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Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1505637> since 2016-06-21T15:16:16Z

Published version:

DOI:10.1111/jdv.12535

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This is the author's final version of the contribution published as:

Fava, P; Astrua, C; Cavaliere, G; Brizio, M; Savoia, P; Quaglino, P; Fierro, Mt1.. Intestinal involvement in toxic epidermal necrolysis. A case report and review of literature.. JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY. 29 (9) pp: 1843-1845.
DOI: 10.1111/jdv.12535

The publisher's version is available at:

<http://doi.wiley.com/10.1111/jdv.12535>

When citing, please refer to the published version.

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<http://hdl.handle.net/2318/1505637>

Intestinal involvement in toxic epidermal necrolysis. A case report and review of literature

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A 62-year-old Nigerian female was referred to our Institution for the onset of erythematous targetoid lesions rapidly evolving into progressive epidermal detachments. Due to an upper respiratory infection in a personal history of chronic bronchitis, amoxicillin was started by general practitioner a week before the onset of the cutaneous lesions.

At clinical examination, purple to brown macules were present, together with wide detachments involving trunk and limbs for more than 30% of body surface area (BSA) (Fig. 1a). Buccal, ocular and genital mucosae were involved too. The Nikolsky sign was positive. Patient had fever (39.5°C) and tachycardia (>120 per min). At the admittance, glucose value was 15.78 mmol/L, sodium 129 mmol/L, creatinine 2.48 mg/dL, urea 32.5 mmol/L, bicarbonate 29 mmol/L. Laboratory test failed to demonstrate Mycoplasma and HIV infections. Serial blood cultures were negative. The clinical suspect of toxic epidermal necrolysis (TEN) was confirmed by skin biopsy; day one SCORTEN (severity-of-illness score) was six.

Amoxicillin was stopped and replaced by clarithromycin. High-dose intravenous immunoglobulins (IVIG) were started at a total daily dose of 0.75 g pro kg for four consecutive days together with a systemic steroidal treatment with prednisone 1 mg/kg daily. Fever rapidly resolved, but clinical scenario remained severe with wide disepitelized areas, electrolytic imbalance and worsening renal failure. Three days after the end of IVIG treatment, patient developed severe abdominal pain with stypsis, fever and faecal vomiting; general conditions rapidly deteriorated. Tests for Cytomegalovirus DNA and Clostridium difficile toxin resulted negative. Abdominal CT scan suspected an intestinal infarction with abdominal dropsy and diffuse mucosal oedema. Explorative laparotomy confirmed the presence of an intestinal infarction, thus the patient underwent intestinal resection. Histological examination of the bowel revealed a diffuse, but not complete inflammatory necrosis of the mucosa together with a transmural inflammation, according to the suspect of an intestinal involvement of toxic necrolysis (Fig. 1b). Despite the transfer to intensive care unit, patient died for multiorgan failure in few days.

TEN and Stevens Johnson Syndrome (SJS) are rare, potentially fatal, cutaneous adverse reactions involving skin and mucous membranes, generally caused by drug assumption. SJS/TEN are characterized by more or less severe epidermal detachment presenting as blisters and areas of denuded skin as a consequence of a massive keratinocytes apoptosis.[1]

Sharing similar aetiology and clinical features, SJS and TEN are considered distinct variants within the same disease spectrum. From a clinical point of view, cutaneous manifestations range from erythematous or violaceous, macules and patches, to bullae, erosions and skin necrosis. Commonly are classified as SJS, patients with <10% of the BSA affected, whereas TEN is defined as an involvement >30% of BSA.[2, 3]

Even if mucosae are often affected, gastrointestinal involvement by TEN/SJS has been rarely reported. Sometimes the relationship between SJS/TEN and intestinal symptoms is hard to demonstrate and the two conditions could be considered as distinct concomitant entities; more frequently, gastrointestinal involvement could be under diagnosed.

We collected all Entrez-PubMed articles about intestinal involvement in patients who developed SJS/TEN since 1985 and reviewed 14 cases, including our own (Table 1). The few cases described in literature are in the majority characterized by acute, inflammatory, not infective diarrhoea; mortality rate is high (57.1%).[4-11].

To date, scanty data are available in regard as the stimuli that leads to keratinocytes massive apoptosis, even if it is generally accepted that in the majority of cases this phenomenon is mediated by drug-specific cytotoxic T lymphocytes via the perforin/granzyme pathway; more recent findings demonstrated the importance of granulysin as the main mediator of this mechanism.[12, 13]

This is a rare case of TEN with a documented intestinal infarction. This report confirms that prognosis in SJS/TEN patients is led not only by the percentage of BSA involved, but also by the extracutaneous disease extension.

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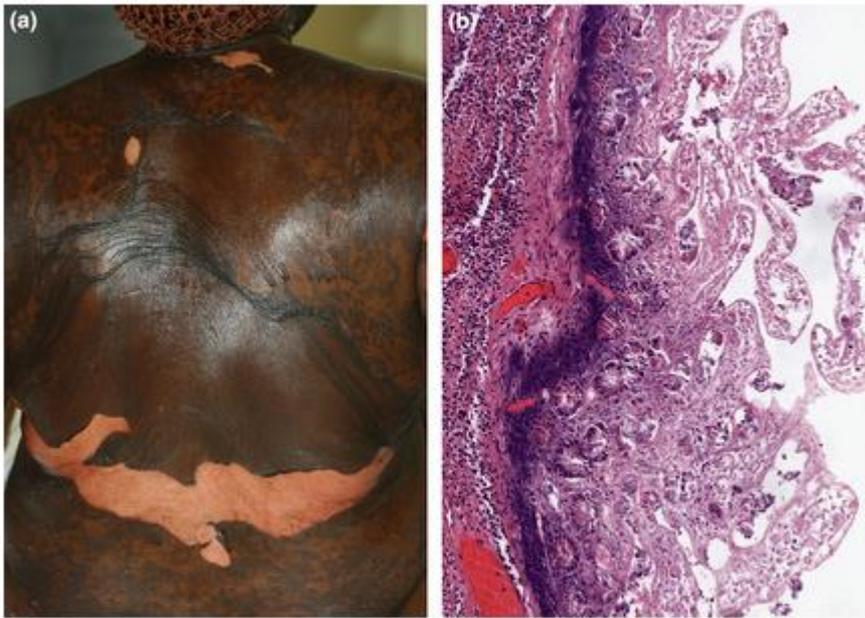


Figure 1 (a) Purple to brown macules were present, together with wide detachments involving trunk and limbs for more than 30% of body surface area. (b) A diffuse, but not complete inflammatory necrosis of the mucosa together with a transmurial inflammation, according to the suspect of an intestinal involvement of toxic necrolysis.

Author	Patients (No.)	Age	Sex	GI symptoms	Treatment	Evolution
Zweiban, 1986	3	36	Male	Dysphagia + Hematemesis	Corticosteroids	Death
19	Male	Dysphagia	Corticosteroids	Resolution		
41	Female	Cramping umbilical pain + Diarrhoea + Hematemesis and melena	Corticosteroids	Death		
Chosidow, 1991	4	41	Male	Abdominal pain + Bloody diarrhoea + Hematemesis	Ileal resection	Resolution
38	Female	Abdominal pain + Bloody diarrhoea	NA	Death		
34	Female	Abdominal pain + Bloody diarrhoea	NA	Death		
55	Female	Abdominal pain + Bloody diarrhoea + Hematemesis	NA	Death		
Sugimoto, 1998	1	46	Female	Hematemesis + Bloody diarrhoea	Corticosteroids + Cyclophosphamide	Death
Carter, 1993	1	69	Female	Hematemesis + Abdominal pain and rectal bleeding	Corticosteroids + Ileal resection	Resolution
Joly, 1992	1	48	Female	Diarrhoea + Malabsorption syndrome	Bowel resection	Resolution
Powell, 2006	1	17	Male	Watery diarrhoea	Antibiotics + Hydrocortisone	Resolution
Jha, 2012	1	23	Male	Abdominal pain + Stool mixed with blood and mucous	Corticosteroids + Antibiotics	Resolution
Pradka, 2014	1	28	Male	Abdominal distension	IVIg + Bowel resection	Death
Fava, 2014	1	62	Female	Faecal vomiting	Corticosteroids + IVIg + Bowel resection	Death

IVIg, intravenous immunoglobulins.

Table 1. Intestinal involvement in SJS/TEN: review of literature