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Case Report

Multiple myeloma extramedullary relapse at the sellar and suprasellar region after autologous stem cell transplantation

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ABSTRACT

Background: The effectiveness of autologous stem cell transplantation (ASCT) in preventing the development of central nervous system (CNS) plasmacytomas in multiple myeloma (MM) patients is not well understood. An ASCT patient who developed CNS extramedullary (EM) lesions is presented. The literature was reviewed for similar cases in which the transplant did not prevent the development of CNS lesions.

Case Description: A 42-year-old female was evaluated after complaining of a sudden severe headache and complete vision loss. Two years before, she was diagnosed with MM and treated with systemic chemotherapy and an ASCT. The patient was in remission; however, a new brain magnetic resonance imaging showed a sellar and suprasellar mass. Additional smaller lesions were identified at the parietal convexity and the splenium. Due to the history of MM and evidence of multiple intracranial lesions, it was suspected that the lesions were secondary to EM disseminated disease. Due to the sudden loss of vision, the patient underwent a right frontotemporal craniotomy with subtotal sellar/suprasellar tumor resection to decompress the optic nerves. Histopathological examination of the lesion confirmed an immunoglobulin A (IgA) EM sellar and suprasellar plasmacytoma.

Conclusion: In the majority of MM patients with CNS involvement, ASCT did not prevent the development of EM sellar plasmacytomas. The IgA subtype is associated with more aggressive disease biology for CNS relapses.

Keywords: Extramedullary, Multiple myeloma, Plasmacytoma, Relapse, Sella, Stem cell, Suprasellar, Transplantation

INTRODUCTION

Multiple myeloma (MM) is a plasma cell proliferative disorder displaying an abnormal increase of monoclonal immunoglobulins. The overall 5-year survival rate ranges from 40% to 82%.[23] High-dose chemotherapy with autologous stem cell transplantation (ASCT) is the mainstay treatment.[4,6,7,29,34] ASCT significantly improves the remission rate and minimal residual disease of MM patients.[23] In patients with MM, deposits of plasma cells can cluster together to form tumors (plasmacytomas) in several body areas. The most frequent mechanism causing soft-tissue plasmacytomas is direct growth from skeletal tumors by disrupting the cortical bone.[27] Other mechanisms for their formation include hematogenous spread or clonal heterogeneity in which a new clone population resistant to previous treatments develops.[5,27] Plasmacytomas may

require neurosurgical management if they involve the skull, brain, or spine. Extramedullary (EM) plasmacytomas outside the bone marrow are highly radiosensitive, with 80–100% local control rates.[10,18] About 13% of MM patients develop EM plasmacytomas, occurring in 7% of newly diagnosed cases or 8% later in the disease.[31]

Central nervous system (CNS) involvement of MM is rare, occurring in 0.7–1% of the patients.[1,22,24,28] It can emerge in newly diagnosed, relapsed, or refractory MM patients; however, it is more frequent in relapsed cases and younger patients.[1,16,21,28] The median time from MM diagnosis to CNS involvement is approximately two years.[16] It has a poor prognosis, with <7 months of overall survival from the onset of CNS involvement, despite receiving systemic chemotherapy, radiotherapy, and intrathecal injections.[1,5,16,28] Abdallah *et al*. showed that patients who received only systemic chemotherapy when the primary MM diagnosis was established had a significantly shorter 8-month median time to CNS myeloma diagnosis compared to those patients who received systemic chemotherapy and ASCT, with a median time of 32 months.[1] The study by Liu *et al*. suggested that for MM patients with CNS involvement, ASCT can improve the prognosis.[21] However, in most studies, the benefit of ASCT in patients with CNS disease appears to be limited.[1,28] The effectiveness of ASCT in preventing the development of CNS plasmacytomas is not well understood. This report presented an MM patient with an ASCT who later developed CNS EM lesions. The literature was reviewed for similar cases in which the transplant did not prevent the development of CNS lesions.

CASE REPORT

A 42-year-old female was evaluated at the emergency department (ED) after experiencing a severe headache and sudden complete vision loss. Two years before, she was diagnosed with MM and treated with systemic chemotherapy and an ASCT. She was in remission; however, eight months before her current evaluation, a right intracranial occipital dural base lesion was identified, for which she received fractionated radiotherapy. Three months later, brain magnetic resonance imaging (MRI) showed a significant reduction in the lesion size. During the two months before her evaluation at the ED, she noticed a slow but progressive visual acuity loss; however, she did not seek medical attention until she developed complete vision loss. A new brain MRI at the ED demonstrated a sellar and suprasellar mass measuring 1.9 cm anteroposterior × 2.1 cm transverse × 3.2 cm craniocaudal, showing avid contrast enhancement causing significant compression on the optic chiasm superiorly [Figure 1]. The lesion had an invasion of the right cavernous sinus and extended inferiorly into the right sphenoid sinus and anteriorly into the ethmoidal air cells. A 2.4 cm parietal dural-based lesion and a 1.5 cm lesion at the splenium of the corpus callosum were also identified.

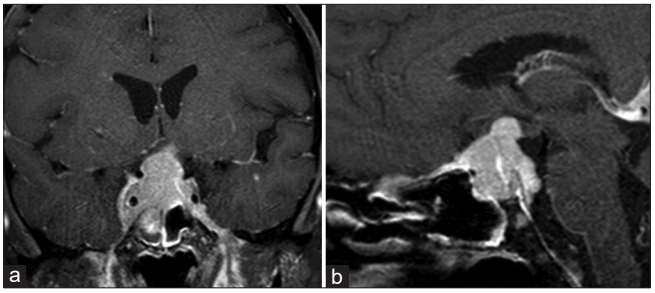

Figure 1: Brain magnetic resonance imaging with gadolinium T1-weighted (a) coronal and (b) sagittal images showing a large sellar/suprasellar mass with avid contrast enhancement with invasion of the right cavernous sinus and encasement of the right carotid artery.

On physical examination, the patient had bilateral optic nerve swelling with no light perception. Bilateral six-nerve paresis was present. Motor and sensory examinations were normal. Due to the history of MM and evidence of multiple intracranial lesions, it was suspected that the lesions were secondary to her disseminated disease. Due to the sudden loss of vision, the patient underwent a right frontotemporal craniotomy with subtotal sellar/suprasellar tumor resection to decompress the optic nerves. The histopathological examination of the lesion was compatible with an immunoglobulin A (IgA) plasma cell neoplasia, CD19 positive, and negative for kappa or lambda light chain. She died three months later from her disseminated disease without receiving additional chemotherapy or radiotherapy.

DISCUSSION

Plasmacytomas are tumors that should be considered in the differential diagnosis for lesions involving the sella even in the absence of known MM, especially when cranial nerve paresis is present.[10,18] However, these patients should be rigorously monitored for progression to MM.[18] DiDomenico *et al*. showed that in 45% of the patients with a sellar plasmacytoma, the initial plasmacytoma diagnosis led to the diagnosis of MM.[10] For patients with known MM and parasellar masses, the treatment plan should include a combination of induction therapy, immunomodulatory drugs, radiotherapy, and systemic therapy.[10,18,28] In the review of sellar and clival plasmacytomas by Lee *et al*., 67% of the patients were alive at a median follow-up of 12 months.[18] However, 18% of them develop parasellar recurrences.

Relapse of MM after ASCT usually presents with a recurrence of plasma cells in the marrow.[22] Some authors have reported that the presentation of localized EM plasmacytoma after ASCT in MM patients is very unusual.[11,26] However, in the study by Zeiser *et al*., the relapse rate after ASCT was 63%.[34]

Alegre *et al*. reported that 52% of MM patients relapsed or progressed after ASCT.[2] In their study, among the patients with relapse, 14% presented EM presentations with multiple plasmacytomas as the predominant symptom, carrying a significantly shorter median overall survival.[2] Yue *et al*. showed that among newly diagnosed MM patients where ASCT was used, 57% had disease relapse during follow-up, including 24% of patients with EM relapse.[33] EM relapse of MM is often resistant to existing treatments and has an extremely poor prognosis.[8,33] Survival analysis showed that EM relapse patients had significantly worse median overall survival than patients with relapse but without EM involvement.[33] Plasmacytoma occurrence at relapse in patients with upfront ASCT is significantly associated with a poor prognosis.[8]

CNS involvement following ASCT has been described in very few MM patients. Isolated CNS relapse after ASCT is extremely rare, with only 14 cases reported.[20,22] Among the isolated CNS relapse cases, 43% had parenchymal lesions.[3,5,22,25,29,32] Despite ASCT, the prognosis after CNS relapse is extremely poor, with a very short median survival.[14,20,22,25,29] For MM patients who are ASCT candidates, IgA MM has been recognized as a risk factor that adversely affects survival.[9,12] Li *et al*. noticed that more patients with EM plasmacytoma at the time of MM diagnosis carried the IgA subtype than those without plasmacytoma.[19] Seftel *et al*. showed that IgA MM patients have a significant risk of CNS relapse after ASCT.[29] In the study of MM patients with CNS involvement by Jurczyszyn *et al*., 27% of them had the IgA subtype.[16] Among the 14 patients with isolated CNS relapse after ASCT, 43% had the IgA subtype. The IgA subtype was present in 50% of the patients with parenchymal CNS lesions. These findings suggest that the IgA subtype is associated with more aggressive disease biology for CNS relapses.

This report highlighted an MM patient with an EM lesion at the sellar/suprasellar area that developed two years after receiving an ASCT. After reviewing the literature, four case reports of sellar/suprasellar plasma cell tumors were identified in which the patient received a stem cell transplant during the disease process.[13,15,17,30] The case presented by Khan *et al*. is similar to that reported herein, where the lesion developed after the patient received the ASCT.[17] However, the patients reported by Fukai *et al*. and Sinnott *et al*. underwent stem cell transplants after they were operated on for the plasmacytic lesion in the Sella.[13,30] For both cases, the MM diagnosis was established after the seller plasmacytoma was operated on.[13,30] The patient presented by Jiang *et al*. did not undergo surgery for the sellar lesion as a diagnosis of MM was made a few days before the scheduled surgery, being treated with radiotherapy, chemotherapy, and ASCT with complete remission.[15] The patients presented by Fukai *et al*., Khan *et al*., and Jiang *et al*. received a peripheral ASCT.[13,15,17] However, the patient presented by Sinnott *et al*. received a bone marrow ASCT.[30] Interestingly, the IgA subtype was not identified in any of the four sellar cases, with 75% of them having light chain MM. Similar to all 14 patients with isolated CNS relapse after ASCT, in the present case, the transplant did not prevent the development of an EM sellar plasmacytoma.

CONCLUSION

In the majority of patients with CNS MM involvement, ASCT did not prevent the development of EM sellar plasmacytomas. The IgA subtype is associated with more aggressive disease biology for CNS relapses.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent is not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author confirms that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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