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Imaging of extraosseous intracranial and intraspinal multiple myeloma, including central nervous system involvement☆

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ABSTRACT

Involvement of the central nervous system by multiple myeloma is rare and has a very poor prognosis. Magnetic resonance imaging of the head and spine plays an important role in diagnosing central nervous system involvement with multiple myeloma. We retrospectively analyzed the imaging features of pathology-proven extraosseous intracranial and intraspinal multiple myeloma from 2002 to 2013. The most common imaging manifestations were extraaxial nonosseous spinal lesions, cranial nerve involvement, and intracranial extraaxial nonosseous lesions. Different sites in the central nervous system may be affected by multiple myeloma, often simultaneously, producing a variety of imaging appearances.

1. Introduction

The central nervous system (CNS) is affected by multiple myeloma in approximately 1% of all cases, and such involvement is a dire prognostic sign [1–10]. Intracranial myeloma constitutes less than 1% of intracranial tumors and can occur as a solitary (primary) plasmacytoma in addition to being a manifestation of systemic multiple myeloma [11]. Central nervous system myeloma takes many forms, including localized intraparenchymal or dural-based lesions and CNS myelomatosis involving leptomeninges or cranial nerves [1,3,12]. It can manifest as a combination of different sites of lesions such as intraparenchymal and dural based [4]. The central nervous system may be involved at all stages of multiple myeloma by direct invasion from contiguous bone lesions or by hematogenous spread with parenchymal infiltration resulting from CNS myelomatosis or dural-based lesions [1,2,7,12,13]. Autopsy studies in patients with leptomeningeal myeloma demonstrated that circulating myeloma cells can infiltrate arachnoid veins diffusely, spilling over into the cerebrospinal fluid (CSF) [13].

Clinical manifestations are nonspecific and may include headache; nausea and vomiting; paraparesis; cranial nerve palsies; mental status changes; and, rarely, seizures [4,5,9,12,14,15]. When the patient's neurological symptoms are not better explained by hypercalcemia, hyperviscosity, drug neurotoxicity, or spinal cord compression, imaging and direct analysis of CSF become necessary [4,9,10,15]. Of all imaging studies, magnetic resonance imaging (MRI) is the most sensitive for detecting leptomeningeal disease and cranial nerve infiltration [7,8].

Typical imaging findings of dural plasmacytoma or mass-like intracranial myeloma include iso- to hyperdensity on computed tomography (CT), T1 iso- to hyperintensity and marked T2 hypointensity on MRI, and high vascularity that may be documented on intraarterial digital subtraction angiography [12]. Restricted diffusion and elevated perfusion parameters may also be present [12]. Intracranial lesions may have perilesional edema, focal calcifications, or intralesional hemorrhage [4]. Differential diagnosis includes meningioma, sarcoma, lymphoma, metastatic carcinoma, plasma cell granuloma, infectious meningitis, and leptomeningeal carcinomatosis [4,12]. Magnetic resonance imaging findings are often nonspecific, and differentiation of leptomeningeal myelomatosis from infectious meningitis requires clinical and laboratory correlation [8,12]. Final diagnosis is made by direct biopsy of localized masses and/or by detection of monoclonal plasma cells in the CSF [1,4,10,15].

The median interval from diagnosis of multiple myeloma to diagnosis of CNS myeloma is 6–18 months, although, rarely, CNS involvement may be the initial presentation of multiple myeloma [5,6,9,15]. While CNS myeloma is usually associated with a higher tumor burden and circulating plasma cells, a significant minority of patients with CNS myeloma appear to be in clinical remission at the time of lesion detection [4,10,15]. The development of CNS myeloma in patients who are otherwise in remission may reflect the poor penetration of the blood brain barrier by most drugs used to treat multiple myeloma [1]. A strong association between leptomeningeal myelomatosis and biological markers of aggressive multiple myeloma has been found [2,5,6,9,16].

☆ Conflicts of interest: Thomas Naidich: royalties from Elsevier. Katya Shpilberg, Steven Esses, Michael Sacher, Mary Fowkes, Ajai Chari: none.

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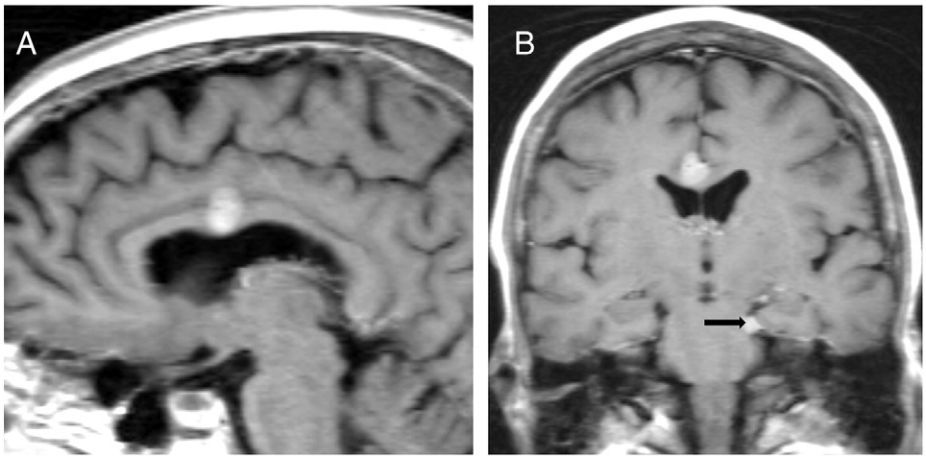

Fig. 1. Patient 2. A 63-year-old woman. (A) Sagittal T1-weighted (T1W) postcontrast MRI demonstrates an enhancing mass within the body of the corpus callosum. (B) Coronal T1W postcontrast MRI shows an enhancing nodule in the left perimesencephalic cistern (arrow) in addition to the callosal mass.

Predictors of poor survival include cytogenetic abnormalities (especially translocations and deletions of chromosome 13 and deletions of 17p13.1, which affect the p53 tumor-suppressor gene), plasmablastic morphology, high lactate dehydrogenase levels, and other concurrent extramedullary manifestations [2,5,6,9,16].

Treatment of CNS myeloma usually consists of aggressive systemic and intrathecal chemotherapy, and autologous stem cell transplantation [1,4,6,9]. Agents such as thalidomide and lenalidomide, which penetrate the blood brain barrier, as well as a novel drug bortezomib with immunomodulatory properties are showing promise [17,18]. Cranial and spinal irradiation may also aid survival [1,4,9,11]. Despite the available therapies, patients with CNS myeloma have a poor prognosis, with a median survival ranging from 1 month for those who show no initial response to therapy to up to 5 months for those who have at least an initial response to therapy [3].

The purpose of this study is to investigate the imaging manifestations of extraosseous intracranial and intraspinal multiple myeloma, including involvement of the central nervous system.

2. Materials and methods

Following institutional review board approval, we obtained a list of 33 multiple myeloma patients with confirmed or strongly suspected intracranial and intraspinal involvement from our department of oncology. These patients were followed at our institution between 2002 and 2013. We searched these patients' electronic medical records and contacted the department of pathology for their CSF and biopsy results, and searched picture archiving and communication system (PACS) for their neuroimaging studies. All patients who had CSF positive for multiple myeloma and had neuroimaging studies available for our review were included in this study. Patients without positive CSF were included only if they had biopsy-proven intracranial or intraspinal myelomatous lesions that were not primarily osseous. Ten patients were excluded from analysis because CSF or biopsy results of the CNS lesions were negative or unavailable. Of these, five had biopsy-proven primarily osseous myelomatous lesions with minor secondary involvement of or mass effect upon the brain or spine.

The final study group of 23 patients included 15 males (65%) and 8 females (35%) ranging in age from 45 to 76 years (median age, 58 years). Their symptoms included altered mental status/ confusion, lethargy, seizures, diplopia, facial numbness, back pain, extremity weakness, and bowel/ bladder incontinence. All of the included patients had an established diagnosis of multiple myeloma prior to neuroimaging. The specific Durie–Salmon stage was known in seven patients, one of whom was stage IA, two were stage IIIA, three were stage IIIB, and one was stage III (unspecified).

The neuroimaging studies of these 23 patients were classified into 8 different patterns of involvement: intraparenchymal brain lesions (Fig. 1), intracranial extraaxial nonosseous lesions (Figs. 1 and 2), intracranial leptomeningeal enhancement (Fig. 3), cranial nerve involvement (Fig. 4), intramedullary spinal lesions (Fig. 5), extraaxial nonosseous spinal lesions (Fig. 6), spinal leptomeningeal enhancement (Fig. 7), and negative imaging studies. The lesions were also classified as "pure CNS infiltration" (or intraparenchymal lesions) versus "non-CNS intracranial and intraspinal lesions". The prevalence of each pattern was calculated.

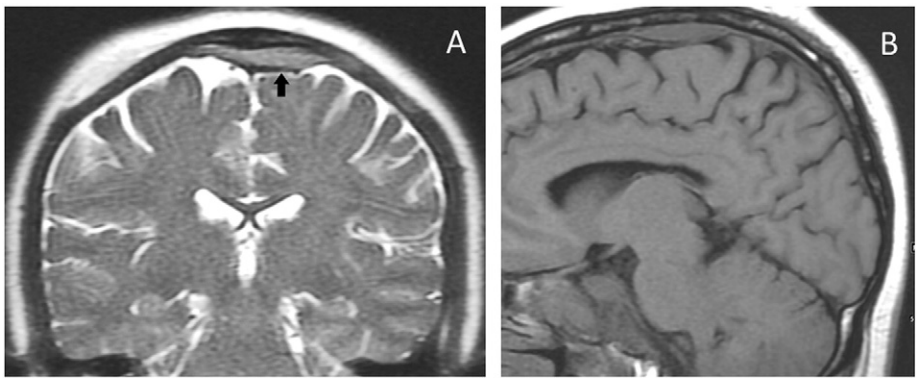

Fig. 2. Patient 8. A 51-year-old man. Coronal T2-weighted (T2W) (A) and sagittal T1W (B) MR images demonstrate an intracranial nonosseous subdural mass (arrow) that is T2 isointense to mildly hyperintense and T1 isointense to white matter.