Carbamazepine induced severe cutaneous vasculitis

Sir,
Adverse drug reaction is a very common presentation in any skin outpatient department (OPD). These reactions can vary from self limited maculopapular eruption to fatal conditions like toxic epidermal necrolysis. Drug induced vasculitis is one of them and approximately 10-15% of acute cutaneous vasculitis cases are due to drugs.

Leukocytoclastic vasculitis (LCV) involves mainly small vessels in the skin and generally manifests as palpable purpura on the lower extremities. Other features include hemorrhagic bullae, ulcers, nodules, and occasional digital necrosis.

Some common drugs which can cause cutaneous vasculitis include penicillins, sulphonamides, NSAIDs, quinolones, propylthiouracil, allopurinol, procainamide, antiepileptics and recently anti-TNF agents.

Among the antiepileptic drugs phenytoin, barbiturates and carbamazepine are used commonly. Carbamazepine is a drug widely used in the treatment of partial and generalized tonic clonic seizures, trigeminal neuralgia and other pain syndromes, affective disorders and paroxysmal symptoms of multiple sclerosis. Common side effects are diplopia, dizziness, headache, nausea, and drug rash. Less common side effects include blood dyscrasias, toxic hepatitis, hyponatraemia, orofacial dyskinesia, and cardiac arrhythmias. Relatively common cutaneous adverse reactions of carbamazepine include erythematous, morbilliform, urticarial or purpuric eruptions, toxic epidermal necrosis and photosensitivity. Rarely LE-like syndrome, dermatomyositis, and erythema multiforme and carbamazepine hypersensitivity syndrome (CHS) have been reported.

Carbamazepine as a cause of cutaneous vasculitis appears extremely rare and we could find only a few such reported cases in the literature.

Here, we report a case of carbamazepine induced severe necrotizing cutaneous vasculitis.

A 45-year old male, known case of grand mal epilepsy was on treatment with phenytoin 100 mg thrice daily since five years. Despite this he had an epileptic episode and phenytoin was changed to carbamazepine 200 mg twice daily. One week after starting carbamazepine, he began to develop multiple painful red raised lesions bilaterally over the legs, joint pains in both knees and ankles and swelling of both feet. He also complained of generalized weakness and malaise. He was normotensive and non diabetic. There was no history of fever, respiratory or urinary complaints, jaundice, connective tissue disease, an underlying malignancy or recent vaccinations.

On examination, there were multiple palpable purpuric tender plaques and papules with hemorrhagic vesicles and necrosis at places over both lower legs [Figure 1]. There was also severe edema around both ankles and joint movements were painful. Palms, soles and mucous membranes were normal. His vital parameters were within normal limits. No other cutaneous or systemic abnormality was found. A clinical diagnosis of drug induced vasculitis was made. Carbamazepine was already discontinued by neurologist.

Investigations revealed hemoglobin 14 gm%, erythrocyte sedimentation rate of 40 mm at the end of one hour, white blood count 11,200 mm$^3$ and platelets 2,22,000 mm$^3$.

Blood coagulation profile, liver and kidney function tests, urine and stool analysis, and throat swab revealed no abnormality. Rheumatoid factor, antinuclear antibody was negative and complements three and four were normal. A skin biopsy taken from a representative lesion revealed epidermal necrosis and a dense perivascular lymphohistiocytic infiltration with fibrin deposition in the vessel walls, red blood cell extravasation, neutrophilic nuclear dust, and endothelial swelling suggestive of leukocytoclastic vasculitis [Figure 2].

On clinicopathologic correlation a diagnosis of carbamazepine induced leucocytoclastic vasculitis was made.

Patient was given on clavulanate potentiated amoxicillin 625 twice daily for seven days, oral prednisolone 50 mg daily with ranitidine 150 mg twice daily, aspirin 300 mg twice daily, oral calcium and potassium supplement with local wound care and bed rest. After 10 days prednisolone was tapered to 40 mg daily and colchicine 0.5 mg twice daily.
was added. No new lesions were seen. Pain and swelling reduced gradually. The patient is being followed up and is symptomatically better.

Carbamazepine is known to cause systemic vasculitis rarely. Carbamazepine-induced granulomatous necrotizing angiitis with acute renal failure has been reported.[3‑5] No systemic problem was found in our patient. Carbamazepine induced Kawasaki-like syndrome has also been reported.[6] There is also a report of carbamazepine induced thrombocytopenia and leucopenia complicated by Henoch-Schönlein purpura symptoms. However purely cutaneous leukocytoclastic vasculitis is reported only once.[7]

Drug-induced vasculitis represents approximately 10% of acute cutaneous vasculitis cases. It can be difficult to diagnose and is often a diagnosis of exclusion. Other causes for cutaneous vasculitis such as infections, autoimmune diseases or neoplasms, must be excluded. Early recognition and withdrawal of the precipitating medication is mandatory to improve the outcome.[8]

Carbamazepine is a commonly used drug and the dermatologist should be aware of this rare side effect. We report this case to increase awareness among dermatologists about this rare side effect of carbamazepine.

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