

Oesophageal Involvement in Familial Benign Chronic Pemphigus

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Sir,

Familial benign chronic pemphigus or Hailey-Hailey disease (HHD) is a chronic, recurrent, autosomal dominant genodermatosis featuring suprabasal acantholysis and affecting primarily the flexural areas. Mucosal involvement has been very rarely reported and can involve oral (1), conjunctival (2), vaginal (3), or in very rare instances oesophageal mucosa (4). We report here a woman with gingival and oesophageal specific lesions of HHD, resulting in iron-deficiency anaemia.

CASE REPORT

A 58-year-old woman with previously familial HHD diagnosed on anamnesis, typical histological pattern and a negative direct immunofluorescence study on lesional skin was referred for iron-deficiency anaemia in 1998. The lesions involved neck, sub-mammary and inguinal folds, associated with frequent gingival ulcerations since the age of 36 years. Her mother, aunt and two sisters were also affected by cutaneous lesions only. Microcytic anaemia (Hb = 10.8 g/dl with mean corpuscular volume (MCV) = 74 fl) was detected in routine blood tests, prompted by mild exertional dyspnoea, whereas previous Hb levels and MCV were normal in 1992 (12.5 g/dl and 92 fl, respectively).

Upper and lower digestive endoscopies showed superficial erosions in the lower oesophagus, no lesion in the gastric or duodenal mucosa, a caecal polyp, and lesions of angiodysplasia in the left colon. A biopsy of the oesophageal lesions showed an intraepithelial cleft with acantholysis, but without dyskeratosis, along with a limited inflammation in the underlying chorion, overall reminiscent of specific lesions of HHD.

The patient had no history of gastrointestinal reflux and is not known as smoker or alcohol consumer. She denied any medication intake, especially non-steroidal anti-inflammatory drugs. Thus, a non-specific erosion of the oesophagus can be excluded and the diagnosis of oesophageal HHD was retained.

The patient was then treated with oral iron and thalidomide 100 mg daily. The angiodysplasia was left untreated. Her skin and gingival lesions improved over the following 6 months, and Hb level was restored to normal (14.8 g/dl) one year after the treatment was started. Thalidomide was stopped after 3 years because of peripheral neuropathy. However, her skin condition remained stable but a second endoscopy performed 5 months after the end of thalidomide therapy showed new oesophageal erosions, histologically consistent with Hailey-Hailey lesions.

DISCUSSION

To date, oesophageal involvement in HHD has been reported only once, in a 74-year-old woman suffering from cutaneous HHD since the age of 25 years. Oesophageal involvement was discovered after an episode of dyspnoea, weakness, and epigastric distress. Oesophageal biopsy specimens found a subepithelial blister with acantholysis and no dyskeratosis, favouring a specific Hailey-Hailey lesion.

Our patient had a previously diagnosed HHD with chronic cutaneous and gingival involvement. Microcytic anaemia prompted upper- and lower-digestive tract investigations, which displayed superficial oesophageal erosions, histologically compatible with HHD. Hb level and MCV returned to normal levels after iron supplementation and thalidomide treatment. It is then likely that the oesophageal localizations of the disease were the reason for chronic gastrointestinal blood loss, and that mucosal as well as skin lesions were improved by thalidomide treatment. Recurrent oesophageal lesions were found by upper gastrointestinal endoscopy performed after thalidomide was stopped. In our patient, a Koebner phenomenon on the oesophagus appears unlikely, according to the lack of risk factors for oesophageal diseases such as reflux oesophagitis or ulceration.

Almost all blistering skin condition may lead to specific oesophageal lesions (5), including autoimmune bullous diseases, such as pemphigus, bullous and cicatricial pemphigoid, and epidermolysis bullosa acquisita since the target antigens of circulating antibodies are also present in mucous membranes. Conversely, specific oesophagus involvement in HHD seems to be very rare, since only one case has been previously published to date. Recently the cause of HHD has been identified as mutation in ATP2C1, encoding a calcium pump present in the skin and other stratified epithelia (6, 7). Accordingly, it is likely that oesophageal mucosa express this gene as well, and that its dysfunction lead to specific erosions, as in our patient.

The occurrence of a microcytic anaemia in a patient with HHD should thus lead to a search for specific erosion of the mucous membrane by all adequate means.

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