Drug reaction with eosinophilia and systemic symptoms mimicking Kawasaki disease

Sir,

Drug reaction with eosinophilia and systemic symptoms (DRESS) is one of the most difficult adverse drug reaction patterns to diagnose due to its wide spectrum of manifestations mimicking autoimmune, infective or neoplastic diseases. Here, we report a child who developed DRESS closely resembling Kawasaki disease (KD).

A 6-year-old boy (body weight 14 kg) was referred to our tertiary care institution as a case of KD not responding to treatment with intravenous immunoglobulin G (IV IG). His medical history revealed cerebral palsy and myoclonic seizures. He was receiving sodium valproate for the past 2 years, phenytoin for 6 months and lamotrigine (started at 12.5 mg daily dose, which was increased to 25 mg daily after 7 days) for the past 3 weeks. The child was admitted 7 days back in a nearby hospital with high-grade fever, generalized pruritic maculopapular rash [Figure 1], bilateral non purulent conjunctivitis, dryness and scaling of lips, strawberry tongue [Figure 2], cervical and axillary lymphadenopathy and facial and pedal edema. He developed hypotension on the 2nd day of admission (necessitating dopamine infusion). Laboratory investigations revealed polymorphonuclear leukocytosis, elevated erythrocyte sedimentation rate and C-reactive protein levels and 2 times elevation of liver transaminases. Peripheral smear analysis showed 9% atypical lymphocytes and eosinophilia with no evidence of malarial parasites or blast forms. Ultrasound examination of abdomen and pelvis, electrocardiogram, echocardiography and chest radiography were within normal limits. Antinuclear antibody profile and serology for human immune deficiency virus infection, infectious mononucleosis, leptospirosis, typhoid fever, rickettsia, dengue, chikungunya and hepatitis B, C and A infections were negative. Blood culture was sterile. Though there was no evidence of cardiac involvement, as the child satisfied the criteria for KD, a provisional diagnosis of KD was made.[1] IV IgG administered at a dose of 400 mg/kg body weight per day for 5 days achieved only correction of hypotension. Hence, the child was referred to us.

At the time of admission in our institution his temperature was 40°C, respiratory rate 28/min and blood pressure was 100/70 mm mercury on the right upper limb in the supine position. A repeat echocardiogram was again within normal limits. Further investigations revealed the persistence of liver function derangement and an absolute eosinophil count of 1586. We considered the possibility of DRESS to lamotrigine as he satisfied the criteria for definite DRESS as per RegiSCAR DRESS validation scoring.[2,3] Substituting lamotrigine with levetiracetam and introducing prednisolone (1 mg/kg body weight) tapered over 3 weeks achieved resolution of the disease.

Clear temporal relationship between the onset of drug intake and the appearance of adverse event and the resolution of symptoms following withdrawal of the suspected drug along with clinical course of the disease and the investigation data ruling out most of the other probable etiologies was suggestive of probable drug reaction on Naranjo probability scale.[4]

Rash involving more than 50% of body surface area (1 point), lymphadenopathy in two different anatomical sites more than 1 cm in size (1 point), atypical lymphocytes in peripheral smear (1 point), AEC above 1500 cells/mm^3 (2 points) and negative serology for ANA and infections due to hepatitis A, B and C viruses and sterile blood culture (1 point) in our patient added to a score of 6 indicating definite DRESS according to RegiSCAR DRESS validation scoring.[2,3]

A higher risk for lamotrigine induced drug reaction is noted in children especially, those co-medicated with sodium valproate.[5]

There are standard guidelines regarding the initial dosing and subsequent titration of lamotrigine so as to minimize the risk of adverse drug reactions.[6] Non-adherence to this might have contributed to the adverse event in our patient.

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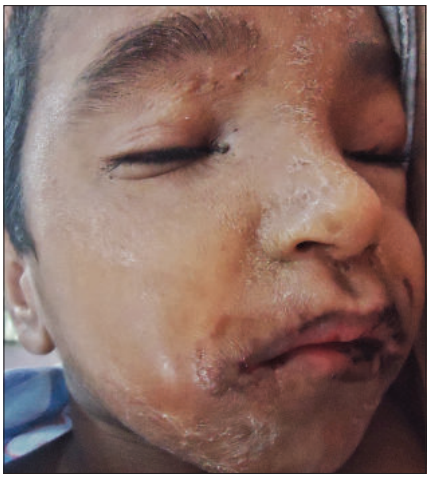

Figure 1: Maculopapular rash and scaling on face

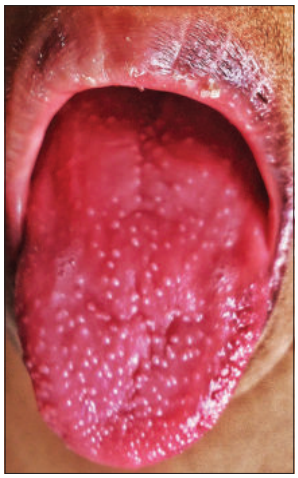

Figure 2: Strawberry tongue

Drug reaction with eosinophilia and systemic symptoms especially in children is often difficult to distinguish from viral exanthema. Reactivation of human herpes viruses (HHV), especially HHV 6 and 7 are well known to precipitate severe DRESS. Currently, it is believed that the term drug-induced hypersensitivity syndrome should be used to differentiate severe DRESS with HHV reactivation from less severe forms without any evidence of viral reactivation.[7] Irrespective of the reactivation status both types of patients are managed with the withdrawal of the culprit drug and the administration of steroids. The HHV 6 reactivation status in our patient remains unknown.

The major challenge we faced was in distinguishing between DRESS and KD. Both these conditions are diagnoses of exclusion. Many clinical features are shared by both including persistent fever, rash, cervical lymphadenopathy, conjunctival congestion, systemic involvement and dermatological manifestations, including strawberry tongue as observed in our patient.[8] DRESS should be considered in any patient who has been started on drugs (in the past 3 months) well known to induce it.

Drug reaction with eosinophilia and systemic symptoms closely mimicking KD has been reported following lamotrigine and aromatic anticonvulsants.[9,10] Conversely Chinen and Piecuch. reported an instance when KD was misdiagnosed as DHS.[11]

Kawasaki disease usually responds well to IV IgG within 72 h of administration. IV IgG resistant KD is rarely reported which is treated with methyl prednisolone pulse therapy. This possibility was unlikely in our patient as IV IgG resistant KD is a severe form, but repeated echocardiography was within normal limits in our child.[12,13]

The French Society of Dermatology recommends systemic steroids with IVIG (400 m g/kg for 5 days) for DRESS with life - threatening signs and opined that IVIG without steroids may not guarantee the desired outcome as happened in our patient.[7] IV IG act by forming immune complexes that block IgG Fc receptors and by neutralizing autoantibodies.[14]

We report this case to stress the significance of considering DRESS when any patient who has started taking drugs known to produce this adverse reaction during the past 3–4 months, presents with pyrexia of unknown origin and also to highlight the importance of systemic steroids in the treatment of DRESS.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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