Blastoid mantle cell lymphoma involving skin and orbit with hypercalcemia: A case report and literature review

Juan Li¹, Han Ma², Xizuhen Tong¹,*, Chang Su¹, Dong Zheng¹, Mei Chen¹, Chun Lu²

¹Department of Hematology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510080, China
²Department of Dermatology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510630, China

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ABSTRACT

Mantel cell lymphoma is one of the small B-cell non-Hodgkin’s lymphomas and usually involves lymph nodes, bone marrow, spleen, liver, gastrointestinal tract, and Waldeyer’s ring, but rarely skin and orbit. A 53-year-old man presented skin nodules and plaques on the head, trunk, and lower extremities for half a month, and the left peri orbital region swelled 4 days ago. Serum calcium and lactate dehydrogenase were increased to 3.12 mmol/L (normal 2.03–2.65 mmol/L) and 853 U/L (normal 71–231 U/L), respectively. Histopathologic examination of the skin nodule revealed tumor cells infiltrated nodular distribution in the dermis and subcutaneous tissue. Immunophenotyping of the abnormal lymphocytes indicated positive reactions for L26, CD79a, Bcl-2, Cyclin D1, and Ki-67 (>80%), but negative for CD5, CD21, CD23, CD38, CD3, CD10, UCHL-1, TdT, MPO, CD30, ALK, CD117, and CD34. Fluorescence in situ hybridization analysis with the CCND1/IGH probe revealed a fusion signal on the abnormal lymphocytes. The final diagnosis was a rare case of blastoid mantle cell lymphoma involving skin and orbit with hypercalcemia. Following the R-Hyper-CVAD treatment plan, the patient achieved a quick and excellent recovery on the 6th day. Unfortunately, the patient eventually died of pneumonia one month later.

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Introduction

Mantel cell lymphoma (MCL) is a rare B-cell non-Hodgkin’s lymphoma with a poor long-term prognosis. Skin involvement occurs in only 2–6% of all cases of MCL, but is seen in 17% of stage IV patients.¹ It is important for the dermatologist to realize and master the primary clinic presentation and pathologic features of the skin, as these will help in early and correct diagnosis of the disease. We report a case of blastoid mantle cell lymphoma involving skin and orbit with hypercalcemia.

Case report

A 53-year-old man presented with dark purple nodules and plaques on the left temporal region, right palpebra frontalis (Figure 1A), abdomen (Figure 1B), and bilateral lower extremities for ½ month, and the left peri orbital region swelled 4 days prior to his initial visit to our department of dermatology. Physical examination revealed significant superficial lymph node enlargement and splenomegaly. Serum calcium and lactate dehydrogenase (LDH) were increased to 3.12 mmol/L (normal 2.03–2.65 mmol/L) and 853 U/L (normal 71–231 U/L), respectively. The agarose gel electrophoresis showed monoclonal immunoglobulin IgM (κ chain). Positron emission tomography computed tomography scan showed multiple areas of abnormal uptake in lymph nodes, back wall of pharynx, and spleen. Bone marrow aspirate revealed active myeloid proliferation and 42% of lymphoblast was observed. Flow cytometry displayed CD20 (93.7%), CD22 (91.0%), human leukocyte antigen (HLA)-DR (99.3%), CD19 (82.9%), CD79a (95.2%), cytoplasm K (98.0%), CD2 (51.5%), and CD15 (32.7%). CD13, CD56, CD41, CD61, and CD42a were all negative. Histopathologic examination of the skin nodule in the neck revealed atypical lymphoid cells (Figure 2B) infiltrated nodular distribution in the dermis and subcutaneous tissue (Figure 2A). Immunophenotype of the abnormal lymphocytes indicated positive reactions for L26 (Figure 2C), CD79a, Bcl-2, Cyclin D1 (Figure 2D), Mum-1 (partly), and Ki-67 (>80%), but negative for CD5 (Figure 2D), CD21, CD23, CD38, CD3, CD10, UCHL-1, TdT, MPO, CD30, ALK, CD117, and CD34. The translocation t(11:14) juxtaposes the cyclin D1 gene (CCND1) at 11q13 to the immunoglobulin heavy chain (IgH) promoter locus at chromosome 14q32.

* Corresponding author. Department of Hematology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510080, China. Tel.: +86 20 85253017; fax: +86 20 87957319.
E-mail address: tongxz05@sina.com (X. Tong).

¹ These two authors contributed equally to this paper.
which may be implicated in the pathogenesis and development of lymphomas, and can be found in virtually all cases of MCL by using fluorescence in situ hybridization (FISH) techniques. The patient’s result of FISH analysis with the CCND1/IGH probe revealed a yellow fusion signal on the abnormal lymphocytes (Figure 3). Based on the cytological characterization of the infiltrated tumor cells (monomorphic sheets of small- to medium-sized blasts with finely dispersed chromatin mimicking lymphoblastic lymphoma) and clinical data, the diagnosis was blastoid MCL (stage IVB) with hypercalcemia. R-Hyper-CVAD chemotherapy was delivered: rituximab 700 mg d0 (only 50 mg was used as the patient did not tolerate it well because of chilling and fever), cyclophosphamide 1.5 g q12h d1−3, vincristine 2 mg d4 and d11, theprubicin (THP) 90 mg d4, and dexamethasone 40 mg d1−4 and d11−14. Three days later, serum calcium became normal. On the 6th day, the lesions on the temporal site of the head, abdomen, and bilateral lower extremities had significantly diminished. Edema around the orbit ameliorated, and the patient could open his eyes (Figure 1). Unfortunately, the patient eventually died of pneumonia 1 month later.

Discussion

MCL is mostly found among adults with a median age ranging from 60 to 65 years and a high male-to-female ratio. At presentation, there is involvement of lymph nodes (75%), spleen (massive splenomegaly in 45–60% of cases), liver (hepatomegaly in 35%), Waldeyer’s ring, bone marrow (>60%), blood (13–77%), and extranodal sites, especially the gastrointestinal tract. Less commonly, skin, lung, breast, soft tissue, salivary glands, and orbit are involved. According to cytological characterization, MCL could be divided into four types: classical, blastoid, small cell, and pleomorphic. The cells of MCL are usually positive for CD5, CD43, CD19, CD20, CD22, CD79a, and CD79b, and negative for CD3, CD23, CD11c, CD10, and Bcl-6. Especially, MCL characteristically display nuclear positivity for cyclin D1 (bcl-1), which is strongly associated with all variants of this lymphoma, including the small group of CD5-negative cases.

Because skin lesions are visible, many cases are firstly diagnosed by the dermatologist. Among 18 cases of MCL reviewed by Canpolat et al, with cutaneous infiltration at the first clinical visit, dermal lesions were found in 11 patients on trunk and face, in three on upper and lower limbs, and in two on lower limbs. Most of the lesions were nodules, and a few were maculapapules and purple plaques. Sen et al reported five cases of MCL involving skin, among which four had blastoid cytological feature without the expression of CD5. Evidence claimed that MCL with cutaneous infiltration had a universal involvement and pessimistic prognosis. Most of such patients died as a result of the progression of disease or ineffectiveness of combined chemotherapy, with a median survival period of 33 months after being diagnosed. This case conformed to the record of documents in terms of cutaneous lesion, cytological characterization, and immunohistochemistry feature.

B-cell lymphoma is less frequently associated with hypercalcemia. Hypercalcemia is also strongly associated with an aggressive
phenotype and/or disease progression in B-cell non-Hodgkin’s lymphoma. Hattori et al. demonstrated that macrophage inflammatory protein-1α (MIP-1α), an osteoclast-activating factor produced by mantle lymphoma cells, may contribute to the development of hypercalcemia. It likely acts through receptor-activator of nuclear-factor kappa B ligand expression in tumor cells and/or stroma cells, as indicated in multiple myeloma and adult T-cell leukemia/lymphoma. Furthermore, MIP-1α is also involved in the development of an aggressive phenotype on MCL by stimulating proliferation of these lymphoma cells.

Now, MCL is generally treated more aggressively than in the past. Unfortunately, with the current treatments, including very aggressive approaches, MCL remains an incurable disease. Age >65 years and elevated β2-microglobulin and LDH levels were adverse prognostic factors, with 5% of toxic deaths due to neutropenic sepsis and secondary myelodysplastic syndrome or acute leukemia, with a risk...
of secondary malignancies of 6%. The patient received the treatment strategy of R-Hyper-CVAD according to the advice of Dreyling et al. and achieved a quick and excellent alleviation of symptoms, as evident from the skin manifestation and the level of serum calcium. However, secondary pneumonia was the direct cause of death.

References