Long-term remission of subcutaneous panniculitis-like T-cell lymphoma with central nervous system involvement: A case report

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Abstract. Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is an indolent cutaneous T-cell lymphoma with a favourable prognosis. The reported incidence of central nervous system (CNS) involvement in SPTCL is extremely low. SPTCL with CNS involvement is a fatal disease with no optimal treatment. The present study presents the case of a 27-year-old man who initially presented with erythematous nodules on the left buttock and left inguinal lymph node enlargement. A skin biopsy resulted in a diagnosis of SPTCL. Subsequent to diagnosis, the patient developed CNS involvement and underwent treatment of fotemustine, teniposide and dexamethasone, and complete remission was achieved for 78 months. To the best of our knowledge, this is the first case report of secondary CNS SPTCL with long-term remission. Accumulating evidence shows that this CNS-directed regimen can be effective in SPTCL with CNS involvement and in other CNS lymphomas.

Introduction

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a cytotoxic cutaneous T-cell lymphoma of predominantly α/β T-cell origin, which has an excellent prognosis, particularly when there is no association with haemophagocytic syndrome (HPS) (1,2). The incidence of SPTCL is <1% of all non-Hodgkin lymphoma cases. SPTCL is most common in young adults with a median age of 36 years (range, 9-79 years) and has a female predominance with a male to female ratio of 0.5 (2). Patients with SPTCL typically present with multiple subcutaneous nodules in the extremities and trunk, and are often treated with doxorubicin-based chemotherapy and radiotherapy (3). In SPTCL without an association with HPS, the first treatment to be considered should be systemic steroids or other immunosuppressive agents (1,2). CNS involvement occurs in ~5% of all systemic lymphomas, although its rate varies depending on the histology and stage of the lymphoma (4,5). The rate of CNS involvement is undoubtedly higher in other lymphomas such as aggressive non-Hodgkin’s lymphoma (NHL) (30-50%) (6). Regarding cutaneous T-cell lymphoma, a limited number of studies have reported of CNS involvement. CNS involvement in cutaneous T-cell lymphoma is fatal, and no consensus is currently available regarding optimal treatment. Therefore, the present study aimed to investigate and discuss optimal treatment strategies.

Case report

A 27-year-old male was admitted to The First Affiliated Hospital of Zhengzhou University (Zhengzhou, Henan, China) on September 1, 2008. The patient presented with erythematous nodules on the left buttock and left inguinal lymph node enlargement that had been apparent for 9 months. The patient was diagnosed with SPTCL based on a skin biopsy (x400 magnification; Fig. 1A) according to the World Health Organization European Organization for Research and Treatment of Cancer classification of primary cutaneous lymphomas (7). The biopsy revealed lobular panniculitis with massive atypical lymphoid infiltrates, as well as inflammatory infiltration of the subcutaneous fat and histiocytes. The rimming of fat cells by atypical T lymphocytes in the subcutaneous fat was also visible, consistent with a diagnosis of SPTCL. The surgical specimen was fixed in 4% formalin, embedded in paraffin and stained with hematoxylin and eosin. Microscopic analysis identified a number of medium-sized lymphocytes infiltrating fatty lobules mixed with histiocytes. Immunohistochemical analysis revealed that the skin lesions were positive for cluster of differentiation (CD)3, CD43, CD99, leukocyte common antigen and B-cell lymphoma-2, and negative for CD20, CD79a, CD45RO, paired box protein Pax-5, CD10, CD23, CD4 and CD8. The immunohistochemical staining was positive for T-cell receptor-βF1 (x400 magnification; Fig. 1B).

Physical examination confirmed erythematous nodules on the left buttock and left inguinal lymph node enlargement. Laboratory assessments were conducted and revealed the following: White blood cell (WBC) count, 8.34x10⁹/l (normal range, 4-10x10⁹/l); absolute neutrophil count, 4.76x10⁹/l; (normal range, 2.7-7.7x10⁹/l); haemoglobin, 142 g/l (normal range, 110-160 g/l); and platelet count, 198x10⁹/l (normal range, 150-450x10⁹/l).
range, 100-300×10^9/l). The results of the liver function assessments were identified to be elevated as follows: alanine aminotransferase, 159 U/l; aspartate aminotransferase, 71 U/l; serum total bilirubin, 11.6 µmol/l; direct bilirubin, 3.9 µmol/l; indirect bilirubin, 8 µmol/l; and albumin, 51.1 g/l. The level of lactate dehydrogenase (LDH) was 251 IU/l and the β2-microglobulin level was 1.76 mg/l. Renal function parameters were within normal ranges, with a blood urea nitrogen level of 6.4 mmol/l and a serum creatinine level of 65 µmol/l. Bone marrow aspirate and biopsy showed no evidence of lymphoma. Computed tomography scans revealed mediastinal and axillary lymph node enlargement. Based on the clinical presentation and imaging findings, the patient was staged as T3bN2M0 according to the tumour-node-metastasis classification system for primary cutaneous lymphomas other than mycosis fungoides and Sézary syndrome (8). There was no relevant personal or familial medical history. The patient was immunocompetent and human immunodeficiency virus-negative.

The patient was treated with 4 cycles of the cyclophosphamide, epirubicin, vincristine and prednisolone (CHOP) regimen (750 mg/m² cyclophosphamide by infusion, day 1; 50 mg/m² doxorubicin by infusion, day 1; 1.4 mg/m² vincristine by infusion, day 1; 100 mg/m² prednisolone taken orally, days 1, 2, 3, 4 and 5) from September 5, 2008 to November 18, 2008, which resulted in partial remission for 3 months. The patient subsequently received 4 cycles of the etoposide, methylprednisolone, cytarabine and cisplatin regimen (40 mg/m² etoposide by infusion, days 1, 2, 3 and 4; 500 mg methylprednisolone by infusion, days 1, 2, 3 and 4; 2,000 mg/m² cytarabine, day 5; 25 mg/m² cisplatin, days 1, 2, 3 and 4) from December 2, 2008 to February 3, 2009, which resulted in complete remission for 8 months. The patient then underwent radiation therapy (36 Gy in 20 fractions; 1.8 Gy per fraction) targeted to the cutaneous tumours for 4 weeks from February 10, 2009 to March 10, 2009.

At 6 months after the completion of treatment, the patient developed a progressive headache, nausea, vomiting, numbness of limbs and blurry vision. During admission, this clinical status rapidly declined, and the patient collapsed into a coma. A magnetic resonance imaging (MRI) study of the brain with gadolinium contrast showed no apparent changes to the brain parenchyma and leptomeninges, or to the eyes (Fig. 2). A stereotactic biopsy was not performed as there were no significant lesions. Cerebral spinal fluid (CSF) analysis revealed the following: WBC...
generalized correlation with a poor prognosis, with few long-term survivors. The relapse of systemic lymphoma within the CNS is a barrier. The relapse of systemic lymphoma within the CNS is generally correlated with a poor prognosis, with few long-term survivors following treatment with conventional therapy (10). Observations suggest that high-dose methotrexate (HD-MTX) and whole-brain radiotherapy (WBRT) are sufficient to treat CNS lymphoma. However, the optimal regimen for HD-MTX has not been firmly defined (11). Despite the fact that the patients who undergo high-dose chemotherapy and autologous stem cell transplant have improved outcomes, the majority of patients with CNS relapse of systemic lymphoma will not be candidates for such an aggressive approach. So, it is highly likely that therapeutic outcomes have now reached a plateau and that further innovations are urgently required to facilitate treatment of CNS lymphomas, particularly for the aging population, among whom a significant proportion cannot tolerate high-dose chemotherapy and/or WBRT (12-14).

The success of treatment depends on effective CNS-directed therapy. In the present study, an FTD regimen was selected based on the pharmacokinetic properties of the drugs and dose levels that were aimed at delivering effective chemotherapy to the CNS. The patient received the FTD regimen and subsequently achieved a CR, with long-term survival. A study by Wu et al demonstrated that the FTD regimen can be effective in primary and secondary CNS lymphomas (15). Fotemustine is known to penetrate into the CNS, and has been investigated previously in a number of brain tumours (16). Teniposide was included in this regimen as it is more lipophilic to cross the blood-brain barrier and is also eliminated at a slower rate (17). Glucocorticoids (prednisone and dexamethasone) play an essential role in the treatment of systemic lymphoma. Clinical studies have shown that dexamethasone has a longer half-life and greater CNS penetration. However, the use of glucocorticoid in CNS lymphoma is controversial due to steroid-induced diagnostic delay. Even if CNS lymphoma is confirmed, steroid use should be tapered off as quickly as possible (11). Moreover, dexamethasone may cause numerous adverse effects, including infection, bone fracture, osteonecrosis, mood and behavioural problems, and myopathy (18). The patient in the present study developed bilateral osteonecrosis of the femoral heads due to the use of dexamethasone. However, treatment with such glucocorticoids can produce rapid symptomatic improvement (11); the FTD regimen has an acceptable toxicity profile and could be the template for such a regimen. Therefore, the relative efficacy of dexamethasone is dose-dependent and must be carefully weighed against toxicity, and research is required to optimize supportive care to prevent and manage glucocorticoid toxicities. Intrathecal chemotherapy has been historically used and was recommended for high-risk lymphoma patients. However, Deng et al (19) reported that its effectiveness in diffuse large B-cell lymphoma patients is uncertain.

In conclusion, involvement of the CNS in SPTCL is a rare complication and is associated with a poor prognosis. To the best of our knowledge, this is the first case report of secondary CNS SPTCL with long-term remission. The study indicates that the FTD regimen can be effective in SPTCL with CNS involvement.

References


