Erythema dyschromicum perstans (ashy dermatosis) during the treatment with infliximab in a child with Crohn disease

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ABSTRACT

Introduction. Erythema dyschromicum perstans (EDP) or ashy dermatosis is a rare, benign acquired disease characterized by macular hyperpigmentations. The cause of EDP is unclear although some drugs, toxic agents and internal disorders have been associated with this dermatosis.

Objective. Presentation of the first case of the association between EDP and Crohn disease treated with infliximab.

Case report. We present a case of a 15-year-old boy with Crohn disease who was treated with infliximab. During the treatment asymptomatic, hyperpigmented macules on the trunk were observed. Based on clinical and histopathological features the diagnosis of erythema dyschromicum perstans was established.

Conclusions. Erythema dyschromicum perstans may be associated with Crohn disease and infliximab.

INTRODUCTION

Erythema dyschromicum perstans (EDP) is an acquired, mild dermatosis of unknown aetiology, rare in the Caucasian population. The condition is characterized by greyish ash-coloured patchy eruptions. The etiopathogenesis of EDP is not completely understood [1, 2]. There is a known link between EDP and other disorders and medications, however EDP has not so far been reported as accompanying inflammatory bowel diseases or biological therapy.

OBJECTIVE

To present a previously unreported association between EDP and Crohn’s disease (CD) treated with infliximab.

CASE REPORT

A 15-year-old boy received consultation at the Department of Dermatology, Venereology and Allergology of the Medical University of Gdansk in May 2011 due to greyish ash-coloured patchy eruptions located on the trunk (Figs. 1 A and 1 B), which had been observed since 2009. The patient reported no other skin conditions. In September 2007, the patient began therapy with infliximab (receiving a total of 17 doses of the drug) due to CD which was diagnosed in 2002. No extraintestinal manifestations of the disease were observed. Due to remission of CD, the drug was discontinued in March 2011. Aside from the history of gastrointestinal disorder, the emergence of cutaneous lesions could not be correlated with any other factors (medications, toxic substances, concomitant diseases). A histopathological assessment
of a skin biopsy revealed discrete vacuolization of the stratum basale and scattered melanophages (Fig. 2). Based on the clinical and histopathological features, the diagnosis of EDP was made. Photoprotection and emollients were prescribed. The cutaneous lesions were found to have regressed within 4 months (Figs. 3 A and 3 B).

**DISCUSSION**

Erythema dyschromicum perstans was first described in 1957 by Ramirez [3]. Based on the clinical presentation of skin eruptions the author originally termed the condition *dermatosis cenicienta*. Since that time, the disorder has been reported in medical literature under various names: *ashy dermatosis, lichen planus pigmentosus, idiopathic eruptive macular pigmentation* or *los cencientos* [2]. Erythema dyschromicum perstans is uncommon in the Caucasian population, and children make up only 8–10% of all EDP patients [4]. Erythema dyschromicum perstans lesions are manifested as asymptomatic greyish ashcoloured, occasionally brown-grey, patches with an erythematous peripheral margin, often barely distinguishable, measuring 1–2 mm in width. The patches usually have a symmetric distribution. The most common sites of involvement are the trunk and proximal arms and legs. Less frequently involved is the skin of the face and neck. Characteristically, the palms and soles, the scalp and mucous membranes are EDP-free [1]. Histopathological findings include the presence of a sparse perivascular lymphocytic infiltrate in the dermis, and numerous melanophages. At an early stage of skin involvement, typical features include vacuolization of keratinocytes in the basal layer, presence of cytoid bodies, lymphocytic epidermotropism and pigment incontinence [1].

The etiopathogenesis of the condition remains unclear. Several infectious agents have been proposed as implicated in the development of EDP, including viruses (hepatitis C virus, human immunodeficiency

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**Figure 1 A, B.** Erythema dyschromicum perstans. Grey-brownish macular hyperpigmentation on the skin of the trunk

**Figure 2.** Erythema dyschromicum perstans – histopathologic feature: single melanophages in the papillary dermis
virus) and parasites (whipworm infestation). There have been reports of EDP accompanying endocrinopathies (hypothyroidism) and vitiligo. Some authors have theorized that in some cases EDP is a variant of lichen planus. Toxic substances (pesticides, radiographic contrast media) and medications also seem to be major etiological factors. There have been cases of EDP linked to the treatment with sodium nitrite, benzodiazepines, chlorothalonil, ethambutol, omeprazole and antibiotics [1, 2, 4–9].

Because of unclear etiopathogenesis the treatment of EDP is difficult. There have been medical reports describing therapy with photoprotective, keratolytic, antimalarial and antihistamine agents, topical and systemic glucocorticosteroids, dapsone, antibiotics, griseofulvin, clofazimine, ascorbic acid, laser treatment and chemical peels [1, 5]. The multitude of therapeutic options attests to their limited efficacy. In the case discussed here, because of the moderate severity of skin involvement and absence of any subjective symptoms, a wait-and-see attitude was adopted.

Inflammatory bowel diseases, CD included, have a very broad range of dermatological symptomatology. Skin lesions accompanying these conditions are identified in between 2% and 34% of all patients [10]. The most common dermal manifestations of CD are pyoderma gangrenosum and erythema nodosum, however medical literature also includes accounts of a number of other skin conditions [10]. Sladek and Ćmiel [11], who examined clinically a total of 146 children with CD, identified dermatological manifestations of the disease (aphthosis and erythema nodosum) in 26.7% of their patients. Studies by Mierzwa et al. [12] corroborate the finding that aphthosis is the most common dermo-mucosal symptom accompanying CD in children and adolescents.

The introduction of biologic medications has been a breakthrough in the therapy of rheumatic, gastrointestinal and dermatological diseases. Due to their widespread use, the spectrum of adverse effects caused by biologic drugs is quite well-known. Lee et al. [13] observed adverse skin reactions in 35 out of 150 patients (23.3%) treated with anti-TNF-α agents due to rheumatic conditions. In 45.7% of cases cutaneous reactions presented as psoriatic or eczematous lesions. Viral, bacterial or fungal infections were confirmed in 37.1% of study patients. There were also isolated cases of dermatitis herpetiformis, leukocytoclasis vasculitis and alopecia areata. Other reported skin abnormalities accompanying biological therapy include pustular lesions, non-specific vesicular skin eruptions and necrotizing fasciitis [14, 15]. Moreover, biologic drugs have a relatively high potential for the induction of lupus erythematosus [16]. A review of medical literature has revealed one case of hyperpigmentations occurring during anti-TNF-α treatment. Kelley et al. [17] reported acquired dermal melanocytosis in a psoriasis patient treated with infliximab. An important report in the context discussed here is that by Bovenschen et al. [18]. The authors described three cases of eruptive benign melanocytic naevi in CD and psoriasis patients who were treated with infliximab, etanercept and alefacept. Similar skin lesions are also observed in other patients with ha-
ematological or iatrogenic immunosuppression [19]. According to what seems to be the most convincing pathogenetic hypothesis, immune suppression affects the expression of the melanocyte-stimulating hormone, which in turn has an impact on neogenesis and melanogenesis [18]. The theory also seems to apply to EDP, especially in the light of the fact that the condition has been observed in immune-incompetent patients [6].

The authors have not identified medical reports about any potential link of EDP with CD, and infliximab or other TNF-α blockers. It is not possible to establish unambiguously whether the patient’s cutaneous lesions were associated with CD or infliximab therapy. A coincidental link cannot be ruled out, either. Complete remission of cutaneous lesions seen after the discontinuation of treatment seems to suggest a correlation between EDP and biological therapy, especially that histopathological findings were consistent with the residual phase of the disease. Since EDP often presents as a mild, asymptomatic, transient and often subclinical condition, patients may have a tendency not to report any symptoms. Also in the case discussed here neither the patient himself nor his family regarded the skin lesions as a major health problem.

Summing up, according to the authors’ knowledge the case presented above, which is interesting both from the dermatological and gastroenterological perspective, is also the world’s first report about EDP coexisting with infliximab-treated CD. The case corroborates the link existing between the two medical disciplines, and expands the knowledge of this rare and little known condition.

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