EJGO European Journal of Gynaecological Oncology

Case Reports

An immunological explanation behind the acantholytic dermatosis of vulvocrural area

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Summary

The acantholytic dermatosis of the vulvocrural area (ADVA) is a rare skin disorder of unknown etiology, described for the first time by Chorzelski *et al.* in 1984. It is characterized by solitary or multiple skin-coloured to white, smooth papules or plaques, involving the genitocrural region, in particular the vulva. Here, the authors refer a case of ADVA in an 80-year-old female patient affected by recurrent endometrial carcinoma. The immunohistochemical investigation demonstrated the exclusive presence of G immunoglobulins inside the skin lesions, so indicating a paraneoplastic immunological action. The findings shed light on the etiopathogenetic mechanisms at the basis of this still scantly known nosological entity.

Key words: Acantholytic dermatosis of the vulvocrural area; Endometrioid carcinoma; Paraneoplastic syndrome; Immunoglobulins; Immunohistochemistry; Histology.

Introduction

Different paraneoplastic syndromes can appear in course of uterine neoplasms [1-4]. They can involve various apparatuses, among which also the skin and mucous membranes, determining a pemphigus or a pemphigus-like condition [5-7]. The acantholytic dermatosis of the vulvocrural area (ADVA) is a rare skin disorder of unknown etiology, described for the first time by Chorzelski *et al.* in 1984 [8]. It is characterized by solitary or multiple skin-colored to white, smooth papules or plaques, involving the genitocrural region, in particular the vulva [9, 10]. A new rare case of ADVA, recently observed in a woman affected by recurrent endometrial carcinoma, is here reported. Its pathogenesis has been found secondary to an immunological mechanism, as demonstrated by the immunohistochemical researches.

Case Report

An 80-year-old female was submitted to hysterectomy with bilateral salpingo-oophorectomy for a well-differentiated endometrioid carcinoma of the uterus, invading the outer half of the myometrium and involving the isthmus, with negative peritoneal cytology, at FIGO Stage IB (Figure 1). Two years later the patient manifested postmenopausal vaginal bleedings, and a recurrence in the vaginal cupola was ascertained by histology. Laboratory tests indicated an increased value of specific markers, such as CA125 and CA19.9. A positron emission tomography revealed activity in the pelvis and in the left pulmonary lower lobe. Contemporaneously, a dermatological eruption occurred at the level of the vulva and anterior perineum, consisting in non-pruritic white papules. Biopsy of the skin lesions showed marked hyperkeratosis with irregular acanthosis, alternated to areas of epidermal parabasal fissuring and serrated acantholysis; only a scanty infiltrate of inflammatory cells, devoid of eosinophils and intermingled with occasional telangiectasias, was observed (Figure 2). The histochemical research for fungi, performed by Grocott stain, resulted negative, too. These findings appeared compatible with a diagnosis of ADVA, also taking into account the absence of a previous Darier's disease and a family history negative for Hailey-Hailey disease.

Results

The paraffin-embedded bioptic specimen was submitted to further immunohistochemically study. After deparaffinization, hydration, endogenous peroxidase blocking, and heat-induced antigen retrieval, the tissue sections were incubated for 30 minutes at room temperature with anti-IgA (polyclonal; prediluted), anti-IgD (polyclonal; prediluted), anti-IgE (polyclonal; prediluted), anti-IgG (polyclonal; prediluted) and anti-IgM (polyclonal; prediluted). Biotinylated secondary antibody was applied and the staining product detected with avidin-biotin complex against a haematoxylin counterstain. Detection of the staining reaction was achieved by an enzyme conjugated polymer complex adapted for automatic stainers, with 3-3' diaminobenzidine tetrahydrochloride as chromogen. The immunohistochemical investigation revealed the exclusive presence of IgG in the areas of acantholysis, mainly in the

Revised manuscript accepted for publication February 16, 2017

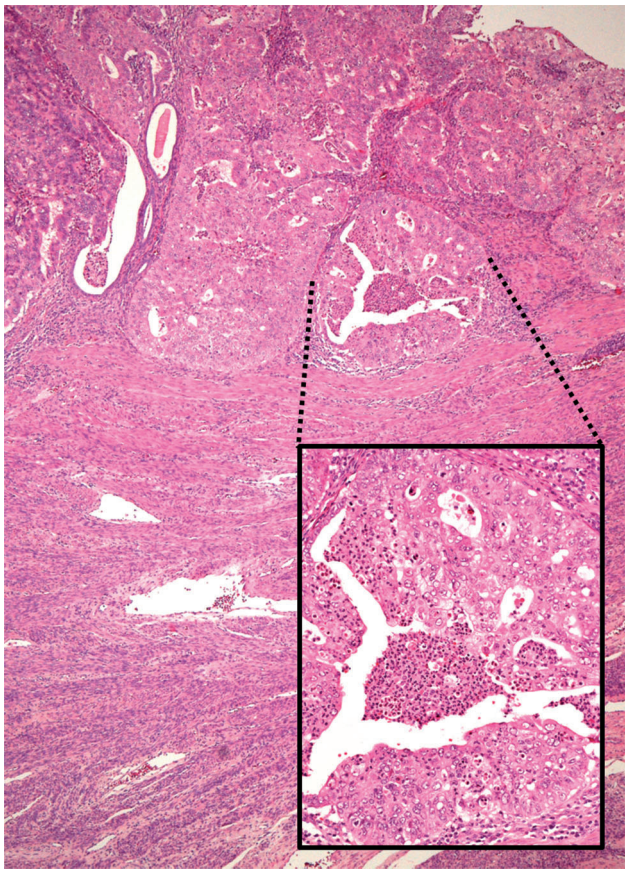

Figure 1. — On Hematoxylin & Eosin, the endometrioid carcinoma of the endometrium infiltrates the outer half of the myometrium (original magnification ×10). The insert (×20) shows carcinomatous elements with prominent nucleoli and mitotic figures; in the lumen of the neoplastic gland, numerous neutrophils and inflammatory cells are also observable.

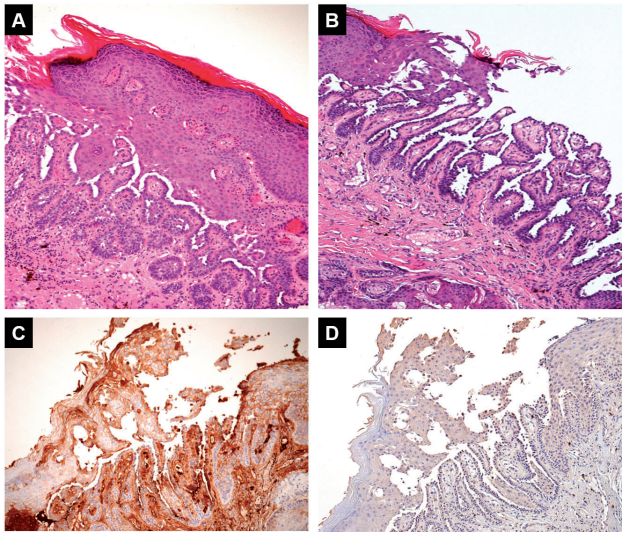

Figure 2. — Papular acantholytic dermatosis of the vulvocrural area: epidermal parabasal fissuring (A: Hematoxylin & Eosin, ×10) and serrated acantholysis (B: Hematoxylin & Eosin, ×10) are well noticeable. In the same areas, the presence of IgG has been ascertained by immunohistochemistry (C: ×10); no reactivity has been found for IgA, IgD, IgE, and IgM (D: ×10).

intercellular spaces and around the acantholytic cells. The patient was treated with an oral corticosteroid therapy, which allowed a frank regression of the dermatosis, and pelvic radio-treatment plus general chemotherapy were associated for the recurrent cancer.

Discussion

In the present case, ADVA appears as a localized form of paraneoplastic disease, connects with the other more frequent pemphigus or pemphigus-like dermatoses. The linkage with these more frequent dermatologic syndromes is represented by a common process of acantholysis, and by the presence of immunoglobulins inside the proper acantholytic lesions [11]. This agrees with the detection of the same IgG in the pemphigus bullae [12]. We can interpret this finding as an activated immunological reaction, promoted by the concomitant tumor, and expressed by the production of antibodies against the neoplastic cells [13-15]. Subsequently, they can also attack the normal tissue components, in the present case, tonofibrils and desmosomes of the epidermal cells, favouring the appearance of paraneoplastic clinical signs [16]. In this target tissue, the persistence of IgG is explained by their innate cytophilic propensity [17]. On the other hand, the IgG do not promote an immediate vigorous immunological response, but they behave as long-acting molecules, supported by a mechanism of immunological memory, evocated by tumoral antigenic stimuli on some immune clones [16, 17]. The multifocal neoplastic recurrence, especially involving the lung, facilitated the blood release of tumoral antigens in the present case. In conclusion, for the first time, the authors have detected the presence of tissue IgG in ADVA, and, therefore, an immunological substrate has been disclosed for this disease.

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