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*Case Report*

# Intracranial plasmacytoma arising from dura mater secondary to multiple myeloma and presenting with sudden lethal intracerebral hemorrhage: A case report and literature review

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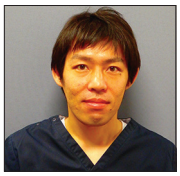

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## ABSTRACT

**Background:** Intracranial and central nervous system's involvement with multiple myeloma (MM) is a clinically rare manifestation. Furthermore, the development of intracranial plasmacytoma without bone involvement is much rarer. Herein, we report the case of massive intracerebral hemorrhage form intracranial plasmacytoma that arose from the dura mater without bone involvement.

**Case Description:** A 71-year-old woman, who had been diagnosed as MM and treated 2 years prior, developed sudden lethal intracerebral hemorrhage from the intracranial plasmacytoma. Massive hemorrhage was observed after a rapid tumor growth in the middle fossa. Immediate hematoma evacuation and tumor resection allowed the patient to avoid severe neurological deficits and lethal conditions.

**Conclusion:** A close follow-up by neuroimaging studies is essential in cases of intracranial plasmacytoma in MM patients and early intervention with surgical resection or radiotherapy should be considered.

**Keywords:** Intracerebral hemorrhage, Intracranial plasmacytoma, Multimodality, Multiple myeloma

## INTRODUCTION

Intracranial and central nervous system involvement with multiple myeloma (MM) is a rare clinical presentation, affecting <1% of patients with MM.[9] The most common neurological manifestations are the myelopathy and polyneuropathy from the spinal cord compression, secondary to vertebral column involvement.[3,15] Lytic lesions of the skull are also commonly observed in MM, arising from the diffuse skeletal involvement.[6]

Intracranial involvement without any bone involvement associated with MM is extremely rare.[14] Due to its rarity, the clinical features and optimal therapeutic approaches are currently unclear. Herein, we report a 71-year-old woman with sudden lethal intracerebral hemorrhage from intracranial plasmacytoma that arose from the dura mater without bone involvement. The massive hemorrhage emerged from the intracranial plasmacytoma after a rapid tumor growth.

Urgent surgical hematoma evacuation and tumor resection allowed the patient to avoid severe neurological deficits and lethal condition. This rare disease manifestation in MM patients is significant and highlights the importance of optimal management of MM with intracranial involvement.

## CASE REPORT

A 69-year-old woman was diagnosed with immunoglobulin (Ig) A lambda-type MM and was treated with 8 cycles of chemotherapy bortezomib-dexamethasone (VD) and lenalidomide-bortezomib-dexamethasone (RVD lite) as well as autologous peripheral stem cell transplantation. She underwent complete remission (CR). After 15 months, she presented with neck pain and paralysis in her left arm. Spinal magnetic resonance imaging (MRI) showed extramedullary infiltration in the left C4 and C5 spinous processes and multiple lytic lesions in the upper thoracic vertebra, indicating a recurrence of MM. Systemic treatment was started with daratumumab, bortezomib, and dexamethasone (D-Vd) and focal irradiation (30 Gy/10 Fr) for spinal lesions. During this time, brain MRI was used to screen for intracranial lesions.

Brain MRI with contrast medium [Figure 1a] revealed a thickened dura mater in the left middle fossa. No abnormal findings were observed in the adjacent skull base. Since the lesion was small and asymptomatic, 3 months of chemotherapy were administered and a follow-up imaging was performed. On MRI [Figure 1b], the lesion of the left middle fossa showed remarkable expansion, arising from the dura mater. Since the mass was expanding rapidly, tumor resection with the histopathological examination was planned.

However, a week after MRI, she developed an acute onset of headache followed by disturbance of consciousness and right-sided hemiparesis. She was brought to the emergency room by ambulance. On arrival, she was unable to follow commands and exhibited aphasia and right-handed hemiparesis. A computed tomography (CT) scan [Figure 2a] revealed a large intracerebral hemorrhage with a significant mass effect in the left temporal region. CT scan [Figure 2b] revealed an enhancing region that extended intraparenchymally, a slight enlargement of the tumor itself was also observed. At this time, no apparent abnormal findings were observed in the adjacent skull base of the middle fossa.

An urgent operation for both the hematoma evacuation and tumor resection was performed. After a temporal craniotomy and dural incision, the intraparenchymal hematoma was promptly evacuated. A reddish rather soft mass was observed directly connected to the hematoma, which arose from the dura mater of the middle fossa. The tumor was detached from the dura mater of the middle fossa followed by gross total removal of the tumor. Since there were no tumor invasion and no connection between the outer layer of the dura mater and adjacent sphenoid bone in the middle fossa, these structures were intentionally preserved. Finally, duroplasty was performed, the bone flap was returned, and the skin was normally closed. The resected tumor was sent for a histological examination. Hematoxylin-eosin staining [Figure 3a] showed diffuse proliferation of the plasmacytoid cells with clumped nuclear chromatin and eccentric eosinophilic cytoplasm [Figure 3b]. Additional immunohistological studies revealed proliferating CD138-positive cells, which are markers of the plasma cells, and a positive immunoreactivity to IgA lambda [Figure 3c]. These intraoperative and pathological findings indicated that the dura mater originated from the intracranial MM.

The postoperative course was uneventful and her hemiparesis and aphasia resolved immediately. Postoperative MRI [Figure 4] confirmed a thorough tumor and hematoma evacuation. Two weeks after the surgery, the patient was referred for further oncological treatment. Multimodality treatment was initiated consisting of proteasome inhibitor carfilzomib and dexamethasone (Kd), intrathecal chemotherapy (15 mg methotrexate, 40 mg cytarabine, and 4 mg dexamethasone), and radiation with 30 Gy/10 Fr for the tumor bed. The patient was discharged from the hospital

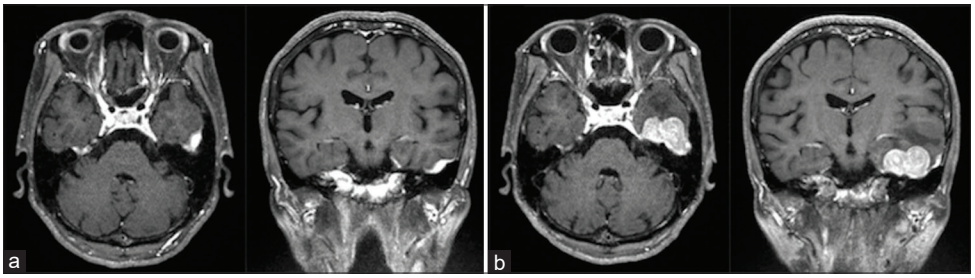


**Figure 1:** Axial and coronal contrasted T1-weighted magnetic resonance (MR) imaging. (a) MR imaging 3 months before the onset of intracerebral hemorrhage revealed a thickened dural lesion in the left temporal region with homogenous contrast enhancement. No abnormal findings in the contiguous skull base were observed (b) MR imaging 1 week before the onset showed that the extra-axial lesion expanded to 33 × 33 mm mass.

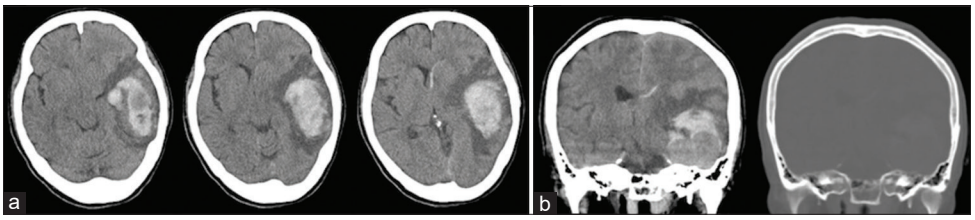


**Figure 2:** Preoperative axial and coronal noncontrasted computed tomographic (CT) scan demonstrating a mass in the left temporal lobe is associated with intraparenchymal hemorrhage extending posteriorly and superiorly. (a) Axial CT images showing a significant mass effect, including the displacement of the left ventricle and midline shift (b) Coronal CT images indicated that the tumor had no adjacent bony lesions.

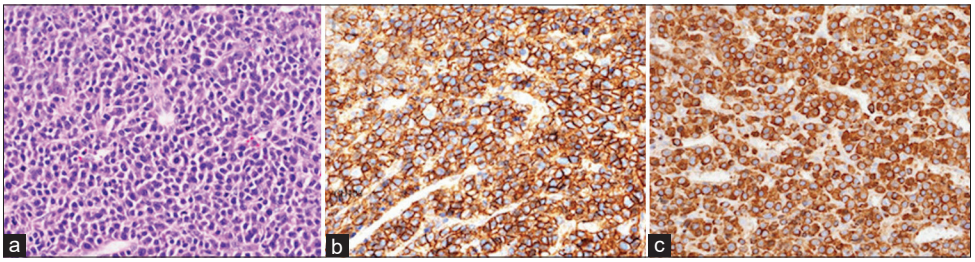


**Figure 3:** Histopathological and immunohistochemical examinations of the surgical specimen (a) A histopathologic study with hematoxylin-eosin staining shows diffuse proliferation of plasmacytoid cells, with clumped nuclear chromatin and eccentric cytoplasm (b) Immunohistochemical examination demonstrating the immunostaining of CD138, a marker of plasma cells, indicating the proliferation of CD138-positive cells (c) Immunohistochemical examination revealed that the plasma cells were monoclonal staining with lambda.

without any observable neurological deficit. She remained in a CR state for 6 months after surgery.

## DISCUSSION

We here report a case of intracranial MM arising from the dura mater without bone involvement. This rare intracranial mass exhibited rapid growth in a few months, followed by a lethal intracranial hemorrhage from the tumor itself. The urgent operation, hematoma evacuation, and tumor removal allowed the patient to recover from a severe neurological sequela.

Among the intracranial involvement in patients with MM, dural involvement usually occurs due to the direct extension of a plasmacytoma of the skull.[1,7] In contrast, primary dural involvement without skull lesion, called extramedullary plasmacytoma, is rare and can cause diagnostic difficulties by mimicking the more common lesions, particularly the meningiomas.[4] In a recent review of intracranial involvement of MM,[7,12] the incidence of central nervous system involvement in previously diagnosed MM patients appears to be on the rise. It is hypothesized that novel chemotherapeutic agents (such as thalidomide, lenalidomide, and bortezomib) may alter the natural history of the disease by changing the tumor microenvironment.[5] Other considerable factors for the increased incidence include the greater sensitivity of modern imaging and the improved survival rate of patients with MM treated by novel monoclonal antibodies for relapsed or refractory MM.[11] In line with these hypotheses, the present case developed central nervous system problems after several cycles of treatment with novel chemotherapeutic agents (lenalidomide and bortezomib). Hematogenous dissemination might have resulted in the formation of primary dural plasmacytoma after chemotherapy. Although it was difficult to definitively diagnose the primary dural plasmacytoma at that time, the screening MRI [Figure 1a] incidentally confirmed the presence of intracranial extra-axial mass. Since the mass grew rapidly over the 3 months, we were able to diagnose the mass as plasmacytoma before the histopathological examination, as the clinical course was atypical as meningioma [Figure 1b].

Hemorrhage from intracranial plasmacytoma is a rare and severe presentation. There have only been a few case reports, as summarized in [Table 1].[3,6,13] Harper *et al*.[6] reported the first case of intracranial hemorrhagic plasmacytoma. A 71-year-old woman with a history of MM developed a lethal acute subdural hematoma from intracranial plasmacytoma, which arose from the greater wing of the sphenoid bone. Despite immediate removal of the hematoma and tumor, the patient remained comatose and died 5 days later. Reddy *et al*.[13] reported a patient with MM with fatal intracerebral and subdural hemorrhage from a plasmacytoma located in the parenchyma of the temporal lobe. In this case, a hematoma evacuation with the right temporal lobectomy was performed but the patient died 2 days later. Similar to

**Table 1:** Past reports of hemorrhage from intracranial plasmacytoma in patient of multiple myeloma.

| Author (year) | Age, sex | Tumor location | Tumor origin | Type of hemorrhage | Postsurgical therapy | Follow-up period | Outcomes |
|---|---|---|---|---|---|---|---|
| Harper *et al*., 1982 | 71, F | Lt. middle fossa (sphenoid bone) | Skull | SDH | None | 5 days | Death |
| Reddy *et al*., 2007 | 44, M | Rt. middle fossa (temporal lobe) | Parenchyma | ICH+SDH | None | 2 days | Death |
| Crowley *et al*., 2010 | 54, M | Lt. middle fossa (dura of sphenoid ridge) | Dura mater | ICH | Chemotherapy + radiation | 4 years | CR |
| Present case | 71, F | Lt. middle fossa (dura of sphenoid ridge) | Dura mater | ICH | Chemotherapy + radiation | 6 months | CR |

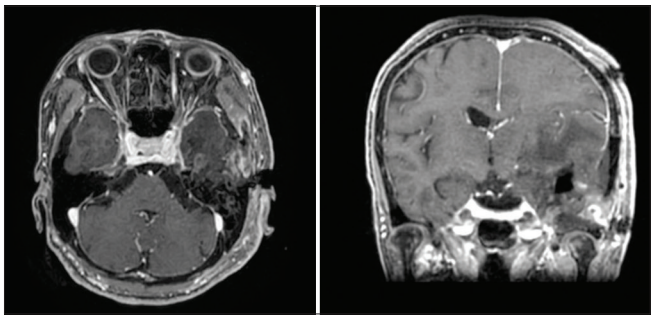

**Figure 4:** Postoperative axial and coronal contrasted T1-weighted magnetic resonance imaging showing the temporal mass and associated hematoma was removed.

our case, Crowley *et al*.[3] reported a patient with intracranial plasmacytoma without an adjacent bone lesion. The patient developed a massive intracerebral hemorrhage from the tumor located in the middle fossa. In their case, emergent surgery and subsequent focal irradiation and chemotherapy resulted in long-term survival without recurrence of MM. As shown in [Table 1], the mortality from a hemorrhage of intracranial plasmacytoma is relatively high. Two of the past three reported patients died within several days after a hemorrhage although emergent surgery was performed. The high mortality, coagulability impairment associated with MM itself, and the side effects of prior chemotherapy and radiation therapy may be attributed to the massive hematoma formation. In addition, the location of the predilection site for intracranial plasmacytoma may also be a reason for poor prognosis. In all cases, including ours, plasmacytoma was mainly located in the middle fossa (1 sphenoid bone, 1 intraparenchyma of the temporal lobe, and 1 dura of temporal base). Hematoma expansion near the lower temporal lobe directly leads to uncus herniation, which promotes the compression of the brain stem and may there exacerbate its damage.

The involvement of the central nervous system in MM is lethal, with a survival time of 6 months.[2] There currently is no consensus on the treatment for patients with a central nervous system involvement.[9] The optimal treatment may include intrathecal chemotherapy and systemic chemotherapy that cross the blood–brain barrier, combined with or without radiotherapy.[8,9] In addition, a biopsy or tumor resection followed by radiotherapy is recommended for skull base intracranial plasmacytoma.[10] In the present case, intracranial plasmacytoma grew rapidly despite the administration of systemic chemotherapy with daratumumab, bortezomib, and dexamethasone. Immediately after tumor expansion during the 3 months, massive hemorrhage from the tumor developed. This indicates that close follow-up by neuroimaging studies is essential in cases of intracranial plasmacytoma in MM patients. Furthermore, early intervention with surgical resection or radiotherapy should be considered.

## CONCLUSION

There is currently no established treatment for intracranial MM. At present, tailored combined therapy with chemotherapy, radiotherapy, and surgical resection is chosen as appropriate for each patient. In our case, intracranial plasmacytoma secondary to MM grew rapidly, resulting in severe intracerebral hemorrhage. Since the hemorrhagic manifestation of intracranial plasmacytoma tends to lead to poor prognosis, it is important to recognize the possibility of hemorrhage from tumor in actual clinical settings, as shown in the presented case. Close follow-up by neuroimaging studies and early intervention with surgical resection or radiotherapy is recommended in such case.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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