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Case Study

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Cutaneous Intravascular/Angiotropic Lymphoma Following a Septic Shock Episode. Case Report and Literature Review

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Abstract

Angiotropic lymphoma is a rare aggressive disease characterized by exclusive or predominant accumulation of malignant lymphoid cells within the lumen of small arteries, veins and capillaries. We describe a 74-year-old female patient who presented at the department of dermatology with widespread cutaneous telangiectasia and generalized edema. No neurologic symptoms were present during the course of these clinical manifestations. After close-up examination and further laboratory and radiological studies, the final diagnosis of cutaneous intravascular lymphoma was made in the histopathological report. Immunochemistry evaluation confirmed a B-cell subtype. Diagnosis of this rare disease, in most cases, is achieved by surgical biopsy. The biopsy and immunohistochemistry have increased the chances of an ante mortem diagnosis. Afterward, the patient was referred to Hematologic Department to follow the combined chemotherapy treatment, which resulted to be successful, and the cutaneous lesions began to disappear.

Keywords: Angiotropic, Lymphoma, Immunohistochemistry, Telangiectasia

Introduction

Angiotropic lymphoma is an extremely rare, aggressive subtype of B-cell lymphoma, characterized by a malignant proliferation of B-lymphocytes within the intraluminal space of capillaries, venules or small arteries of the organs. Intravascular (angiotropic) lymphoma was first described by Pfleger and Tappeiner in 1959 as "angioendotheliomatosis proliferans systematisata." Originally, the proliferating intravascular cells were thought to be of endothelial origin, but the immunohistochemical studies have established that they are B, or rarely T, lymphoid cells [1-4]. The lymphoma presents itself with nonspecific features that usually turn out to be misleading in the path of finding the proper diagnosis [1]. Men and women are equally affected by it [2]. It has a vividly wide representation, especially on the skin and central nervous system although practically every single organ can be affected by a great variety of clinically different presentations. The mechanism for the selective intravascular trapping of neoplastic cells in angiotropic lymphoma remains mostly unknown. The prognosis of this aggressive cutaneous lymphoma is poor because of late diagnosis and therapy in the majority of cases the course of IL is generally fatal, and most patients die within 1 year after the diagnosis except for purely cutaneous cases.

Case Report

A 74-year-old female patient was presented at the Department of Dermatology because of some widespread lesions in her body that put her in great discomfort. She also complained of a general fatigue. The lesions began one and a half year ago, initially localized on a small area but then began to spread all over her body. Before the skin lesions appeared, she had an episode of an Ischemic stroke. The lesions generally manifested themselves in the trunk and upper extremities. Her past medical history includes anemia, hypothyroidism and recurrent urinary tract infections. During the previous year, she experienced quite an immense weight loss. She mentioned an episode of being bitten by a dog, which resulted in the wound being badly infected, so she needed hospitalization. She experienced sepsis and seizures when hospitalized. Cutaneous lesions began to appear shortly after this incident.

Laboratory Assessments Showed: WBC 3.1 x 10^3/mm^3, RBC 3.43 x 10^6/mm^3 Hemoglobin 9.1 g/dl, Hematocrit 29.9 %, PLT 145 x 10^3/mm^3. Immunological tests showed ANA +, anti dsDNA -, ENA screen 1.6, scl 70 -, RO52 +, JO1 -, SSA -, SSB -, SM -, A-AMA -. Glucose 85 mg/dl, LDH 278 U/L, ALP 66 U/L, total protein 7.0 g/dl, albumin 4.0 g/dl, urea 40 mg/dl, creatinine 0.8mg/dl, AST 23 U/L, ALT 9 U/L.

CT-Scan of the Cranial Region Showed: Hyper dense right suprabulbar lesion infiltrating the cortex. (MRI examination was suggested). Regarding the thoracic region the scan images showed cardiomegaly and axillary lymph nodes, no mediastinal lymph nodes, bilateral interstitial pulmonary fibrosis was encountered. A small nodule in the right lung was noted.

Clinical examination showed generalized edema and hepatosplenomegaly along with a widespread of cutaneous telangiectasia and pathological angio-genesis on skin. Lesions were indurated on palpation. She did not show any palpable regional lymphadenopathy but she had some swellings in the neck area.

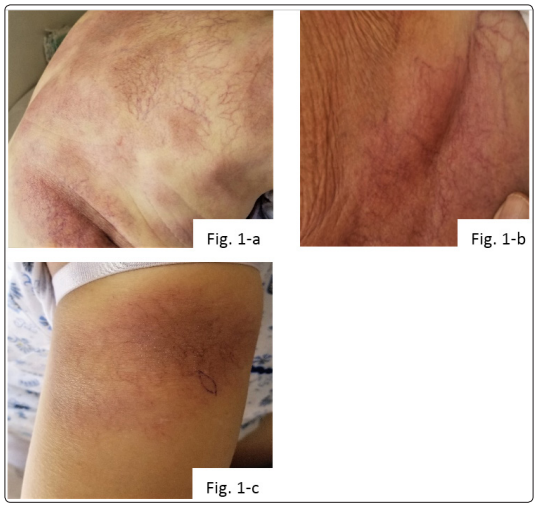

Figure 1 (a-c): Clinical examination revealed dilated blood vessels typical of telangiectasia. These lesions were noted sparsed all over the skin of the shoulders, arms and neck, the latter characterized by some swelling

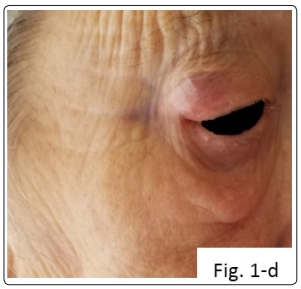

Figure 1-d: Examination of the face showed periorbital edema

According to her clinical presentation and laboratory values a presumptive diagnosis of connective tissue disorder was firstly given. Clinical differential diagnosis included mixed connective tissue disease, scleroderma, mastocytosis (telangiectasia macularis eruptiva perstans), mycosis fungoides, B-cell lymphoma and idiopathic multifocal fibrosclerosis.

The lesion was excised for further histopathological examination.

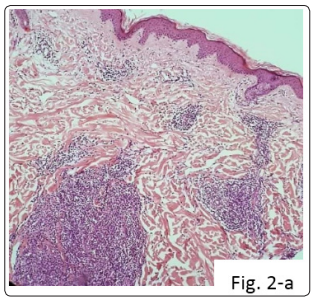

Figure 2-a: H&E stained sections revealed atypical lymphoid proliferation around the vessels within the dermis and in some areas filling lumen of the vessels

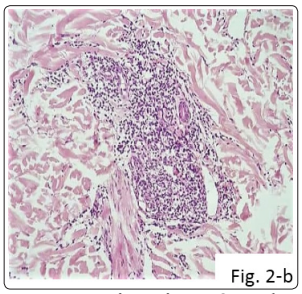

Figure 2-b: Medium power view in H&E showing perivascular infiltrates around the vessels and neoplastic cells filling the lumen of the vessels

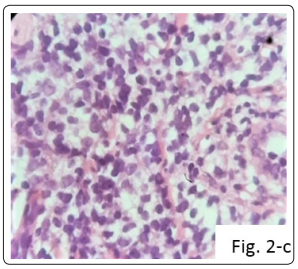

Figure 2-c: High power view showing large pleomorphic lymphoid cells with pleomorphic nuclei

Light microscopic findings in the H&E-stained sections from the skin biopsy showed showed dilated small vessels throughout the whole thickness of the dermis with periadnexal accentuation and large hyperchromatic cells filling the lumen of the vessels within the dermis. Histopathologically, the differential diagnosis included other entities showing intravascular proliferation, especially reactive angioendotheliomatosis. Further microscopic examination revealed predominant intra and perivascular accumulation of atypical lymphocytes, suspicious of a proliferative lymphoid disorder, so further immunostains were required.

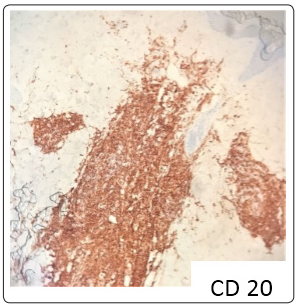

Figure 3-a: CD 20 is intensively positive within the tumor cells, revealing their immunophenotype of mature peripheral B- cells.

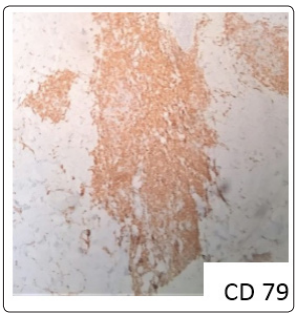

Figure 3-b: CD79a expression in the tumor cells, confirming their B cell origin

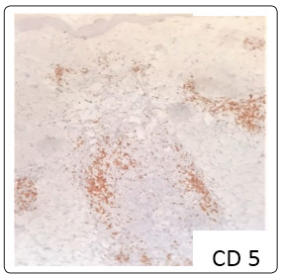

Figure 3-c: CD5 expression on immunostaining of formalin-fixed, paraffin-embedded sections, the neoplastic cells around the vessels and intravascular, showed strong positivity for CD5

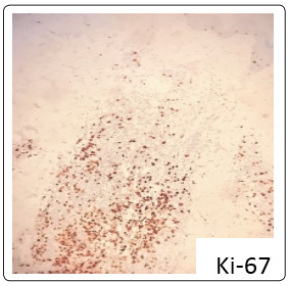

Figure 3-d: Ki67 showing a relatively high proliferation rate within the tumor cells.

The neoplastic cells showed positivity for lambda chain, CD20, CD79, CD5 and BCL-2. No expression was noted with CD10 antibodies and Cyclin-D1. Ki67 was intensively positive in the neoplastic cells showing a high proliferation rate (up to 65%). CD20 and CD79a immunostains were strongly positive on the neoplastic cells within the vascular structures, confirming the diagnosis of angiotropic large B-cell lymphoma. Histopathological examination in H&E stained sections and Immunohistochemistry evaluation concluded the diagnosis of Intravascular/angiotropic lymphoma. Molecular biology studies could not be done in our country. The patient was referred to the hematology department for further treatment. She began the combined chemotherapy with rituximab, endoxane and systemic glucocorticosteroids. Rituximab was divided in 6 cycles, 21-28 days apart from each other.

Discussion

Angiotropic lymphoma is a rare subtype of large B-cell lymphoma. The estimated 5-year survival reported by the EORTC is 50%. Intravascular/angiotropic lymphoma is a multiorgan disease, with the skin and central nervous system being most commonly affected [3]. The immunophenotype of B cell lineage is a phenotypically heterogeneous form of large B cell lymphoma. On the basis of CD5 expression, two subgroups with a presumed different histogenesis have been recognized, but the biologic significance of CD5 expression in angiotropic lymphoma of B cell lineage remains unclear [4-7]. In reference to its rarity and variability of the clinical presentations, it is very difficult to diagnose it antemortem. The skin is the second most common site of involvement. As dermatologists, we should never underestimate the appearance of an unusual widespread cutaneous telangiectasia and pathological angiogenesis on skin, as it may be an important representational feature of an underlying aggressive type of lymphoma [8]. An effective communication and collaboration between dermatologist and pathologist is crucial to make an accurate diagnosis and start the appropriate treatment [9]. The course of the disease can be rapidly fatal if left untreated, given the fact that even a banal infection could be life threatening because of the weak immune system caused by the disease (the dog bite in our case report) [10]. An aggressive therapy may result in the improvement of the clinical course and prolong the time of remission, increasing the survival rate on these patients. Although the prognosis is poor, it has improved with the recent introduction of rituximab to combination chemotherapy [11-23].

Conclusions

The clinical, histopathologic and immunohistochemical features of the skin lesions investigated in this study fulfill the criteria for the diagnosis of Intravascular/angiotropic lymphoma of B cell lineage. It is yet unclear whether cutaneous angiotrophic lymphoma is a unique entity or represents a heterogeneous disease within the spectrum of large B cell lymphomas. However early detection, accurate diagnosis and appropriate chemotherapeutic management can be promising to increase the disease-free survival rate.

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