Paraneoplastic leukocytoclastic vasculitis in chronic lymphoid leukemia

ABSTRACT

A 50-year-old female who was a known case of chronic lymphoid leukemia (CLL) developed ecchymoses, purpuric spots with papules, some nodules (1-3 mm) and crusts all over the body associated with severe burning and itching along with exaggeration of CLL. The lesions were more prominent on lower limbs and face. Skin biopsy was reported as leukocytoclastic vasculitis. These lesions regressed after treatment with leukeran and glucocorticoids.

INTRODUCTION

Leukocytoclastic vasculitis is a small-vessel systemic vasculitis characterized by the involvement of the skin as palpable purpura. Systemic manifestations include, most frequently, fever, arthralgias and arthritis; and, less commonly, renal, neurological or gastrointestinal compromise. This disorder is caused by hypersensitivity mechanisms associated with different antigens, mainly in infections, drugs or autoantigens in connective tissue diseases.

In 1986, Longley et al. first suggested that malignant neoplasms might produce antigens and consequently cause paraneoplastic vasculitis. In the same year, McLean established two necessary criteria to define paraneoplastic vasculitis: first, the simultaneous appearance of both vasculitis and neoplasms; and second, their parallel course. From that date to 1993, Kurzrock and Cohen identified a total of 200 patients with both cancer and paraneoplastic vasculitis reported in the world literature, of whom 88 presented cutaneous leukocytoclastic vasculitis. Most of these cases of vasculitis occurred in patients with hematological malignant neoplasms (two-thirds of the total number of cases of paraneoplastic vasculitis).

The pathogenetic mechanisms for the development of paraneoplastic vasculitis remain unknown. In addition, the significantly stronger association between vasculitis and hematological malignancies as compared with solid tumors, as well as the different tendency for each hematological disorder to develop vasculitis, is poorly understood. The incidence of paraneoplastic vasculitis in patients with CLL is very low – approximately 0.1-2%. We report here a case of paraneoplastic vasculitis in a patient with CLL.

CASE REPORT

A 50-year-old female patient presented to radiotherapy oncology outpatient department (OPD) on November 7, 2001, with complaint of swelling bilateral neck since one month. There was no history of B-symptoms. She was not suffering from any chronic illness.

On examination, her general condition was good and she was not anemic. There was left level II, 1 x 1 cm; and level IV, 1.5 x 1 cm, lymph node. Bilateral axillary lymph nodes were also enlarged (2 x 2 cm). Her chest, cardiovascular and abdominal examinations were within normal limits.

On investigation, her hemoglobin was 11.4 gm%; total leukocyte count, (TLC) 202,000; lymphocytosis, 80%; platelets, 3.01 x 10^5; and erythrocyte sedimentation rate, 26 mm in first hour. On her peripheral blood film, red blood cells were normocytic normochromic, with no abnormal cell; white blood cells were in high limit; and platelets were adequate. Fine needle aspiration cytology from the neck nodes was reported as low-grade non-Hodgkin’s lymphoma. Her chest X-ray and ultrasound of abdomen were normal. Bone marrow aspiration was reported as CLL [Figure 1].

With the diagnosis of stage I (A) CLL, she was started on leukeran 5 mg and prednisolone 10 mg – both twice daily, with weekly complete blood counts, till
her TLC was 30,500, when leukenan and prednisolone were reduced to once daily. She was all right till January 30, 2004, when she developed small papules, blisters with erythematous nodules in bilateral gluteal regions. These subsided after taking acyclovir. The lesions reappeared on April 8, 2004 and progressed to back. At that time her TLC was 103,000; therefore, prednisolone and leukenan doses were made ‘twice daily.’ The lesions subsided subsequently.

On August 28, 2004, she developed ecchymoses, purpuric spots with papules, some nodules (1-3 mm) and crusts all over the body associated with severe burning and itching. These used to subside on their own and itching was controlled with antihistamines. Subsequently, she developed small erythematous nodular rashes over face and neck on October 30, 2004. Patient was referred to dermatology OPD, where biopsy from the skin lesion was taken and it was reported as leukocytoclastic vasculitis [Figure 2]. There was no evidence of infection (pyogenic bacteria; fungal, mycobacterial and viral infections; pneumocystis carinii). Hemoglobin was 11.2 gm%, TLC was 28,100, platelets were 2.01 x 10^5, renal and liver function tests were normal. Blood cultures, HIV test, cytomegalovirus, Epstein-Barr virus, hepatitis B and C, antinuclear antibodies and rheumatoid factor were negative. Dose of prednisolone was increased to 25 mg and leukenan 5 mg once daily; lesions subsided subsequently. Her last follow-up was on April 12, 2005; there were no such lesions.

**DISCUSSION**

The association between lymphoma and vasculitis is rare. Cutaneous leukocytoclastic vasculitis is the most frequently observed paraneoplastic vasculitis; this clinicopathological type constitutes nearly 30-40% of all paraneoplastic vasculitis. In 1997, Hayem et al reported that in most patients with cutaneous leukocytoclastic and paraneoplastic vasculitis, the associated tumoral disease is a hematological malignancy (90%), being only 10% of the cases in relation to solid tumors. The majority of individuals with leukocytoclastic vasculitis secondary to hematological disorders suffer from lymphoid neoplasms, most commonly lymphoproliferative (nearly 20% of cases) or myelodysplastic syndrome (3-5% of cases). Among lymphoid malignancies, the association between hairy cell leukemia and leukocytoclastic vasculitis, polyarteritis nodosa or temporal arteritis is the most common.

Many variations have been observed in the time between the onset of vasculitis and of malignancy. In more than 50%, it occurs before or concurrent with cancer, but the common feature in all of them is the tendency towards vasculitis healing, once treatment of CLL has been started. Our patient presented marked improvement in cutaneous lesions after starting oral corticosteroids treatment along with specific treatment with leukenan for CLL.

In general, the signs and symptoms of paraneoplastic vasculitis are similar to those in patients who do not suffer from an underlying cancer. Histological features of leukocytoclastic paraneoplastic vasculitis do not differ from those identified in different etiological vasculitis.[1] Our patient’s skin biopsy specimens showed characteristic features of leukocytoclastic vasculitis characterized by polymorphonuclear cell infiltrates, nuclear dust and fibrinoid changes in small dermal vessels.

The mechanisms of vasculitis associated with malignancy are complex, including formation of immune complexes, polyclonal activation of B-lymphocytes, monoclonal immunoglobulin activation, antibodies directed toward endothelial antigens, direct effect of malignancy on vascular wall or adverse reactions...
to anticancer drugs.[9] CD5-positive B cells present in certain lymphoproliferative disorders such as CLL, may have a role in these mechanisms, producing autoantibodies and monoclonal immunoglobulins with various autoantibody activities.[10]

The prognosis of paraneoplastic vasculitis depends primarily on the availability of effective treatment for the underlying malignancy. As expected for a paraneoplastic syndrome, cutaneous lesions heal after surgical removal or radiation therapy of the cancer.[6]

When a curative treatment of the neoplasm is not possible, paraneoplastic vasculitis responds to treatment with glucocorticoids alone or in combination with immunosuppressive agents.[4] In a majority of cases, deaths are due to metastatic or recurrent tumor rather than to vasculitis complications.[2,4] In conclusion, we believe that in our case, two factors suggest the paraneoplastic etiology of the vasculitis. First, its manifestations during the course of CLL. Second, the vasculitis and neoplasm followed a parallel course, with improvement in both disorders when treatment was started and later recurrences of the skin lesions coinciding with aggravation of the CLL.

Association between CLL and vasculitis is rare. Commonly manifests as cutaneous vasculitis without systemic involvement. Paraneoplastic effect of vasculitis is not constant and evolves without the influence of malignancy or treatment. Lesions usually subside with the treatment of the underlying disease.

**REFERENCES**


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