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CASE REPORT

Meningeal involvement in multiple myeloma

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Key Clinical Message

A patient with multiple myeloma with a mass in the nasopharyngeal was diagnosed. He received melphalan autograft and radiotherapy, and obtained complete remission. He relapsed 3 months later, with meningeal involvement and without systemic relapse. He received intrathecal and systemic chemotherapy, without neurological improvement and died 4 weeks after relapse.

Keywords

Meningeal involvement, multiple myeloma.

Introduction

The multiple myeloma is a hematological malignancy characterized by the development of a clone of plasma tumor invading hematopoietic marrow. In its usual form, it involves bone marrow plasma cell infiltration, a monoclonal immunoglobulin in blood and/or urine, and bone involvement.

Marrow is not the only site of plasma cell proliferation. Extra bone infiltration is common at autopsy, and most often clinically silent. Sometimes the extraosseous plasmacytoma is isolated and all organs can be affected.

Meningeal localization of myeloma is a rare presentation and poor prognosis [1–4]. A high myeloma burden, stage III disease, high labeling index, circulating plasma cells in the peripheral blood, and IgA or IgD M protein were the most frequent clinical features of these patients.

We report a case of a patient who developed meningeal involvement 3 months after achieving complete remission after autologous stem cell through multiple myeloma revealed by a nasopharyngeal mass and discuss the presumed mechanism of meningeal involvement. We also speculate that meningeal involvement may occur also in cases with a low myeloma mass and with a disease apparently well controlled by high-dose therapy [4, 5], but who had initially an infiltration from contiguous structures when lytic lesions erode skull and dura mater [6].

Case Report

We report a case of a 41-year-old man who was admitted in our institution for multiple IgG kappa myeloma ISS3 score, in a context of general alteration with 9 kg weight loss, dysphagia to solids, a left laryngeal immobility. The physical examination found a large mass in the nasopharyngeal.

The patient complains of back pain mixed pace without motor or sensory deficit. Brain magnetic resonance imaging (MRI) rating extensive homogeneous cell mass developed at the expense of nasopharyngeal extending into the oropharynx, invading the soft parts of the cranio-spinal shower hinge, part of the skull base, the predominant left temporal fossae, large sphenoid wings being crossed by the tumor process (Fig. 1). The microscopic examination of the tumor's biopsy showed a fragment consisting of nasopharyngeal cohesive sheets of small cells overwritten. Immunohistochemistry noted of CD145+ cells, CD20−, CD3−, CD138+, monotypic lambda with an estimated of 90% proliferation index. MRI of the spine found epiduritis T1 and T5–T6. The PET scanner showed

a large mass developed at the expense of nasopharyngeal extending the skull base and oropharynx. It was no other extranodal localization. The skeletal radiographs showed multiple spinal lesions.

The complete blood count on presentation demonstrated a white blood cell count of 8.1 G/L (segmented neutrophils 61%; band neutrophils 0%; lymphocytes 28%; monocytes 9%; eosinophils 1%; basophils 1%) with hemoglobin level of 9.8 g/dL, and platelets levels of 283 G/L. The electrophoresis of proteins founded monoclonal gammopathy IgG kappa of 44.6 G/L. Serum electrolytes showed hypercalcemia in 3 mmol/L. Béta 2 microglobulin was increased to 5.7 mg/L.

Bone marrow aspiration indicated marrow involvement due to the presence of 40% of plasma cells. Cytogenetic analysis showed a 46, XY karyotype in the bone marrow. Fluorescence in situ hybridization showed 17p deletion. Lumbar puncture including electrophoresis of proteins of the cerebrospinal fluid (CSF) was normal. The patient was treated with VCD regimen, melphalan autograft, radiotherapy of nasopharyngeal and spine. A complete remission has been obtained for 3 months. Autograft was complicated by (1) pulmonary infection, (2) a significant mucositis grade 4 with major malnutrition, and (3) weight loss of 10 kg. Consolidation initially provided by VCD could not be performed.

The patient was readmitted to the emergency department with intensive headache, dysarthria, unsteady gait, and limb weakness, without nuchal rigidity or fever.

Investigations showed negativity of IgG paraprotein and a normal bone marrow. A brain MRI demonstrated a contrast-enhanced dural multinodular thickening next to the right parietal lobe, with focal extensions to the subarachnoid space and vasogenic edema of the underlying brain parenchyma (Fig. 2). The adjacent inner table and diploe of the skull were not involved. A bilateral parenchymal enhancement of the superior cerebellar peduncle was also observed.

A lumbar puncture was performed and showed a low level of glucose (0.4 mmol/L), a high protein level (2.1 g/L), and a high white cell count composed almost exclusively by plasmas cells (Fig. 3), all with neoplastic phenotype CD138 positive.

He received intrathecal administration of 12 mg of methotrexate, 40 mg of cytarabine, and 40 mg of prednisolone, three times per week, and PAD regimen (bortezomib–adriamycine–dexamethasone). There was no neurological improvement with the appearance of confounding signs. He developed a generalized seizure and fell into a coma. He died 4 weeks after relapse.

Discussion

Meningeal localization of myeloma is a rare presentation and poor prognosis. About 65 cases were reported in the literature [1–3] and reviewed by Peterson et al. [4].

The largest series including 14 patients was reported by Chamberlain et al. [1]. A high myeloma burden, stage III disease, high labeling index, circulating plasma cells in the peripheral blood, and IgA or IgD M protein were the most frequent clinical features of these patients.

A hematogenous spread can be hypothesized in plasma cell leukemia, and an infiltration from contiguous

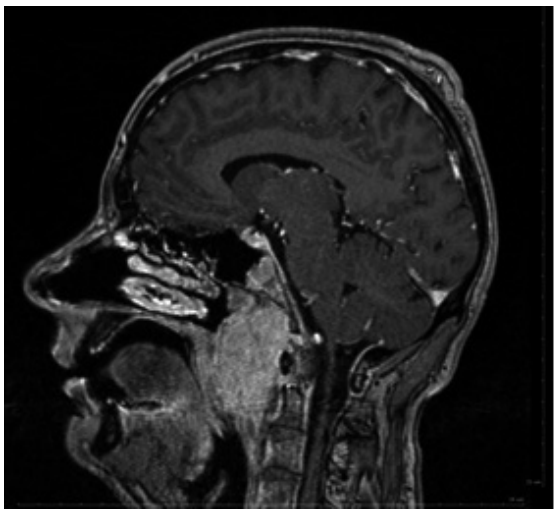

Figure 1. Sagittal view of a 3D-T1-weighted MRI with gadolinium shows extensive homogeneous cell mass invading the soft parts of the cranio-spinal shower hinge, part of the skull base, the predominant left temporal fossae, large sphenoid wings being crossed by the tumor process.

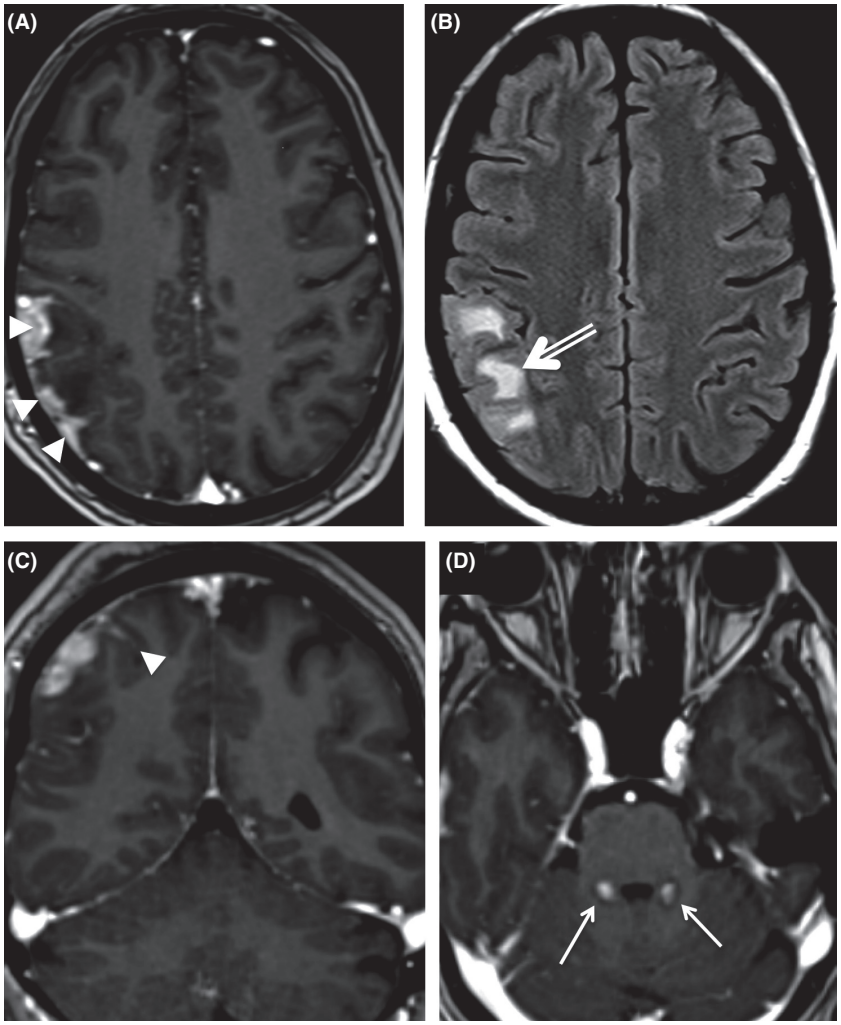

Figure 2. Axial view of a 3D T1-weighted MRI with gadolinium (A) and FLAIR (B) shows an enhanced dural thickening (arrowheads) with a parenchymal edema of the underlying cortex and subcortical white matter (double arrow). Coronal view (C) also reveals an involvement of the subarachnoid space (arrowhead). An axial view of the brain stem shows bilateral parenchymal enhancement of the cerebellar peduncles (arrows).

structures is possible when lytic lesions erode skull and dura mater [6].

Otherwise, a few patients with a CNS relapse had circulating plasma cells (PC) at the first recognition of multiple myeloma (MM): in these patients, PC might have infiltrated the meninges at diagnosis and might have grown during the course of the disease since most of the drugs used in MM treatment and even high-dose melphalan cannot overcome the blood–brain barrier.

This complication appeared in the majority of the patients as a terminal event [7], but it was also reported as a presenting feature of MM [5]. Moreover, a few cases of meningeal involvement were reported in patients who had been successfully treated with high-dose therapy and stem cell rescue and had no overt medullary plasmacytosis [4, 5].

Four patients were described: all presented meningeal involvement a few months (2 or 3) after an autologous stem cell transplant (ASCT) with the attainment of a complete remission and no evidence of residual disease in the bone marrow. The conditioning regimen was high-dose melphalan in three cases and total body irradiation (TBI) plus melphalan in the fourth.

These data confirm that meningeal involvement may occur also in cases with a low myeloma mass and with a disease apparently well controlled by high-dose therapy.

Our report describes a patient with meningeal involvement who had not detectable disease after VCD regimen, melphalan autograft, radiotherapy of nasopharyngeal and spine but who had initially a nasopharyngeal mass invading the base of the skull.

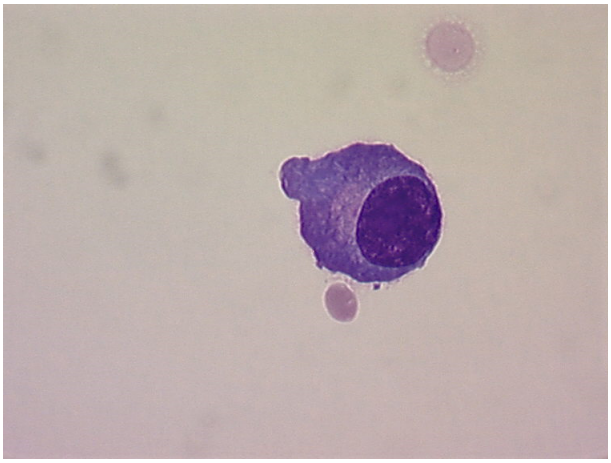

Figure 3. Plasma cells in the cerebrospinal fluid May Grunwald Giemsa (MGG) × 100.

Lumbar puncture is essential for the diagnosis. Although PC can be seen in the CSF in other conditions, both infectious and noninfectious [8], the presence of PC in the CSF of a patient with MM supports the diagnosis of myelomatous meningitis. The definitive proof is the definition of monoclonality of the PC obtained by immunophenotyping or the immunoelectrophoresis of CSF showing an M component [9].

The prognosis of meningeal and cerebral involvement of MM is very poor. On the basis of the 65 cases of meningeal myelomatosis reported mainly as case reports in the literature, with available information about survival, the median overall survival (Kaplan–Meyer) from the time of the diagnosis of the meningitis was 6 weeks [4].

IT chemotherapy [2, 4, 5, 7] and/or craniospinal irradiation [1, 4] were the most common modalities of treatment. The IT given included methotrexate, cytarabine, thiotepa, and hydrocortisone and in some cases it was associated with systemic chemotherapy.

In conclusion, the occurrence of neurological symptoms in a patient with myeloma requires an accurate evaluation with MR and lumbar puncture to detect a possible meningeal or cerebral involvement, when metabolic factors (hypercalcemia, uremia), hyperviscosity, or medullary compression can be excluded. Herein, we confirmed that this hypothesis has to be considered also in patients with a disease apparently responsive to standard or high- dose therapy. There is no consensus toward the modalities of treatment; in our experience, IT chemotherapy and systemic chemotherapy did not have the expected result.

Conflict of Interest

None declared.

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