CASE REPORT

Case of lymphadenopathy with lytic bone lesions

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SUMMARY

Plasmablastic lymphoma, a rare highly aggressive non-Hodgkin's lymphoma subtype, often associated with HIV infection, is a close differential diagnosis of plasmablastic myeloma. The 2 conditions may be morphologically and immunophenotypically identical. However, differentiating between the 2 conditions is critical for adequate patient management. Herein, we describe an unusual case of plasmablastic myeloma with biclonal gammopathy which was initially diagnosed as plasmablastic lymphoma based on lymph node biopsy and immunohistochemistry (IHC) results. The incidental finding of lytic bone lesion on imaging prompted further investigations. The presence of multiple osteolytic lesions, biclonal gammopathy on serum protein electrophoresis and immunofixation, negative Epstein-Barr virus-encoded small RNAs on IHC led to revision of the diagnosis to plasmablastic variant of multiple myeloma. The patient was initially started on bortezomib plus dose-adjusted EPOCH chemotherapy for plasmablastic lymphoma. Subsequently, he was treated with RVD (lenalidomide, bortezomib, dexamethasone) regimen for plasmablastic myeloma and he achieved stringent complete response after 4 cycles.

BACKGROUND

Plasmablastic myeloma is a very close differential diagnosis of plasmablastic lymphoma. At times, it may not be possible to differentiate between the two conditions. Treatment of the two conditions is different and it requires more aggressive approach for plasmablastic lymphoma. It is important to take into consideration the presence of associated clinical features while diagnosing this condition. Incidental finding of osteolytic lesions prompted us for further investigations and led to revision of diagnosis.

CASE PRESENTATION

A man aged 55 years was admitted with symptoms of high-grade fever, cough and haemoptysis. He also reported rapid enlargement of left cervical lymph nodes for the past 1 month. On examination, he had crepitations in the right infra-axillary area. There was no hepatosplenomegaly or bone tenderness. Complete blood count showed anaemia, and leucocyte and platelet counts were normal. Sputum culture sensitivity revealed growth of *Streptococcus pneumoniae* and no AFB was detected. HBsAg was negative; anti HIV-I,II and anti-HCV antibodies were non-reactive. Histopathology and immunohistochemistry (IHC) of cervical lymph node biopsy were consistent with the diagnosis of plasmablastic lymphoma (figure 1).

Staging CT scans and bone marrow biopsy were performed, and therapy was started with bortezomib plus dose-adjusted EPOCH chemotherapy regimen in view of the aggressive nature of plasmablastic lymphoma. Contrast-enhanced CT scan chest incidentally detected osteolytic lesions in D10 and L1 vertebral body and partial collapse of D2 vertebra, and prompted further workup (figure 2). X-ray skeletal survey showed multiple punched out osteolytic lesions in the skull. Serum protein electrophoresis and immunofixation revealed biclonal gammopathy comprising IgG κ and IgA λ monoclonal paraprotein bands (figure 3). As plasmablastic lymphoma is strongly associated with EBV infection, IHC of lymph node biopsy for EBER (Epstein-Barr virus-encoded small RNAs) was performed. IHC for EBER was reported negative (figure 4). Bone marrow aspiration and biopsy were consistent with multiple myeloma with 42% clonal plasma cells, including 4% plasmablasts (figure 5). The diagnosis was revised to plasmablastic variant of multiple myeloma. Treatment protocol was changed to RVD (bortezomib, lenalidomide and dexamethasone) regimen and monthly injections of zoledronic acid. The patient achieved stringent complete response (sCR) after four cycles of RVD but was not willing for early autologous stem cell transplant. At present, he is on induction therapy with RVD and has completed 11 cycles until November 2016. Maintenance therapy with bortezomib has been planned after completion of 12 cycles of induction therapy.

INVESTIGATIONS

Complete haemogram: haemoglobin: 9 g/dL, MCV: 84 fL, MCH: 30 pg, total leucocyte count: $4 \times 10^9/L$, platelets: $156 \times 10^9/L$.

Figure 1 Lymph node biopsy: sheets of plasma cells causing effacement of lymph node architecture (HE $\times 40$).

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Figure 2 Osteolytic lesion.

Figure 3 Serum protein immunofixation—biclonal bands (IgA lambda and IgG κ).

Blood urea: 37 mg/dL, creatinine: 1.0 mg/dL, serum calcium: 9.6 mg/dL.

Sputum culture: Heavy growth of *S. pneumoniae*.

Lymph node biopsy: Diffuse effacement of lymph node architecture by sheets of plasmablastic cells.

Immunohistochemistry: Positive for CD138, Bcl-2, MUM 1, EMA and negative for CD20, CD10, CD45, CD56, Bcl6, c-MYC, EBER. κ light chain restriction present. Ki-67 labelling index 85%. Findings were consistent with plasmablastic lymphoma.

CT scan chest: The right lower lobe showed patchy consolidation. Enlarged lymph nodes were seen at precarinal, subcarinal and bilateral hilar regions. There was partial collapse of D2 vertebral body. Lytic lesions were seen in D10 and L1 vertebral body.

Figure 4 Immunohistochemistry of the lymph node showing negative Epstein-Barr virus-encoded small RNAs.

Figure 5 Bone marrow aspiration showing immature and atypical plasma cells (100 $\times$ Leishman Geimsa stain).

CT scan abdomen: Pelvic and retroperitoneal lymphadenopathy.

Serum protein electrophoresis: M γ spike present—In gamma-globulin region (3.89 g/dL).

Serum immunofixation electrophoresis: Biclonal gammopathy in the form of IgG κ and IgA λ paraprotein bands.

Bone marrow aspiration and biopsy: 42% clonal plasma cells including plasmablasts.

Bone marrow immunophenotyping: CD45 negative, CD138 and CD38 positive, CD19 negative.

Anti HIV-I,II antibody: non-reactive.

X-ray skull: multiple punched out lytic lesions.

SPEP, IFE, Serum free light chain assay after four cycles: normal (stringent CR).

DIFFERENTIAL DIAGNOSIS

- Plasmablastic lymphoma
- Plasmablastic myeloma

TREATMENT

The patient has received 11 cycles of RVD therapy until November 2016.

OUTCOME AND FOLLOW-UP

The patient achieved stringent CR after four cycles and he continues to be in sCR.

DISCUSSION

Plasmablastic myeloma accounts for almost 10% of all newly diagnosed cases of myeloma.¹ The incidence of plasmablastic lymphoma is not defined, although it is a rare entity. Plasmablastic myeloma is a very close differential diagnosis of plasmablastic lymphoma. Both the conditions may be morphologically and immunophenotypically identical and it may not be possible to distinguish between the conditions on the basis of histopathology and IHC alone.² Plasmablastic lymphoma is a very aggressive disease and hence differentiating between the two conditions is important. Plasmablastic lymphoma is considered to be a subtype of diffuse large cell lymphoma and is more commonly found in HIV-positive individuals. It accounts for 2% of all HIV-associated lymphoma. In retrospective analysis of published cases, HIV-positive cases constituted 63% of all cases. In about 70% cases, Epstein-Barr virus encoded RNA can be documented indicating strong association with EBV infections.³ Oral cavity involvement is seen in 44% of cases and lymph node and bone involvement are seen in 7% and 4% of cases, respectively, in plasmablastic lymphoma.³ Histopathological features consist of the presence of large immunoblasts or large plasma cells that express plasma cell markers and lack B-cell markers.⁴ Immunoblasts are positive for CD79a, IRF-4/MUM-1, BLIMP-1, CD38, CD138 and EBER and are negative for the B-cell markers CD19, CD20 and PAX-5.² Plasmablastic myeloma express CD138, cytoplasmic Ig, CD38 and are negative for EBER, CD20, PAX-5, BCL-6.² Hence, it may not be possible to distinguish the two conditions solely on the basis of histopathology and IHC. Clinical features which favour multiple myeloma are the presence of monoclonal paraprotein, increased bone marrow plasma cells, osteolytic lesions, renal failure and hypercalcaemia. Apart from these features, detection of myeloma-specific translocation (eg, t(11:14), t(4:14), t(14:16), etc) by fluorescent in situ hybridisation can help in distinguishing the two conditions. However, this investigation was not performed in this case for financial reasons. Lymph node enlargement is also relatively uncommon manifestation of myeloma and is reported only in 1% of the cases.⁵ It is commonly associated with IgA myeloma.⁶ Biclinal gammopathy is also extremely uncommon and is only seen in 1% of cases of myeloma.⁷

The case in discussion had presented with lymphadenopathy but was incidentally found to have osteolytic lesions, which led to further diagnostic workup. The presence of biclinal gammopathy comprising IgG κ and IgA λ paraproteins and bone marrow features suggestive of plasmablastic myeloma, leading to timely diagnosis and initiation of definitive management with achievement of complete response.

Learning points

- Plasmablastic lymphoma and plasmablastic myeloma are very close differential diagnosis and the two conditions may be morphologically and immunophenotypically identical.
- The diagnostic workup should include serum protein electrophoresis with immunofixation, bone marrow biopsy and imaging studies in addition to lymph node histopathology and immunohistochemistry including Epstein-Barr virus-encoded small RNAs.
- Clinical correlation is of utmost importance in accurate diagnosis and definitive treatment for the two conditions.

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