Pagetoid dyskeratosis of the forehead

Sir,

Pagetoid dyskeratosis (PD) is an incidental histologic finding seen in various types of skin lesions, such as nevi, acrochordons, lentigines, milia, and seborrhoeic keratoses. It was first reported in the dermatology literature in 1988 in a variety of benign facial papules.[1] It is considered to be a selective keratinocyte response in which a small part of normal keratinocyte population is induced to proliferate in response to friction.[2] There are cases of PD reported in various anatomic locations. However, it has not been described in a hyperpigmented area of the forehead.

A 35-year-old male patient presented with a 2-year history of gradually progressive pigmentation over his forehead. He denied a history of photosensitivity, use of any commercial preparations on the forehead or excessive rubbing of the forehead. There was no history of application of topical or ingestion of oral medications. The family history was not contributory. Physical examination revealed obesity (body mass index, 34.6 kg/m^2). Dermatologic examination revealed a hyperpigmented area over the forehead [Figure 1a].

Laboratory investigations revealed elevated fasting blood glucose (138 mg/dL, normal 70-110 mg/dL). The fasting plasma insulin, insulin-like growth factor, lipid profile, and postmeal blood glucose levels were normal. A biopsy was done from the hyperpigmented lesion over the forehead that revealed epidermal hyperkeratosis, acanthosis, and papillomatosis. There were singly lying as well as clusters of large, individual keratinocytes with central, condensed pyknotic nuclei, a clear halo, and surrounding pale eosinophilic cytoplasm in the upper half of the epidermis [Figure 1b]. Periodic acid Schiff [Figure 1c] and colloidal iron stainings carried out to see the presence of glycogen and mucin, respectively, in the pale cells were negative. Immunohistochemical stains with cytokeratin 7 (CK7), epithelial membrane antigen (EMA) [Figure 1d], and carcinoembryonic antigen (CEA) were done, all of which were negative.

PD is characterized by the presence of pale, round cells that are usually larger than normal keratinocytes with a condensed pyknotic nucleus, perinuclear halo and pale eosinophilic cytoplasm. These cells are mostly seen in the granular and upper Malpighian layer.[3] They resemble the cells found in Paget's disease, although large atypical nuclei are seen in the latter. The normal pattern of cytokeratin expression is modified in pale cells, which show premature keratinization that contributes to the eosinophilic and condensed cytoplasm.[1] It is thereby considered an epidermal maturation defect. However, there is retention of the intercellular contacts with surrounding cells. There is no acantholysis or parakeratosis. These cells rarely develop keratohyalin granules and appear well defined in the granular layer and ultimately mature into orthokeratotic squamous layer cells.[1]

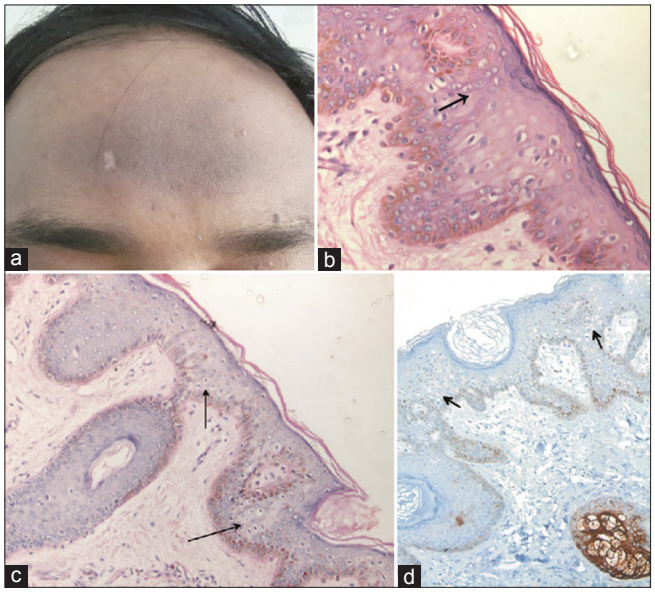

Figure 1: Hyperpigmentation on the forehead; (b) keratinocytes with pyknotic nuclei and perinuclear halo; hematoxylin and eosin, ×400; (c) negative staining of the cells with periodic acid Schiff, ×200; (d) immunohistochemical stain with epithelial membrane antigen showing nonreactivity, ×200

The cells in PD are thought to result from friction. The anatomic locations of the lesions that exhibit PD are usually areas prone to friction, such as the intertriginous areas, trunk, buttocks, face, and the limbs.[3] The presence of pagetoid cells in a biopsy specimen calls for consideration of histologic differential diagnoses, such as extramammary Paget's disease, pagetoid squamous cell carcinoma, and pagetoid melanoma.

Most of the literature on PD comes from the studies done by Val-Bernal *et al*. who have described it in various locations, such as lips,[2] nipple,[4] prepuce,[5] hemorrhoids,[6] and cervix of the prolapsed uterus.[7] Lee *et al*. described PD on the scrotum in a 54-year-old man with scrotal pruritus.[8] It has been described in a 26-year-old woman with longstanding, asymptomatic, light brown patches over the thumb and the webspaces of the hand.[9]

Our patient was diagnosed to have PD on the basis of characteristic histologic features showing epidermal clear cells with a perinuclear halo and negative immunohistochemical examination for CK7, CEA, and EMA. A role of unrecognized rubbing of the forehead causing hyperpigmentation is thought

to be responsible for the appearance of PD in this patient. Although it has been described on the face in variety of benign papules, to our knowledge there are no reports of its occurrence on a pigmented area over the forehead.

In summary, PD is an incidental histologic finding. Awareness of this entity is essential as it represents a frequent diagnostic pitfall and avoids misdiagnosis, thereby preventing unnecessary biopsies and therapies. Although routine histology suffices, in doubtful cases immunohistochemical examination is helpful.

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