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Richter's transformation presenting with superior vena cava syndrome

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ABSTRACT

In the present study, we report a 65-year old man who had been diagnosed earlier as having chronic lymphocytic leukemia and treated for 2 years with fludarabine. He presented to our hospital 2 years later with clinical features of superior vena cava syndrome. The underlying cause was diffuse large B cell lymphoma obstructing the superior vena cava.

1. Introduction

Maurice Richter first termed Richter's transformation (RT) in 1928 as transformation of chronic lymphocytic leukemia (CLL) into an aggressive large-cell lymphoma. Diffuse large B cell lymphoma (DLBCL) represents the most frequent histological type among patients with RT.[1]

The frequency of RT from CLL to DLBCL has been variously quoted to range from 2 to 9%.[1] The median time from the CLL diagnosis to the development of RT varies between 2 and 4 years.[2] RT has a rapidly progressive clinical course, with a 5–8 months median survival.[1]

Superior vena cava syndrome (SVCS) results from a partial blockage of blood flow through this vein.[3] The severity of the symptoms depends on the degree and speed of the superior vena cava obstruction.[4] DLBCL can be extremely aggressive with local compression of vessels or airways.

This case details the second report of a patient with superior vena cava syndrome secondary to Richter's transformation.[5]

2. Case presentation

Here, we report a case of RT presenting with SVCS in a patient with CLL. When he registered in 2007 he complained of a one-month history of weakness and painless swelling of lymph nodes in the cervical, axillary and groin areas. He had no constitutional symptoms such as weight loss, fever or night sweats at the time of presentation. A complete physical examination was performed which revealed hepatomegaly of 2 cm below the right subcostal margin and palpable cervical, axillary and inguinal lymph nodes. They were freely movable in the subcutaneous space, non-tender, rubbery and the biggest one was 3 × 2 cm in diameter. There was no ulceration, retraction or skin dimpling. The spleen was not palpable. Respiratory and cardiovascular examinations were unremarkable.

Laboratory evaluation revealed a WBC count of 103.300/mm3 with 6.8% polymorphonuclear leukocytes, 73% lymphocytes, 14% monocytes, 0.5% eosinophils and 5.7% basophils, and an elevated lactate dehydrogenase (LDH) level (768 U/L). Evaluation of the peripheral blood smear revealed 1% neutrophils, 97% lymphocytes, 1% monocytes, and 1% eosinophils with anisocytosis, normochromic red blood cells and a normal distribution of platelets. Although the majority of lymphocytes showed the classical morphology, a small proportion of them were larger. Smudge and prolymphocytoid cells were also seen. Bone marrow assessment by flow cytometry revealed neoplastic cells positive for CD5, CD19 and

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CD20, and was consistent with CLL. After the diagnosis of CLL was established the patient was entered into a fludarabine treatment protocol. He was followed up with three cycles of chemotherapy for several years.

When he applied to our clinic in 2009, he experienced progressive weakness, dyspnea and headache with facial and cervical swelling, occurring a week before the present hospital admission. The patient had also developed edema of his right arm five days prior. On admission, he was restless, anxious and febrile (38.3 °C) with mild tachypnea (24 breaths/min) and a heart rate of 120 beats per minute. His oxygen saturation, measured by pulse oximetry, was 88% while breathing room air. Physical examination revealed a distended right jugular vein, massive edema of the neck and right upper extremity, and enlargement of the cervical, supraclavicular and axillary lymph nodes. The patient had an ECOG performance status of 3–4.

Chest X-ray taken on admission showed bilateral pleural effusion, cardiomegaly and mediastinal widening (Figs. 1 and 2). An

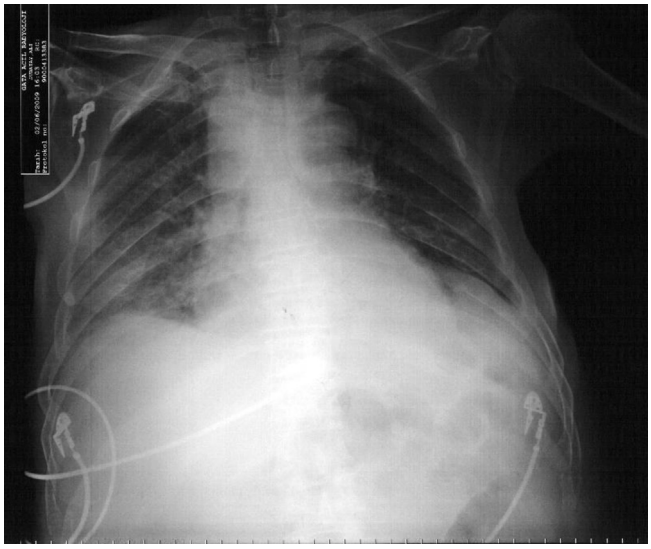

Fig. 1. Bilateral pleural effusion, cardiomegaly and mediastinal widening.

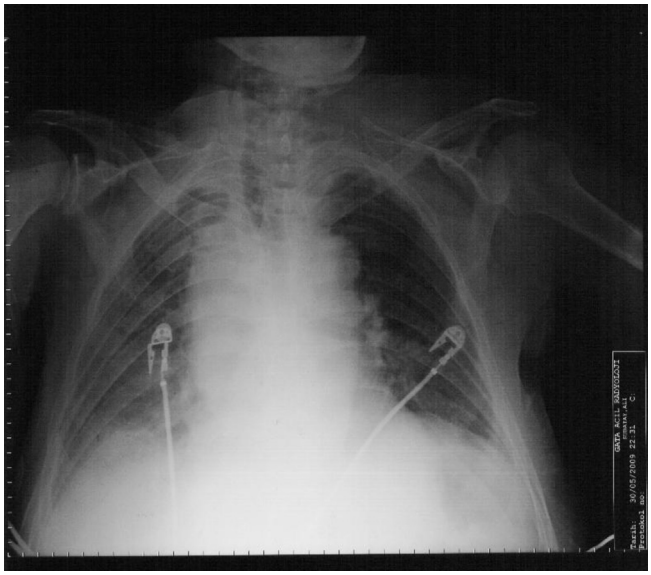

Fig. 2. Bilateral pleural effusion, cardiomegaly and mediastinal widening.

echocardiographic examination revealed pericardial effusion (20 mm in the lateral wall of the right atrium, 16 mm in the posterior wall of the left atrium, 17 mm at the apex of the right ventricle and 9 mm at the apex of the left ventricle) with normal left ventricular systolic function (ejection fraction of 60%). Inferior vena cava diameter and collapsibility were 17 mm and greater than 50%, respectively.

The patient was submitted to left supraclavicular lymph node biopsy, the result of which was diffuse large B cell lymphoma. The microscopic findings of the resected nodule revealed large, atypical lymphoid cells with prominent nucleoli and basophilic cytoplasm. Immunohistochemical staining showed that the neoplastic cells had CD20, CD79a, IgM, kappa light chain and MUM-1 expression. The expression of Ki-67 proliferation index was 70%.

When the diagnosis of Richter's syndrome was established he received both glucocorticoid therapy (dexamethasone, 4 mg every 6 h) and radiotherapy (a total dose of 400 cGy in 2 daily fractions of 200 cGy) to mediastinal area as initial treatment, but unfortunately he died on the second day. Although the disease presented with a rapidly progressive course, there was no laboratory evidence of tumor lysis syndrome in the present patient.

3. Discussion

The onset of RT is a serious complication in CLL patients and is manifested by a sudden clinical deterioration with a rapid development of lymphadenopathy and/or splenomegaly, and deteriorating “B” symptoms. The percentage of patients with elevated serum LDH levels is significantly higher in patients with RT than in those with CLL (50–80% vs. 8%).[6] All of these features were present in our patient.

The most valuable imaging study to identify SVCS is contrast enhanced CT of the chest.[7] MRI may be considered for patients who cannot tolerate the intravenous contrast agent.[8] Venography may be useful when a stent placement or a vascular surgery is planned.[9] In the present case, the existence of SVCS was established through chest X-ray and aforementioned physical findings. Because of his poor performance status, the present patient could not undergo CT scanning or MRI of the chest. It is necessary to perform a biopsy of the enlarging lymphadenopathy (likely site of transformation) to ascertain the diagnosis. Accordingly, the lymph node biopsy confirmed the transformation of CLL into large B cell lymphoma in the present patient.

The goals in the management of SVCS are treatment of the primary malignant process and relief of the life threatening symptoms.[4] Outcomes of patients with RT have historically been reported to be invariably fatal if the disease is left untreated.[10] Both glucocorticoid therapy and radiotherapy were utilized in an attempt to reduce the tumor burden and to relieve symptoms of obstruction. Unfortunately, the patient was non-respondent to these treatment modalities and died within a short time.

Because of its malignant potential, RT should always be considered in the differential diagnosis of SVCS in patients with CLL.

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