Fatal outcome of DRESS syndrome associated with esomeprazole

Sir,

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a severe, potentially life-threatening condition with a mortality rate of about 10%. This syndrome is characterized by the clinical association of fever, rash, and internal organ involvement.[1] It has been described mainly with aromatic anticonvulsants; association with proton pump inhibitors (PPIs) is extremely rare.[2-4] We report a case of DRESS syndrome associated with esomeprazole with fatal outcome.

An 84-year-old woman, with no chronic diseases and no known drug allergies complained of dyspepsia and was prescribed esomeprazole 20 mg/day. On the 8th day after the initiation of treatment, the patient presented with fever and a rash involving the trunk. She was admitted to Habib Thameur hospital (Tunis, Tunisia). Subsequent to the admission, her general condition deteriorated. She was febrile, with a temperature of 38.9°C, and had a diffuse maculopapular rash affecting more than 50% of the skin surface [Figure 1]. No lymphadenopathy was detected. Blood tests showed an increased white blood cells count of 22 × 10^9 cells/L with hypereosinophilia 8.2 × 10^9 cells/L. Liver enzymes were elevated: alanine aminotransferase (ALT) 265 U/L (normal <40 U/L), aspartate aminotransferase (AST) 196 U/L (normal <40 U/L), gamma glutamyl transferase (GGT) 540 U/L (normal <45 U/L) and serum creatinine 280 μmol/L (normal <115 μmol/L) with an estimated creatinine clearance of 25 mL/min. Bacteriological studies were negative. DRESS syndrome was suspected and esomeprazole stopped.

On the 5th day of hospitalization, her general condition worsened with persistent fever. Intravenous methylprednisone 1 mg/kg/day was started, however she continued to worsen despite 5 days of being on systemic corticosteroids. The skin examination revealed desquamation and laboratory tests showed ALT 244 U/L, AST 203 U/L, GGT 622 U/L, and serum creatinine 433 μmol/L. The patient required intubation for respiratory support and transfer to an intensive unit care. Two days later, she died of multiple organ system failure. An autopsy was not done at the family's request.

The diagnosis of DRESS syndrome was made in this patient based on the criteria adopted by the European

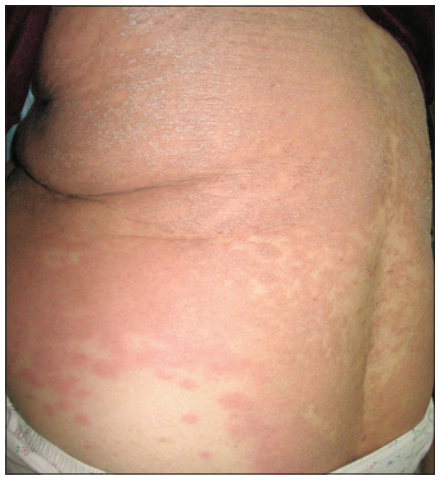

Figure 1: Generalized rash on the trunk

Table 1: Summary of the cases of DRESS associated with PPIs

Ref	Authors	Year of publication	Number of cases	Sex/age	Latency (days)	PPI involved	Symptoms	Patch tests	Fatality
2	Caboni	2007	1	Female/41	20	Esomeprazole	Fever, maculopapular rash, conjunctivitis, cheilitis, eosinophilia, increased liver enzymes	Positive	No
3	Barbaud	2013	5*	Not specified	Not specified	Lansoprazole (1 case) esomeprazole (2 cases) pantoprazole (2 cases)	Not specified	Positive	No
4	Descamps	2014	2	Not specified	Not specified	Omeprazole	Not specified	Not specified	No
Our case			1	Female/84	8	Esomeprazole	Fever, maculopapular rash, eosinophilia, liver and kidney involvement	Not done	Yes

*Among these five cases, three were associated with other drug patch tests positivities: Multiple drug reactivity was retained in these three cases and the responsibility of the PPI could not be determined

group RegiSCAR, which uses a score system based on the presence of symptoms, clinical and laboratory signs.[5] In our case, the RegiScar score was 5: generalized skin rash (1), fever (0), eosinophilia (2), liver and kidney involvement (2).

Esomeprazole was suspected to be the responsible drug for the DRESS syndrome in this case based on Naranjo score.[6] This algorithm is an estimation of the probability that a drug is responsible for an adverse clinical event. It is the sum of scores of 10 items including temporal sequence, biological criteria, existence of alternative causes and effect of withdrawal and re-exposure. The total score is applied for interpretation and varies from doubtful (score of zero of less) to highly probable (score of 9 or more). The Naranjo score for esomeprazole was 4 (possible).

Proton pump inhibitors have been rarely reported as a cause for DRESS syndrome. Eight cases reported in the literature are listed in Table 1; none of these cases were fatal.

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