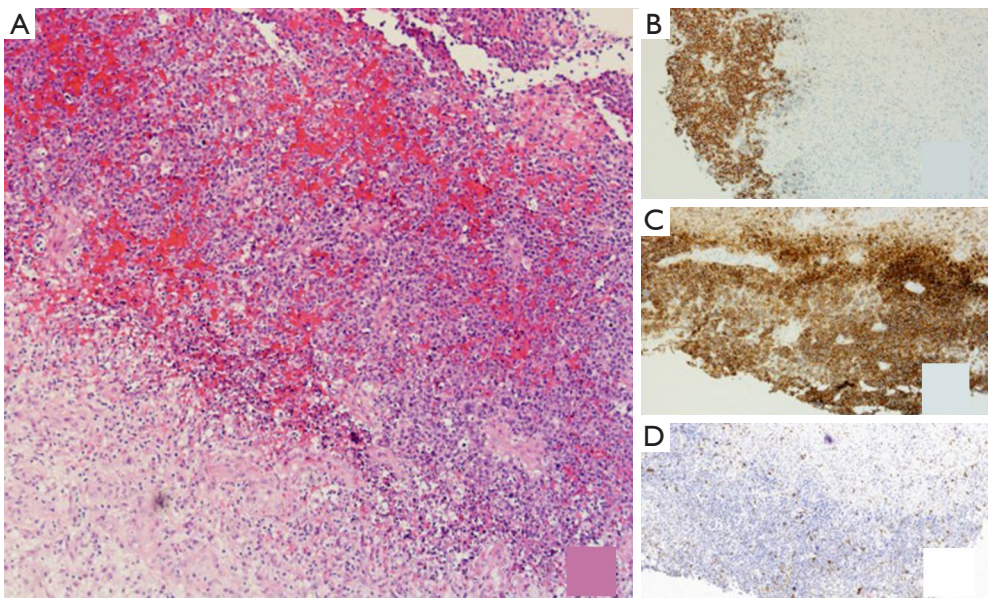

Figure 2 Patient's postoperative pathology results. (A) A histopathological image of the tumor mass (hematoxylin and eosin: 100×) shows abnormalities, intense staining, plasmacytosis, and abundant mitotic activity. Immunohistochemical staining (MHF100 Orthostatic Fluorescence Microscope: 100×), revealed that the tumor cells were negative for (B) CD138, (C) CD38, and (D) CD56.

dexamethasone (IRD) regimen was initiated on March 8, 2023, and the patient was discharged without complications on March 13, 2023.

On April 10, 2023, the patient was re-admitted for regular radiotherapy treatment and MRI showed significant enhancement around the surgical area. Chemotherapy with a pomalidomide + carfilzomib regimen was recommended to the patient. However, the patient's family chose to continue the IRD program on April 12 due to the cost. The patient was admitted to the hospital on May 13, 2023, for regular chemotherapy. A complete examination showed an IgG level of 21.20 g/L; bone marrow examination revealed 5% blast cells and minimal residual disease of 3.12%. Bone biopsy showed a significant increase in Ki-67, indicating

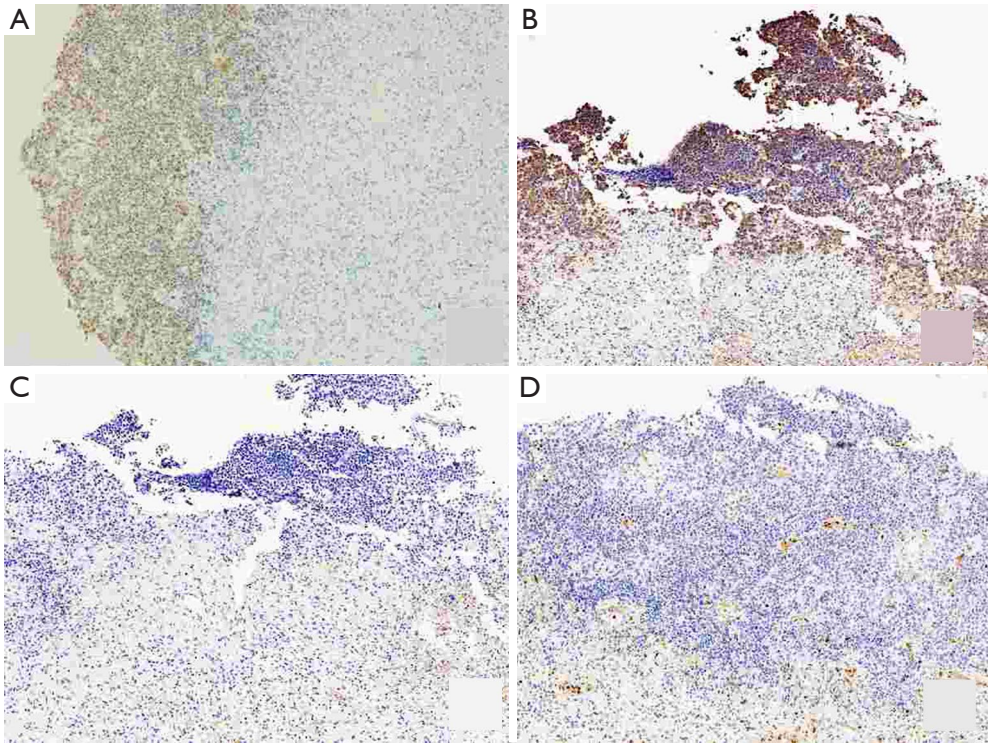

Figure 3 Immunohistochemical staining (MHF100 Orthostatic Fluorescence Microscope: 100×), shows the tumor cells are positive for (A) MUM1, (B) kappa, and (C) lambda (with higher expression of kappa than lambda) and negative for (D) cyclin D1.

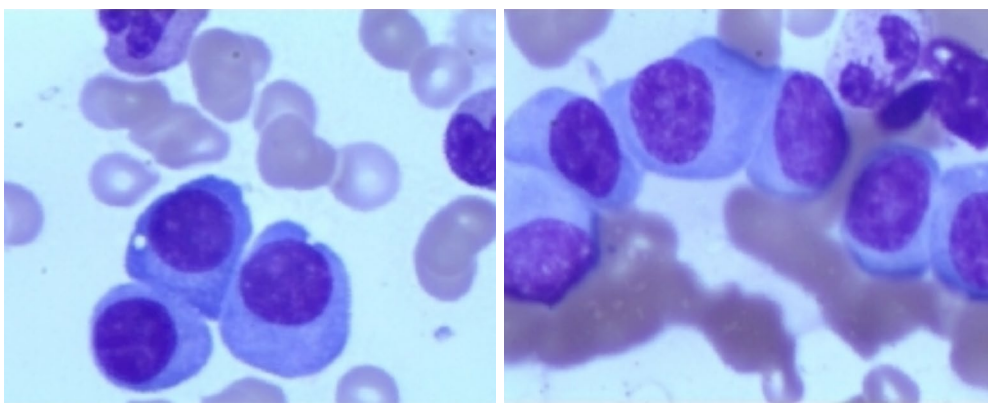

Figure 4 Initial bone marrow puncture (MHF100 Orthostatic Fluorescence Microscope: 400×), results showed active proliferation of nucleated cells with a granulocytic to erythroid (G:E) ratio of 5.56:1, where G =64.0% and E =11.5%. The granulocytic series showed active proliferation with approximately normal proportions and morphology of granulocytes at each stage. The plasma cell system exhibited abnormal proliferation, with immature plasma cells accounting for 10.0%. These cells were round, oval, or irregular in shape, with deep blue cytoplasm and vacuoles. The chromatin of the nucleus was coarse, and the nucleoli were faintly visible.

a poor prognosis. Therefore, intravenous chemotherapy combined with multiple agents was recommended. After consultation, the patient and his family refused and asked to continue ixazomib-pomalidomide dexamethasone regimen (IPD) treatment. Subsequently, the patient successfully completed chemotherapy sessions on May 16,

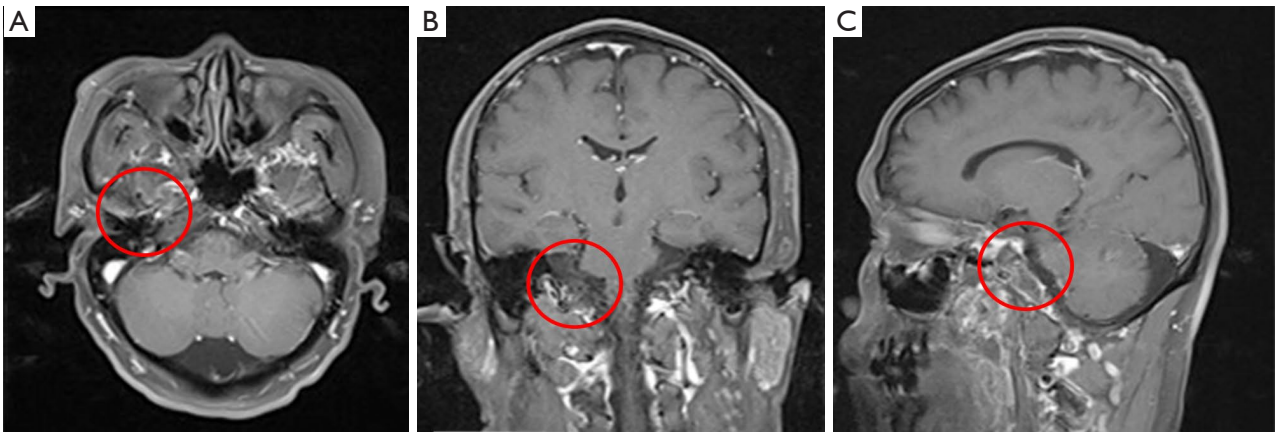

Figure 5 The postoperative 10-month follow-up enhanced cranial MRI (October 1, 2023). (A) Axial, (B) coronal, and (C) sagittal views of show no obvious enhancement or proliferative tissue in the surgical area. The location of the tumor operative zone is circled in red in the figure. MRI, magnetic resonance image.

June 19, and July 24, 2023, and was discharged. During the outpatient follow-up period, the patient's blurred vision and facial numbness improved significantly. Enhanced cranial MRI (*Figure 5*) performed in October showed no obvious enhancement or proliferative tissue in the surgical area. The patient's general condition is currently stable, and regular treatment will continue.

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee of Jinhua Hospital Affiliated to Zhejiang University (approval number: 2021 320-001) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

MM typically proliferates within the bone marrow microenvironment, with extramedullary involvement sometimes occurring in the upper respiratory tract, including the throat and nasopharynx. CNS infiltration is rare in patients with MM (6,7). CNSMM is usually defined as the infiltration of plasma cells in the cerebrospinal fluid, meninges, or brain parenchyma and is only seen in 0.7% of patients with MM. Infiltration can originate from direct spread from adjacent affected tissues or the hematogenous dissemination of malignant plasma cells in the peripheral blood circulation. The overall prognosis is poor (1,8), possibly due to the limited efficacy of intrathecal therapy and radiation, as well as the blood-brain barrier preventing the action of chemotherapy drugs on CNS-infiltrating plasma cells.

The clinical manifestations in patients with CNSMM are primarily related to the regions involved in the CNS, including headaches, seizures, limb weakness, sensory disturbances, and symptoms of cranial or spinal nerve root involvement (1,9). CNSMM don't have unique imaging features compared to common intracranial or spinal bone tumors and vascular disease (10,11). For example, hemangiomas can be described as having a "salt and pepper" look, with a high signal intensity, and exhibiting considerable contrast in enhanced MRI (12). Osteoid osteomas, in comparison, may reveal a radiolucent tumor with surrounding sclerosis, bearing a resemblance to a "sunny-side-up egg" (13) and on. The main imaging diagnosis of CNSMM is based on enhanced MRI of the head or spine showing plasma cell infiltration and substantial tumor lesions, often with visible changes in the enhancing deposits in the leptomeninges (approximately 70%) (14,15). Owing to the broad and nonspecific clinical features of CNSMM and its rarity, CNSMM is prone to misdiagnosis or missed diagnosis. In the present case, the patient presented with numbness in the right facial area, primarily in the distribution of the mandibular branch of the trigeminal nerve. He also exhibited symptoms of extraocular muscle paralysis (i.e., right internal strabismus, exotropia, or diplopia) when looking to the side. Preoperative enhanced cranial MRI confirmed a substantial

tumor occupying the right petrous apex. Considering the location of the lesion, a subtemporal preauricular approach was chosen, and the operation was performed extradurally. The tumor had a tough consistency and abundant blood supply; intraoperatively, it was observed that the tumor invaded the local dura mater, extending anteriorly into the Meckel cave and invading the lateral wall of the cavernous sinus, which matched the patient's symptoms.

The current clinical diagnosis of CNSMM is mainly based on detection of plasma cells or monoclonal Ig in the cerebrospinal fluid, as well as the presence of specific neurological symptoms or confirmation through craniotomy. Examination of the cerebrospinal fluid of patients with CNSMM typically shows increased cerebrospinal fluid pressure and increased protein and lactate dehydrogenase levels. Cytological examination of the cerebrospinal fluid may reveal abnormal plasma cells, although the low number of tumor cells and similar morphology between benign and malignant cells makes diagnosis difficult. Some studies have shown that detection of abnormal free light chains in the cerebrospinal fluid can improve the detection rate and be used for monitoring treatment response (1,16). Su *et al.* (17) and Fisken *et al.* (18) have suggested using flow cytometry to detect monoclonal plasma cells in the cerebrospinal fluid or minimal residual disease for the diagnosis of CNSMM. Plasma cell infiltration in the CNS is often associated with an increase in the expression of the antigen CD56 (75–80% of cases), which is involved in cell proliferation and migration. However, it remains unclear whether CD56 expression is beneficial for the infiltration of MM plasma cells (1,8,16). In this case, the immunohistochemistry results were negative for Bcl-2, CD56, and CD19. Although the antigen shared the same phenotype as normal plasma cells, it was negative for κ light chain and strongly positive for λ light chain, particularly the latter. By combining morphology and immunohistochemistry, the patient was diagnosed with intermediate plasma cell myeloma. Bone marrow aspiration cytology showed an increase in immature plasma cells, further confirming the presence of MM.

However, the optimal treatment plan for CNSMM remains unclear. Currently, the main approaches include local or systemic chemotherapy, targeted therapy, autologous stem cell transplantation, surgery, and intrathecal injection. Jurczyszyn *et al.* (7) emphasized the importance of systemic chemotherapy in 172 patients with CNSMM and the combination of systemic chemotherapy and other treatment modalities to prolong survival. Blood-brain barrier permeability of the selected drug is crucial for treatment efficacy. Bortezomib has a total response rate of 50–80% for relapsed or refractory MM, but its efficacy in CNSMM has not been extensively studied (19). Caballero-Velázquez *et al.* (20) reported that six patients survived >1 year with a combination of thalidomide, intrathecal injection, and radiotherapy (9,21). The treatment and efficacy of hematopoietic stem cell transplantation for CNSMM remains uncertain, and high-dose methotrexate may have potential benefits before transplantation (7). Reviewing domestic and foreign literature, the overall prognosis of this disease is poor, with a median survival of about 3–5 months (4,9,16,22). In the present case, follow-up enhanced cranial MRI 3 months after surgery showed a significant decrease in the size of the lesion, and the patient had been living for 10 months after the CNSMM diagnosis while receiving regular systemic chemotherapy. This may be because the lesion did not breach the dura mater or invade the brain parenchyma, and there was no evidence of leptomeningeal spreading through the cerebrospinal fluid.

Conclusions

CNSMM is a rare condition with a poor prognosis that is difficult to diagnose and treat. A multidisciplinary approach involving hematology, radiology, and pathology can assist in early diagnosis. It is worth exploring whether early intervention in cases of early CNS focal involvement could improve patient survival. For advanced stages, personalized treatment is required, and monotherapy or combination therapy can be considered. Due to the limited treatment experience for this disease, further confirmation is needed through multicenter, large-scale randomized controlled trials.

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Footnote

Reporting Checklist: The authors have completed the CARE

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-511/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee of Jinhua Hospital Affiliated to Zhejiang University (approval number: 2021 320-001) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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