Cutaneous Intravascular Large B-cell Lymphoma
-A Case Report-
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Intravascular large B-cell lymphoma (LBCL), a subtype of extranodal diffuse large B-cell lymphoma, is a rare and usually fatal disease characterized by the presence of lymphoma cells in the lumina of small vessels. Obstruction of blood flow by tumor cells in different organs can cause a variety of clinical manifestations, including the nervous and respiratory systems and skin. Biopsy of the involved organs for pathologic study is needed for establishing the diagnosis. We report a case of intravascular LBCL presenting with an erythematous plaque and neurological problems. The diagnosis was established by pathologic study of a skin biopsy specimen.(Dermatol Sinica 24: 63-66, 2006)

Key words: Intravascular large B-cell lymphoma, Intravascular lymphomatosis, B-cell lymphoma
INTRODUCTION

Intravascular large B-cell lymphoma (LBCL) is a malignant neoplasm characterized by disseminated intravascular proliferation of neoplastic B lymphocytes. The disease predominately affects the skin and central nervous system, but multisystem involvement may also occur. The majority of cases of intravascular LBCL took a rapidly progressive course, and were not correctly diagnosed antemortem. We report a case of intravascular LBCL of the skin presenting as an erythematous plaque.

CASE REPORT

A 78-year-old man was admitted to our hospital in October 2003 with a short history of fever, nausea, vomiting, and progressive weakness. He developed dementia, paraplegia, and urine and stool incontinence since 4 months ago. In 2001, he had been treated for adenocarcinoma of the prostate by hormone therapy and radiotherapy. On physical examination, the patient had decreased muscle power of 4 limbs, and was not even able to maintain an upright sitting position. No lymphadenopathy was found, and there was no palpable enlargement of the liver or spleen. A full blood count revealed hemoglobin: 10.1 g/dl (normal 13.5-17.5), white cell count: 7200 uL (normal 3900-10600), and platelet count: 205000 uL (normal 150000-400000). There was no atypical lymphocyte found. All biochemical tests were within normal limits except for hypoalbuminemia (albumin: 2.6 g/dl, normal 3.5-5.5), increased C-reactive protein (54 mg/L, normal <5), AST (40 U/L, normal 0-34) and an elevated level of LDH (279 U/L, normal 47-140). Autoimmune serology and anti-HIV antibodies were negative. A computed tomographic (CT) scan of the brain showed multiple decreased densities of...
the cerebellum suggesting the presence of multiple cerebellar infarctions. During hospitalization, the patient developed multiple small violaceous papules measuring 2-4 mm in diameter on an ill-defined erythematous plaque located in the left axilla (Fig. 1). The skin lesions clinically resembled senile angioma. A biopsy specimen showed aggregates of malignant tumor cells with large nuclei and prominent nucleoli in the dermal small and dilated vessels with many mitotic figures, neutrophils, and fibrin thrombi (Fig. 2). Neutrophils and hemorrhage are also seen in dermis. The tumor cells were shown to be located within the vessels by endothelial markers CD31 and CD34 (Fig. 3). The large neoplastic cells were positive for CD20, CD30, and negative for CD3, CD5, CD10 and ALK1 (Fig. 4). The majority of the atypical intravascular cells showed high proliferative activity by Ki-67. The results established the diagnosis of an intravascular LBCL.

Chemotherapy was arranged but held because of poor general condition of the patient. Progressive encephalopathy and multiorgan failure developed, and the patient died on day 30 after the diagnosis was made. A postmortem examination was not performed.

**DISCUSSION**

Intravascular LBCL, a subtype of diffuse LBCL in the WHO classification, is a very rare non-Hodgkin's lymphoma with an estimated frequency of <1% of all lymphoma. It was first described by Pfleger and Tappeneiner in 1959 as "angioendotheliomatosis proliferans systemisata". The disease predominately affects the skin and central nervous system, but multisystem involvement may also occur, resulting in a variety of clinical manifestations.

The most common clinical feature in the reported patients of intravascular LBCL is fever of unknown origin. Other important findings, which were present in our patient, are anemia, mental status changes, and cutaneous anomalies. Subcutaneous nodules or masses and indurated plaques are the most frequently reported skin changes. The nodules and plaques are often irregular in shape, and may be raised or flat, soft or firm, violaceous, hemorrhagic or hyperpigmented, and asymptomatic or painful those usually involve lower extremities and lower abdomen. Generalized telangiectasia without underlying skin lesions has also been reported. Besides, senile angioma-like eruptions have been presented.

Intravascular LBCL is often diagnosed postmortem, probably because of the atypical presentation and poor prognosis. Since there is no specific laboratory test or useful tumor marker for the disease, histological confirmation by the biopsy of affected organ is imperative to establish the diagnosis. It is obvious that
biopsy from the brain, kidney, lung or other internal organs carries a high risk, while skin biopsy is easily accessible, and can establish the diagnosis earlier.

Little is known about the etiology and pathophysiology of intravascular LBCL. In the case presented here, radiotherapy for prostatic adenocarcinoma 2 years before lymphoma manifestation may have had an initiating or promoting effect. Interestingly,2 similar cases of intravascular LBCL, previously treated by radiation for carcinoma of larynx and cervix uteri, have been reported recently.12, 13 Furthermore, intravascular lymphoma is observed often in patients with transplantation- or HIV- associated immunosuppression,14, 15 and a relationship with Epstein-Barr virus infection has been proposed.16 Why intravascular LBCL prefers confinement within the vascular lumina remains unclear. Some authors suggested that absence of surface adhesion molecules, which enable lymphocytes to extravasate and infiltrate various organs, may be responsible for the intravascular location of the tumor cells.2, 17

In summary, intravascular LBCL is an extremely rare form of aggressive non-Hodgkin's lymphoma with a very poor outcome. The initiation of an intensive diagnostic work-up is of paramount importance since multiagent chemotherapy is probably effective but only at an early stage of the disease.18 A biopsy of suspected skin lesions may be beneficial for a prompt diagnosis in patients with intravascular LBCL.

REFERENCES