

Pearls & Oysters: Plasma cell meningitis

An uncommon complication of multiple myeloma

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PEARLS

- Meningeal involvement in multiple myeloma is rare and occurs in fewer than about 1% percent of all cases.
- The presence of plasma cells in the CSF is not specific to multiple myeloma and can occur in some infections, especially in immunocompromised patients.
- The most common manifestations include signs of raised intracranial pressure, multiple cranial neuropathies, radiculopathy, and back pain. Seizures are uncommon.
- Clinical examination and imaging may be falsely negative. Large volume (10 mL) of CSF sampling with flow cytometry analysis is the key to diagnosis and may be repeated if necessary. Samples must be processed immediately to ensure cellular viability.

OY-STERS

- Plasma cell meningitis should be sought as a cause of neurologic symptoms in patients with multiple myeloma once other potential complications such as infections, metabolic derangements, hyperviscosity syndromes, peripheral neuropathies (infiltrative or amyloid-related), and mass lesions (plasmacytomas) have been assessed.
- Patients who receive treatment for recurrence of systemic disease may be at a higher risk for developing meningeal disease as most regimens do not have good CNS penetration.
- Plasma cell meningitis is treated with intrathecal chemotherapy with or without radiation. It carries a poor prognosis but early initiation of therapy can lead to clinical response though benefits may not be long-lasting.

We report a case of plasma cell meningitis (PCM) presenting as a first-time seizure.

CASE REPORT Our patient was a 60-year-old man with a medical history of multiple myeloma that had been diagnosed 3 years prior to this presentation. He

had completed chemotherapy then and also received an autologous peripheral blood stem cell transplantation. He had a recurrence about 6 months ago for which he received 2 cycles of chemotherapy with dexamethasone, cyclophosphamide, etoposide, and cisplatin. His last dose of chemotherapy was 4 months ago. He subsequently discontinued follow-up with his oncologist because he had decided to change providers at the time and therefore could not complete his chemotherapy regimen. He now presented to our hospital with a single first-time generalized tonic-clonic seizure with full return to baseline; he also had a mild generalized headache that had started on the morning of presentation. He did not complain of any other neurologic or systemic symptoms. His neurologic examination was entirely nonfocal, including normal funduscopic examination and the absence of meningeal signs. Hematologic evaluation was significant for normocytic anemia and thrombocytopenia, metabolic panel showed mild hypocalcemia, other initial workup including urine toxicology was unrevealing. No lymphopenia or neutropenia was noted. His initial CT head showed multiple lytic lesions in the skull but brain was unremarkable. He had a brain MRI (figure) with contrast that showed patchy areas of leptomeningeal enhancement and subsequent lumbar puncture with CSF analysis showed 258 cells/mm³ with a lymphocytic predominance (63%), protein 124 mg/dL, glucose 69 mg/dL, and CSF electrophoresis showed elevated immunoglobulin G (17%) with a single monoclonal band. CSF cytology showed sheets of immature blasts cells. Flow cytometry confirmed these to be CD38-positive clonal plasma cells exhibiting a single lambda light chain. Further testing for herpes simplex (1 and 2), West Nile virus, adenovirus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus (EBV), human herpesvirus 6, enterovirus, Eastern equine encephalitis, and Saint Louis encephalitis were negative. Fungal and *Mycobacterial* cultures were also negative. He was diagnosed with plasma cell meningitis and intrathecal chemotherapy with craniospinal radiation was planned; however, his disease rapidly progressed, and he died within 2 weeks of his diagnosis.

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Figure MRI in plasma cell meningitis



Gadolinium-enhanced MRI shows leptomeningeal enhancement in our patient with a relapse of multiple myeloma that is indicative of plasma cell meningitis. Presence of monoclonal plasma cells in the CSF confirmed the diagnosis of plasma cell meningitis.

DISCUSSION The terms PCM, myelomatous meningitis (MM), and CNS myelomatosis have been used interchangeably. They refer to a type of leptomeningeal carcinomatosis where there is a spread of multiple myeloma to the meninges. This is characterized by the presence of monoclonal plasma cells in the CSF.¹ Plasma cells are seen in a number of infectious, inflammatory, and infiltrative diseases; they are not specific to MM. Previous authors have noted that their presence in the CSF of patients with multiple myeloma may be suspicious for MM (more so if evidence of monoclonality is seen) than actually diagnostic of MM.² In immunocompromised patients, it is important to evaluate for the presence of coexistent mimics such as viral infections, EBV-related posttransplant lymphoproliferative disorder, and fungal, cryptococcal, spirochetal (especially syphilis), and mycobacterial infections.^{3–5} CNS myelomatosis is usually a late complication of multiple myeloma. MM was seen in all stages of multiple myeloma but is usually a late complication of the disease. One review of 109 cases of CNS myelomatosis found this to be the initial manifestation of multiple myeloma in only 13 cases (11.9%). This study showed confusion, limb weakness, and headaches to be the most common presenting symptoms. Cranial nerve palsies and symptoms of spinal cord involvement such as radicular pains, paresthesias, and paraparesis have also been described. Convulsions were reported in 6% of cases.⁶ The apparent rarity of this condition may stem from underdiagnosis.² The paucity of clinical examination and imaging findings in leptomeningeal carcinomatosis has already been emphasized.⁷ Large-volume (>10 mL) CSF sampling with flow cytometry analysis is required for diagnosis and may be

repeated if necessary. Samples must be processed immediately to ensure cellular viability.⁸ Utility of CSF tumor markers such as $\beta 2$ microglobulin is unclear.^{9,10} Though the exact mechanism of meningeal spread is unknown and remains a matter of speculation, there are numerous reports of meningeal disease manifesting after the treatment of systemic recurrence, as seen in our patient. This may be secondary to the fact that commonly used chemotherapeutic regimens may not penetrate the meninges, thus allowing a sanctuary for growth and recurrence.² There is no standard regimen for the treatment of MM and a combination of intrathecal chemotherapy with or without radiation is usually prescribed. Commonly used intrathecal regimens previously reported include methotrexate or cytosine arabinoside in combination with a steroid such as hydrocortisone.^{2,6} The presence of MM is a sign of poor prognosis, with a median overall survival time from diagnosis of MM to death being only 2 months. No particular chemotherapy regimen has been shown to be superior. Patients who receive craniospinal radiation may have a significantly longer survival than without craniospinal radiation (median survival of 3 months compared to 0.81 months, $p < 0.004$).^{2,6} Through this report we hope to increase awareness among clinicians of this rare complication of multiple myeloma. Early diagnosis and intervention may improve survival, though this effect is not long-lasting and the condition carries a poor prognosis.

AUTHOR CONTRIBUTIONS

Neville Jadeja: manuscript preparation. Krishna Nalleballe: manuscript formatting and design. Jerome Graber: manuscript supervision and critical revision for intellectual content.

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REFERENCES

1. Petersen SL, Wagner A, Gimsing P. Cerebral and meningeal multiple myeloma after autologous stem cell transplantation: a case report and review of the literature. *Am J Hematol* 1999;62:228–233.
2. Lopes da Silva R, Costa I, Prata M, Sousa AB. Plasma cell meningitis: a rare neurological complication of multiple myeloma requiring a high index of suspicion. *Acta Neurol Taiwan* 2011;20:209–212.
3. Shapiro RS, McClain K, Frizzera G, et al. Epstein-Barr virus associated B cell lymphoproliferative disorders following bone marrow transplantation. *Blood* 1988;71:1234–1243.

4. Kalia R, Hennessey K. Plasma cell pleocytosis in HSV-2 aseptic meningitis. *Open J Intern Med* 2013;3:119–120.
5. Carson PJ, Steidler T, Patron R, Tate JM, Tight R, Smego RA Jr. Plasma cell pleocytosis in cerebrospinal fluid in patients with West Nile virus encephalitis. *Clin Infect Dis* 2003;37:e12–e15.
6. Nieuwenhuizen L, Biesma DH. Central nervous system myelomatosis: review of the literature. *Eur J Haematol* 2008;80:1–9.
7. Chamberlain MC, Glantz M. Leptomeningeal metastasis: a response assessment in neuro-oncology critical review of endpoints and response criteria of published randomized clinical trials. *Neuro Oncol* 2014;16:1176–1185.
8. Glantz MJ, Cole BF, Glantz LK, et al. Cerebrospinal fluid cytology in patients with cancer: minimizing false-negative results. *Cancer* 1998;82:733–739.
9. Lee E. Nervous system metastasis from systemic cancer continuum. *Neurology* 2015;21:418.
10. Alsobhi EM, Hashim IA, Abdelaal MA, Aljifri AM, Alshamy AM. Elevated cerebrospinal fluid beta-2 microglobulin as a tumor marker in a patient with myeloma of the central nervous system. *Saudi Med J* 2007;28:128–130.

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