An Unusual Cause of Vascular Purpura: Recurrent Cutaneous Eosinophilic Necrotizing Vasculitis

Sir,

Eosinophilic vasculitis is a common feature of systemic vasculitis such as polyarteritis nodosa and Churg-Strauss syndrome (1) or vasculitis-complicating connective tissue diseases such as rheumatoid arthritis, Sjögren syndrome and systemic lupus erythematosus (2). Dermal perivascular eosinophilic infiltration without any necrotizing vasculitis can be found in the hypereosinophilic syndrome (3), episodic angioedema with hypereosinophilia (4) and Wells’ syndrome (5). However, clinical and histologic necrotizing vasculitis of dermal small vessels with an almost exclusively eosinophilic infiltration and without any features of the aforesaid diseases has only recently been described by Chen et al. and reported as recurrent cutaneous eosinophilic necrotizing vasculitis (6).

Only 3 cases have so far been reported by these authors. We describe here 1 more patient with a similar condition.

CASE REPORT

An 81-year-old woman was first seen in January 1996 with a 2-week history of intensely pruritic, infiltrating, necrotic purpuric and purpuric skin lesions of the lower limbs. She had no history of asthma or allergic rhinitis. She was not a drug user. This was the fourth onset of purpura and skin lesions of different ages were present: the youngest were purpuric and papular and the oldest were necrotic. The lesions were predominantly localized on the legs and feet (Fig. 1). Clinical examination also indicated angioedema of the right hand. The patient complained of recent arthralgia of both ankles and wrists without any sign of arthritis. She had neither fever nor weight loss.

There was no evidence of a peripheral neuropathy and careful examination did not disclose any cardiac, pulmonary, upper respiratory tract, central nervous system or other visceral organ involvement.

Abnormal laboratory findings included the following: white blood cell count 12.6 x 10^9/l with 31% eosinophil cells (3.9 x 10^9/l); normal: 0–0.5 x 10^9/l); erythrocyte sedimentation rate 70 mm/h (normal: 0–29 mm/h); C-reactive protein 48.8 mg/l (normal: 0–6 mg/l); and fibrinogen 5.1 g/l (normal: 2–4 g/l). Renal function as measured by endogenous creatinine clearance was normal. There was neither haematuria nor proteinuria. Liver enzyme level was normal. Serum protein electrophoresis showed hypoalbuminemia at 28.8 g/l (normal: 30–48 g/l). IgA, IgG and IgM serum levels were normal. IgE level was 81 KU/l (normal<91 KU/l). Immunoelectrophoresis of serum and urinary proteins was normal.

Search for antinuclear antibody, performed by immunofluorescence on rat liver, was slightly positive with a homogeneous pattern. A total hemolytic complement (CH50) of 135% (normal: 100±20%) C3 of 1380 mg/l (normal: 750–1400 mg/l) and C4 of 370 mg/l (normal: 100–340 mg/l) were consistent with the inflammatory context. Anti-neutrophil cytoplasmic antibodies, cryoglobulin, rheumatoid factor and hepatitis A, B and C serologic tests were all negative. Multiple urine and blood cultures remained sterile.

Stool examinations for ova and parasites were negative. Myelogram and bone marrow biopsy showed only a mild medullary hypereosinophilia without any morphologic or neoplastic changes. Blood eosinophils of the patient were purified by centrifugation on discontinuous metrizamide gradients (7). After using this separation procedure, a few of the blood eosinophils appeared degranulated and hypodense as seen in the hypereosinophilic syndrome.

Abdominal X-ray, ultrasound examination and computerized tomography did not show any abnormalities. Radiographs of the ankles and wrists were normal as were the electrocardiogram, chest X-ray, echocardiogram and electromyogram. There was no sign of a polyneuropathy or a mononeuritis simplex. Muscle biopsy showed no inflammatory lesions and no evidence of either polyarteritis nodosa or Churg-Strauss syndrome.

A first skin biopsy, performed on the youngest, non-necrotic lesion, revealed a striking, almost exclusively eosinophilic, perivascular infiltration throughout the dermis without any leukocytoclastic vasculitis or amyloid substance deposit (Fig. 2). There was no necrotizing vasculitis but there was evidence of the beginning of endothelial cell damage as demonstrated by the presence of endothelial cell urgence and extravasation of erythrocytes. A second skin biopsy was performed on a necrotic lesion and showed necrotizing vasculitis of a small artery in the deep dermis with almost exclusive infiltration by eosinophils. Using immunohistochemistry, marked deposits of eosinophil-derived neutrotrans, eosinophil peroxi- dase and eosinophil cationic protein were found in the walls of the affected vessels and surrounding areas, with both cellular and extracellular deposition. The epidermis was normal.

The patient was initially given 1 mg/kg prednisone daily and there was a dramatic and immediate improvement in both clinical and laboratory abnormalities. Twelve hours after prednisone was started, the results of laboratory studies showed a normal eosinophil blood count (0.1 x 10^9/l). Similarly, angioedema of the right hand, the youngest skin lesions and the severe itching disappeared rapidly. However, 3 weeks of treatment was needed in order to heal all the necrotic lesions.

The corticosteroids were tapered without any recurrence of skin lesions. Four months after the beginning of the treatment, the patient received 10 mg prednisone daily and clinical examination together with laboratory findings were normal. The corticosteroids were then slowly decreased. An attempt was made to decrease the daily dose of prednisone to <5 mg but purpuric lesions recurred and the

Fig. 1. Vascular purpura with necrotic lesions of the lower limbs.

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corticosteroids were increased in order to control the disease. The patient is still receiving 5 mg prednisone daily. During the last year, no evidence of visceral involvement and no recurrence of the skin lesions have been noticed. She has a normal eosinophil blood count.

DISCUSSION

Peripheral blood eosinophilia, in association with skin lesions and/or angioedema, may be found in many different diseases such as the hyper eosinophilic syndrome and vasculitis affecting small dermal vessels including Churg–Strauss syndrome, Wegener’s granulomatosis, microscopic polyangiitis, drug-related eruptions and vasculitis-complicating connective tissue diseases.

The hyper eosinophilic syndrome is a heterogeneous group of diseases with eosinophilia of >1.5 x 10^9/l persisting for >6 months in the absence of a known cause of raised eosinophil count and in association with systemic involvement or dysfunction either directly related to eosinophilia or unexplained in the given clinical setting (3). Histologically, dermal eosinophilia with perivascular eosinophil infiltration may be observed in this condition. However, true necrotizing vasculitis is very rare and palpable purpura is not a common feature of this disease. Moreover, our patient had no evidence of systemic involvement. Indeed, we did not find any evidence of neurologic, cardiac or pulmonary manifestations, making the diagnosis of hyper eosinophilic syndrome very unlikely.

Cutaneous small-vessel vasculitis in Churg–Strauss syndrome is a neutrophil-rich leukocytoclastic vasculitis. In our patient, the absence of allergic diathesis, lung involvement, mononeuritis simplex, fever and weight loss, in association with the lack of extravascular granuloma and dermal small vessel neutrophil-rich leukocytoclastic vasculitis, allowed us to eliminate the diagnosis of Churg–Strauss syndrome. By the same token, the absence of anticytoplasmic neutrophil antibodies and lung, upper respiratory tract or renal abnormalities is not compatible with a diagnosis of Wegener’s granulomatosis or microscopic polyangiitis.

The drug-related eruptions may be associated with cutaneous vasculitis. However, lymphocytic vasculitis is the most frequent histologic finding, with occasional occurrence of leukocytoclastic vasculitis. None of these symptoms were found in our patient. Moreover, the patient denied any drug consumption.

Hypereosinophilia and eosinophilic vasculitis may be found in connective tissue diseases like rheumatoid arthritis, Sjögren syndrome and systemic lupus erythematosus. Histologically, these diseases are necrotizing vasculitis of dermal small vessels with a predominance of eosinophils intermingled with neutrophilic infiltration. However, our patient had none of the common clinical or paraclinical features of these conditions. Moreover, almost exclusively eosinophilic infiltration without any leukocytoclasia is not a feature of connective tissue diseases with vasculitis. The lack of associated extracutaneous symptoms and the almost exclusively eosinophilic perivascular infiltration were consistent with the diagnosis of recurrent cutaneous eosinophilic necrotizing vasculitis (6).

CONCLUSION

Skin lesions show a rapid response to corticosteroids. The disease follows a benign course but attempts to discontinue systemic steroid therapy always result in recurrence.

REFERENCES


Accepted April 28, 2000.

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