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Case Report

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An Uncommon Complication of Multiple Myeloma in a Post Bone Marrow Transplant patient–Plasma Cell Pleocytosis

Prachi[1,*], Gaurav Sharma[2]

[1]Senior Resident, Department of Pathology, Dharamshila Narayana Super speciality Hospital, New Delhi

[2]Senior Consultant, Department of pathology, Dharamshila Narayana Super speciality Hospital, New Delhi

Corresponding author:

Prachi, Senior Resident, Department of Pathology, Dharamshila Narayana Super speciality Hospital, New Delhi

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Andrei Alimov, Leading researcher (preclinical studies), Docent (academic teaching) Research Center of Medical Genetics, Moscow, Russia

Abstract

Multiple myeloma is a neoplasm of B- cell arising from the germinal centre. An uncommon complication of multiple myeloma is plasma cell pleocytosis, which carries poor prognosis and reduces the patient survival time. Repeated CSF sampling is to be done for monitoring. And this condition is proven with the aid of Cerebrospinal fluid electrophoresis or flowcytometry. We report a case of plasma cell pleocytosis in a 48 year old lady ,who was a diagnosed case of IgG lambda multiple myeloma, post transplant and later on developed plasma cell pleocytosis, which is quite uncommon. The rarity of this case prompted this study.

Introduction

Multiple myeloma is a neoplastic disease of plasma cells, with very few cases showing infiltration of CSF by plasma cells. Normally plasma cells is not a component of CSF. Presence of malignant plasma cells in cerebrospinal fluid leads to the diagnosis of myelomatous meningitis , which is further confirmed by CSF electrophoresis and flowcytometry.[1]

Meningeal involvement in multiple myeloma is very rare and constitutes to around 1 % of all Plasma cell myeloma cases.

Case History

We report plasma cell pleocytosis in cerebrospinal fluid in a diagnosed case of multiple myeloma. Our patient was a 48-year-old woman who was diagnosed with IgG lambda myeloma, 2 years prior to this presentation. She had completed chemotherapy then and also received an autologous peripheral blood stem cell transplantation. The patient was in complete remission for about 6 months, followed by disease progression (M spike 2.0). Her bone marrow biopsy examination revealed

35 % of plasma cells of all the nucleated marrow cells. She was initiated on inj. Daradex (daratumumab/ dexamethasone; orencia (abatacept); melphalan; hydro-cortisone; biodronate) with a dosage of

1. Weeks (1-6)-16 mg/kg IV infusion once weekly (total of 6 doses)
2. Weeks 7-54: 16 mg/kg IV infusion every 3 weeks (total of 16 doses); first dose of the every-3-week dosing schedule is given at Week 7

Weeks 55 onwards until disease progression: 16 mg/kg IV infusion every 4 weeks; first dose of the every-4-week dosing schedule is given at Week 55 and was refractory to the same. Later on , she was put on inj.orencia and low dose melphalan and achieved morphological remission and was planned for Haploidentical bone marrow transplantation.

Post transplant, Day 10, she developed transplant associated thrombotic microangiopathy and was treated with four consecutive therapeutic plasma exchanges and was relieved promptly.

On Day 30, she had low- grade fever. Her haematological parameters showed pancytopenic picture. Her biochemical parameters were within normal limts. In view of this , low grade CMV infection was suspected and was put on antiviral and discharged for the same. At the time of discharge, her LDH was 192.5IU/L.

On day 84, she came with a complaint of ataxia and mild slurring of speech. Sensorimotor examination showed mild sensory neuropathy. Her LDH- 358 U/L, Ferritin- 2140ng/ml. In view of Chronic inflammatory demyelinating polyneuropathy, CSF examination was evaluated . on biochemistry – glucose 43.3mg/dl, protein -2 gm/dl,chloride -74.4U/L.

On clinical pathology, CSF showed 20 cells, with 70 % lymphocytes and 30 % mesothelial cells and was negative for malignancy.

MRI brain revealed evidence of the bilateral periventricular white matter T1/T2 prolongation around occipital horns . No meningeal involvement seen. Features suggestive of Progressive multifocal leukoencephalopathy – immune reconstituition inflammatory syndrome and was given inj hydrocort and biodronate.

She now presented to our hospital with one episode of fever spike with persistent cough and headache and right eye ptosis s. On examination , her spO2 was 97%. There was improvement in her gait and bilateral lower limb neuropathy. She did not complain of any other neurologic or systemic symptoms. Hematologic evaluation was significant for normocytic anemia and thrombocytopenia. No lymphopenia or neutropenia was noted. His initial CT whole body showed metabolically inactive subcentimeter sized intramedullary foci noted in axial and appendicular skeleton . coarse trabeculation noted in entire skeleton with diffuse metabolic active – reactionary / mitotic and subsequent lumbar puncture with CSF analysis showed 100cells/mm^3 with a plasma cells predominance (90 %), protein 79 mg/dL, glucose 69 mg/dL, and CSF electrophoresis showed elevated immunoglobulin lambda (17%) with a single monoclonal band. CSF cytology showed sheets of plasma cells wth occasional binucleated forms are also seen . 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), 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. She was diagnosed with plasma cell meningitis.

Intrathecal chemotherapy with craniospinal radiation was planned; however, his disease rapidly progressed, and he died within 2 weeks of his diagnosis. Table 1

Discussion

Presence of monoclonal plasma cells in cerebrospinal fluid is the characteristic feature of plasma cell meningitis, myelomatous meningitis (MM), and CNS myelomatosis ,hence these terms are have been used

Table 1. Her pre-transplant work up are as follows

Tests done	Results
Complete blood count	Hb- 9.0gm/dl, TLC-14.0/mm3,PLT- 34000/microlitre
Coagulation profile	PT-13.5,INR-0.86,APTT-26.0
CRP-	11.4
Liver function test	Bilirubin- 0.29/0.24, SGOT- 21.6IU/ml, SGPT-13.2IU/ml
Albumin	5.69g/dl
Creatinine /GFR	2.4/22.8
LDH/TSH/FT4	LDH-281 U/L, TSH-1.4 mIU/L ,vit D-32.5ng/ml
Ferritin	1340ng/ml
CMV IgG	42.0- positive
EBV IgG	0.35 Positive
HIV 1 and 2 ,HbsAg,HCV	Non reactive
Toxoplasma IgG/IgM	<3.0
VZV IgG	2.07
Swab (rectal/skin/throat)	Rectal – ecoli ESBL+, CRE negative , Skin- MRCNS
Blood group	B positive
Left ventricular ejection fraction	62%
Bone marrow aspirate and biopsy	Hypercellular marrow, with plasma cell seen in cluster and sheets
Serum free light chain assay	Kappa- 13.30 mg/dl, lambda- 65.00 mg/dl, kappa: lambda- 0.205
Serum protein electrophoresis	M spike – 2.5g / dl

interchangeably.[2] They refer to a type of leptomeningeal carcinomatosis where there is a spread of multiple myeloma to the meninges. Plasma cells are not specific to multiple myeloma , but can be seen in number of infectious,non- infectious , inflammatory, and infiltrative diseases. Hence the further evaluation of viral, EBV – related post- transplant related lymphoproliferative disorder, fungal, cryptococcal, spirochetal and mycobacterial infection is mandatory. CNS myelomatosis is usually a late complication of multiple myeloma .

This study showed fever, headache and limb weakness to be the most common presenting symptoms. The apparent rarity of this condition may stem from underdiagnosis.

Large volume sampling is required for diagnosis and repeated sampling is done if necessary. Flowcytometry of CSF sampling is done to narrow down the diagnosis.

Samples are processed immediately to ensure cellular viability.

The exact pathogenesis of spread to meninges is still unknown and is a matter of speculation still. Commonly intrathecal chemotherapy with or without radiation is prescribed as a part of treatment . the meningeal involvement in multiple myeloma case is rare and carries poor prognosis. None of the treatment is considered superior. The people with irradiation therapy have better and prolonged survival as compared to non irradiated patient . [3]

Conclusion

Plasma cell pleocytosis is a rare entity in case of multiple myeloma. Need to be distinguished from its other differential by CSF flowcytometry and electrophoresis to conclude it as plasma cell pleocytosis in case of multiple myeloma. Early diagnosis and intervention may improve survival, though this effect is not long-lasting and the condition carries a poor prognosis.

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