A 20-year-old girl presented with a one-week history of fever and chills, malaise, generalized erythema (including the face, trunk, back and extremities), edema (initially the face and then lower limbs) and hoarseness (Figure 1).

Physical examination revealed low-grade fever, jaundice, lymphadenopathy (posterior cervical, submandibular, <1 cm, no axillary, no inguinal). Dermatological examination showed diffuse erythema (erythroderma), edema (generalized, especially periorbital and lips), and mild jaundice (scleral and sublingual). No mucosal lesions or nail changes were seen. She had a history of epilepsy since 3 years ago and had been under treatment with sodium valproate until 1.5 month ago when she discontinued the medication. She had an epileptic attack then and therefore carbamazepine was started for her. Positive laboratory findings were anemia, leukocytosis with eosinophilia (20%), elevated liver enzymes, and direct hyperbilirubinemia. Other routine laboratory tests, electrocardiogram, chest x-ray, and viral markers (including HBV, HCV and EBV) were unremarkable. Abdominal sonography revealed thickening of gall bladder and fluid in posterior choledosac.

A punch biopsy was taken from her forearm skin.

What is your diagnosis?

Move on the next page for the answer and discussion.
Diagnosis

Drug reaction with eosinophilia and systemic symptoms (Hypersensitivity Syndrome)

Microscopic findings

Microscopic study revealed the lymphocytic infiltrate and eosinophils in the superficial dermis associated with dermal edema (Figure 2).

The histological finding in addition to the clinical features and lab findings were compatible with the diagnosis of drug reaction with eosinophilia and systemic symptoms (DRESS).

DISCUSSION

Drug reaction with eosinophilia and systemic symptoms (hypersensitivity syndrome) refers to a specific severe drug reaction with systemic manifestations. Fever, lymphadenopathy, rash, and internal organ involvement with marked eosinophilia form the main manifestations. The most frequently involved organ is the liver, followed by the kidneys and lungs 1.

Skin eruption is polymorphic and usually begins as a morbilliform eruption of the face, upper trunk, and extremities which may progress to exfoliative erythroderma. Edema of the face is the hallmark of hypersensitivity syndrome and a frequent finding. The most common etiologies are anticonvulsants, sulfonamides, dapsone, allopurinol, minocycline, and gold salt 1.

The pathophysiology of this syndrome remains uncertain, but a defect in detoxification of causative drug, infections such as human herpes virus type six (HHV 6), and immunological imbalance have been suggested 1. Generally, mortality of the hypersensitivity syndrome is about 10% and more often occurs in patients with severe multi-organ involvement 2.

Hypersensitivity syndrome was first introduced in 1996 by Bocquet et al 2. The accurate incidence of this syndrome is unknown because of the variability in clinical presentations and lack of strict diagnostic criteria 3. Its differential diagnosis includes other cutaneous drug eruptions, acute viral infections, idiopathic hypereosinophilic syndrome, lymphoma, pseudolymphoma, and hepatitis (infectious or autoimmune) 4,5.

Our case had most of the clinical features of the hypersensitivity syndrome with a positive history of the consumption of an anticonvulsant drug for about 6 weeks before the beginning of the eruption. This time period is compatible with the onset of the hypersensitivity syndrome (2 to 6 weeks after administration of the responsible drug) 3.

The first line therapy for hypersensitivity syndrome is corticosteroids. Topical high-potency corticosteroids may be helpful for skin manifestations in milder cases while systemic corticosteroids are recommended for life-threatening organ involvement 1-3.

Before any investigation, we discontinued the responsible drug and after excluding infectious etiologies, prednisolone 30 mg daily was started. Two weeks later, a significant improvement was seen and then prednisolone was tapered to 20 mg daily. She was on 20 mg prednisolone for about one month and after that, the dose was tapered slowly in order to reduce the relapse rate. After 3 months when prednisolone was discontinued, she was symptom free and no recurrence was noted in the follow-up visits.

REFERENCES