

Naevus Comedonicus Immunohistochemical Features in Two Cases

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Accepted February 26, 2003.

Sir,

Naevus comedonicus was first described by Kofmann in 1895 (1). It was arranged in groups or linear patterns along Blaschko's line and located on the face, neck, upper arms, chest and abdomen. It has been well documented that naevus comedonicus occurs as a single entity but occasionally in association with other disorders.

The objective of this study was to analyse the clinical and immunohistochemical features of two patients with extensive naevus comedonicus arranged in groups and linear patterns without non-cutaneous abnormalities.

CASE REPORT

Case 1

A 38-year-old white male was first seen in the Department of Dermatology in 1981. The naevus comedonicus appeared during the first decade and in the following years was complicated by recurrent infections leading to the formation of pustules, cysts, abscesses and fistulas that healed with scars. The patient shows lesions characterized by patches occurring in a unilateral zosteriform distribution over the left side of the trunk, neck and left arm. Few lesions cross the midline (Fig. 1).

Numerous 1–4 mm darkly pigmented and keratotic plugs are clustered in patches that range in size from 1 × 2 cm to 25 × 4 cm. The patches comprise groups of small or large dilated follicular openings and the comedones vary from small pinhead size to large horny structures. Some patches show a cribriform pattern with extruded plugs. Hypertrophic scarring was noted subsequent to infected cysts. The lesions are slightly pruritic.

Case 2

A 37-year-old white male was first examined at the age of 21. The lesion began on the right lumbar region. It was about



Fig. 1. The lesion characterized by patches occurring in a unilateral zosteriform distribution over the left side of the trunk, neck and left arm. Few lesions cross the midline. Patient no. 1.

7 cm in width and descended in the posterior middle line of the sacral region. The lesion was not continuous but instead was interrupted by areas of normal skin. The involved areas were composed of grouped comedo-like lesions, black in colour and ranging in size from 1 to 7 mm (Fig. 2). The black substance was soft and readily expressed. The lesion of the sacral region had been infected and healed scarring, and there was one distinct area of inflammation with purulent drainage.

Methods

Two biopsies per patient were taken from lesional skin. Haematoxylin and eosin-stained sections from formalin-fixed paraffin-embedded sections were prepared. Immunophenotypic studies were performed including positive and negative controls. Sections of 4 µm from the 10% buffered formalin and paraffin-embedded tissue blocks were placed on silane-coated glass slides, deparaffinized and rehydrated. The slides were pretreated in citrate buffer, pH 6.1 at 120°C for antigen retrieval. The sections were then treated with 3% hydrogen peroxide to block endogenous peroxidase activity and with 10% normal horse-radish serum for 20 min at 20°C in a humidified chamber. Primary antibodies used in this study were: monoclonal antibody to proliferating cell nuclear antigen (PCNA), p53 (DAKO Spa, Milan, Italy), intercellular adhesion molecular-1 (ICAM-1), HLA-DR (Novocastra Laboratories Ltd, UK) and CD68. Primary antibodies were incubated for 30 min at room temperature. Immunostaining was performed using the ABC technique. Antigen-antibody complex was visualized by 3-amino-9-ethylcarbazole.

RESULTS

Biopsies from the two patients showed similar features. Histological examination of full thickness sections of involved skin showed numerous comedo-like lesions characterized by dilated follicles filled with keratinous material, the corneocytes arranged in a laminate pattern, and by a peculiar proliferation of epithelium at the bases

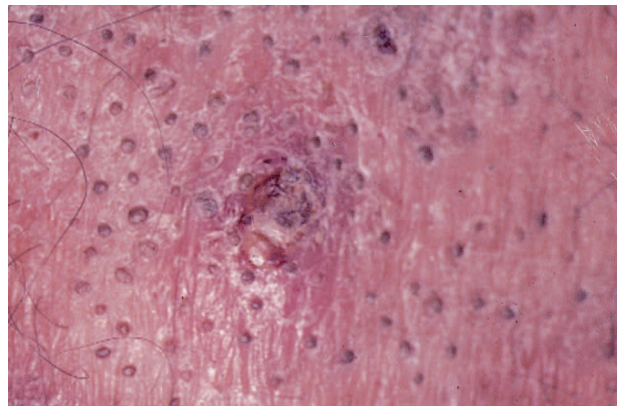


Fig. 2. Grouped comedo-like lesions, black in colour and ranging in size from 1 to 7 mm. There was one distinct area of inflammation with purulent drainage. Patient no. 2.

of the infundibula. The follicular wall was irregularly thickened. Small sebaceous gland lobules were seen in the lower pole of the invagination.

Hair shafts were seen at the base of the invagination. The rete ridges were prominent at the bases of some elongated and particularly widened infundibula-like structures. Several comedonal and infundibula-cyst structures extend near to the subcutaneous fat. The intervening epidermis was hyperkeratotic and some inflammatory infiltrate of histiocytes and lymphocytes was present in the superficial dermis and prevalent near the peculiar proliferation of epithelium at bases of the infundibula, which project bulbous proliferations of keratinocytes.

Immunohistochemical evaluation of the specimens has demonstrated a distribution of PCNA in projecting bulbous proliferations of keratinocytes of dilated and elongated infundibula. The expression of PCNA in the interfollicular epidermis was minimal (results not shown).

Immunoreactivity for HLA-DR was evident in epidermal keratinocytes of the elongated infundibula (Fig. 3). Staining with ICAM-1 was present in the lesional epidermis of infundibula and decreased in the interfollicular epidermal cells and in the endothelial cells within the dermal vascular plexus. The staining for the CD68 was evident in the cells of the dermis predominantly near project bulbous proliferation. Our cases showed non-increased nuclear staining for p53 within the areas of keratinocytes of dilated and elongated infundibula (results not shown).

DISCUSSION

The bizarre follicular structures of the two patients are typical of the naevus comedonicus. Many consider the naevus comedonicus as a hamartoma arising from a defective mesoderm; others consider it an epidermal naevus involving the hair follicle or an appendageal naevus of sweat ducts (2). Naevus comedonicus syndrome can be categorized as a disorder related to the epidermal naevus syndrome group (3). There is no gender or racial

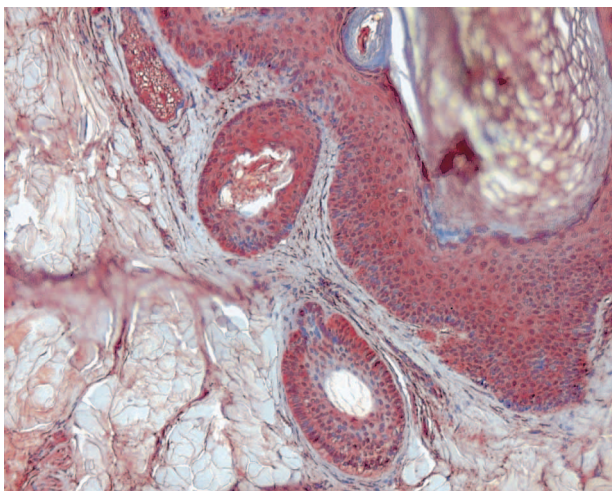


Fig. 3. Immunoreactivity for HLA-DR was evident in epidermal keratinocytes of the elongated infundibula (HLA-DR 160 \times).

predisposition. Generally, the history of onset is at, or shortly after, birth. Distribution is usually unilateral.

Our patients were asymptomatic until inflammation began to appear. This complication tends to come later in life.

The cases studied demonstrated that these lesions represent a focal clonal defect in the growth regulation of keratinocytes of infundibula with an increased expression of PCNA, ICAM-1 and HLA-DR.

PCNA is essential for DNA replication of mammalian cells. The mechanism of the cell-cycle-dependent regulation of the human PCNA promoter is not clear, despite extensive investigation (4). PCNA is a nuclear protein that is expressed in G1-M phases of the cell cycle, but is maximally expressed in late G1-S phases (5).

Our data show that in project bulbous proliferations of keratinocytes of dilated and elongated infundibula the rate of proliferating cells is higher than that of interfollicular epidermis. Thus, within these lesions there may be a primary clonal dysregulation of growth initially which produces a rate of proliferating epidermis of infundibula that is different from the interfollicular epidermis, indicating that this excessive proliferation may cause the formation and development of dilated and elongated infundibula. The immunohistochemical increased expression of PCNA, ICAM-1, HLA-DR and CD68, and non-increased nuclear staining for p53 could explain the less aggressive biological behaviour of the naevus comedonicus.

Genetic and clinical mosaicism in the epidermal naevus has been documented (6). This mutation is suspected in naevus comedonicus. Genetic mosaicism secondary to a postzygotic mutation during development offers the basis for the naevus comedonicus (7). Our patients' illness could also be the result of a genetic defect in the development of the hair follicle.

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