POROKERATOSIS OF MIBELLI
(Review of literature and report of 6 cases)

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Summary

Porokeratosis of Mibelli is a rare hereditary disorder of the skin. The salient features in 6 cases are described with a brief review of the relevant literature. Involvement of the mucous membranes was noted in 2 cases. The clinical picture was quite variable and some of the lesions resembled tinea corporis, warts and neurodermatitis. Histologically cornoid lamella was the pathognomonic feature. An attempt is made to explain the relative rarity of this condition in females on the basis of hormonal factors.

KEY WORDS: Porokeratosis, Genodermatosis, Hormonal Factors, Cornoid Lamella.

Porokeratosis of Mibelli (PM) is a rare genodermatosis characterized by solitary or multiple, asymptomatic, chronically progressive, annular or circular keratoatrophodermas. This entity was initially reported from Italy independently by Mibelli[1] and Resphigi[2] in 1893. Later cases have been described in all races from different parts of the world. In 1962 Butterworth and Strean[3] stated that fewer than 200 cases of this rare disorder have been recorded in literature. A few interesting case reports of this uncommon disorder have also been described from India sporadically[4-9]. In 1966 Chernosky[10] reported a variant of this disorder under the name "disseminated superficial actinic porokeratosis" (DSAP), in which the lesions are mainly seen on sun exposed areas. Guss et al[11] in 1971 reported 8 cases of yet another disseminated variant of this disorder under the name "Porokeratosis plantaris palmaris et disseminata" (PPPD) occurring in the same family.

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Review of Literature

Clinical Pattern :

The nomenclature of this condition as "Porokeratosis" by Mibelli was based on his belief that the disease process always involves the sweat pores. This is not considered true any more by many authors[12-14]. The disease has a distinctsex prediletion for males (3 : 1) and usually starts in the younger agegroup. Characteristically thelesions appear as sharply demarcated, circular to oval, hyperkeratotic plaques with a raised border on the summit of which

runs a linear furrow. The center of the lesion is usually atrophic, non-hairy and anhidrotic. The disease process may occur in a localized or generalized pattern anywhere on the body including the nails and mucous membranes of the mouth, nose, conjuctiva or glans penis[12]. The clinical picture varies considerably and the lesions may appear faint or prominent, small or extensive, atrophic or hypoplastic, hyper or hypopigmented, hypertrophic or verrucous, asymptomatic or pruritic and even erythematous[14]. Several variants occur; these include generalized eruptive[15], punctate[16], linear[17,18], bullous, ulcerative[7], systematized[19], zosteriform[20] and hypertrophic types[21].

DSAP is one of the more commonly encountered variant of porokeratosis[14]. The lesions occur usually in the third or fourth decade of life and are predominantly situated on the sun exposed areas of the body[22-26]. Both sexes are equally affected and the lesions appear as small (0.5–1cm), multiple, superficial, indistinct, bilaterally symmetric papules with a circular keratotic rim. Conspicuously the mucous membranes, palms and soles are spared. The lesions are asymptomatic and often become prominent on exposure to sun light. Probably the phenotypic expression of the gene responsible for the disease is regulated by sun light[14].

PPPD of Guss et al[11] is an uncommon variety of porokeratosis in which the onset usually occurs around 18–22 yrs. with an apparent sex predilection for males (2 : 1). The lesions appear as multiple, circular, keratotic furrows or ridges all over the body, but conspicuously on palms and soles. The mucous membranes are spared[14].

Etiopathogenesis:

It is generally accepted that a regular autosomal dominant gene is responsible for the transmission of PM. Mibelli[1] believing this disorder to be due to hyperkeratosis of the acrosyringeal portion of the eccrine sweat ducts, named it porokeratosis. Further he pointed out that the progress of the lesion is due to successive involvement of new sweat pores. The basic point against the sweat duct origin is that the lesions are seen on the mucous membranes, where there are no sweat glands[11,13]. The cornoid lamella has been noted in relation to sweat glands[1,5,27] but it has been also reported to occur in relation to hair follicles and in areas devoid of cutaneous appendages[14,28,29].

Based on extensive histological studies of PM, Reed and Leone[29] postulated that this is a clonal disease of epidermal cells similar to actinic keratosis and the tendency of these clones to produce disease is probably inherited. In many cases, the latent abnormal clones become clinically overt following an actinic effect. In support of this, they cited the development of malignancy in the lesions of PM. The histochemical and ultrastructural studies of Abdel-Aziz[13] revealed that PM is a heritable metabolic derangement of some epidermal cells, manifesting the disturbance at the active border of the lesion. Taylor et al[30] noted chromosomal instability in the cultured fibroblasts of PM and believed that this may be important for the susceptibility of lesions to become malignant when exposed to UV light, X-ray irradiation and trauma. In support of this view, they further stated that most of the malignancies reported in PM were located on the distal parts of the extremities, where the skin is more prone to the actinic injuries. Macmillan and Roberts[31] reported a curious instance of quiescent PM turning into an extensive systematized form two weeks after kidney transplantation and immunosuppressive therapy. According to these authors,

abnormal clone of cells exist in the epidermis which are regulated by the inhibitory forces exerted by the adjacent normal cells or by certain immune mechanisms. These may have prevented the appearance of macrosocopic lesions. Immunosuppressive therapy impaired probably either of these mechanisms resulting in the development of extensive systematized eruption.

Several instances of epithelial neoplasia have been observed in Porokeratosis of Mibelli[32-35]. Summarizing the available data, Car and Abdel-Aziz[35] stated that squamous cell carcinoma in 14, basal cell epithelioma in 1 and Bowen's disease in 3 cases have been reported.

Microscopic, histochemical and ultra structural studies :

Histologic studies of lesions of porokeratosis have regularly shown the presence of characteristic wedge-shaped porakeratotic cell mass, the cornoid lamella[14]. Below this, the granular cell layer is vacuolated and dyskeratotic. In many cases, a lymphohistiocytic infiltrate is present in the dermis with dilated capillaries. Histochemical studies of the cornoid lamella have revealed increased sulfhydryl and decreased disulfide groups in the parakeratotic cells. The cells contain PAS positive and diastase resistant material with RNA and DNA in the basophilic granules of the nuclei[12,14]. Electron microscopic studies by Sato et al[36] revealed that the cornoid lamella is mainly composed of numerous extremely irregular dark cells and a few dyskeratotic cells.

The present paper presents 6 cases of PM with several interesting features studied in the out-patient clinic of the Skin & V.D. department, Sir Sunderlal Hospital, Institute of Medical Sciences, Varanasi.

Case Reports

Case No. 1

30 years old male patient reported with the complaints of multiple asymptomatic lesions all over the body of 10 years' duration. History of similar lesions was present in the family (Fig. 1). Examination revealed numerous, discrete, circular to oval shaped, variously sized plaques on the face, chest, back, abdomen and extensor aspects

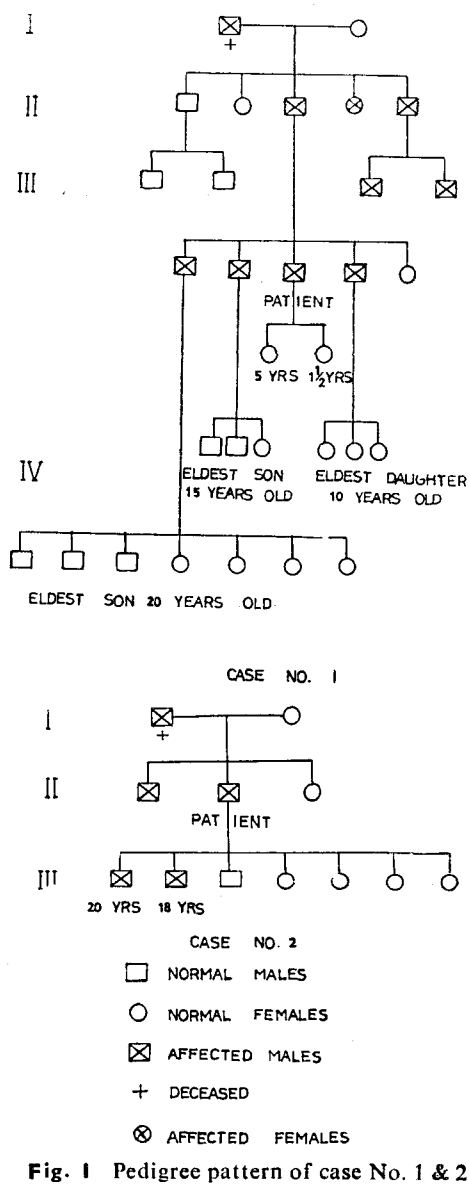

Fig. 1 Pedigree pattern of case No. 1 & 2

of both upper and lower extremities, with raised keratotic border and a groove on the summit. The skin at the centre of the lesion was atrophic (Fig. 2). Histology of one of the lesions showed, hyperkeratosis, cornoid lamella with parakeratotic cells, thinning and vacuolization of the granular cell layer in the subcornoid region and

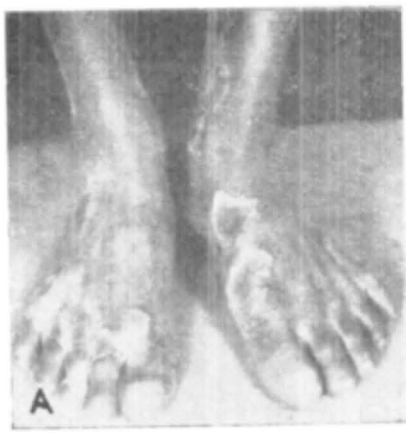

Fig. 2
Typical lesions of PM with a raised horny border traversed by a linear furrow and atrophic center devoid of hair

atrophy of the prickle cell layer was noted at the inner border of the cornoid lamella (Fig 2A). A mononuclear inflammatory infiltrate was observed in the dermis corresponding to the region of cornoid lamella. Neither sweat ducts nor hair follicles were noted in relation to the horny plug. Vitamin A capsules orally given in the dose of 5000 I.U. (1 Cap daily) for a period of 2 months had no effect on the lesion. Repeated intralesional triamcinolone acetonide (0.3 ml of 4 mg/ml) injections into some of the lesions resulted in mild improvement but the results were not convincing.

Case No. 2

35 years old male patient reported to the dermatology clinic with asymptomatic skin lesions of 3 years' duration. Three other family members had similar skin lesions. Examination revealed multiple, discrete, annular, horny plaques on the face, inner surface and outer border of the lower lip, shoulders, abdomen, perianal region, scrotum, extensor aspect of the legs and feet involving the right great-toe nail. Some of the lesions on the back of the thighs resembled tinea corporis. Some of the lesions were thick and gave the impression of warts and others of neurodermatitis (Fig. 3). Histology was consistent with that of porokeratosis of Mibelli. A dilated sweat duct was seen in the dermis in

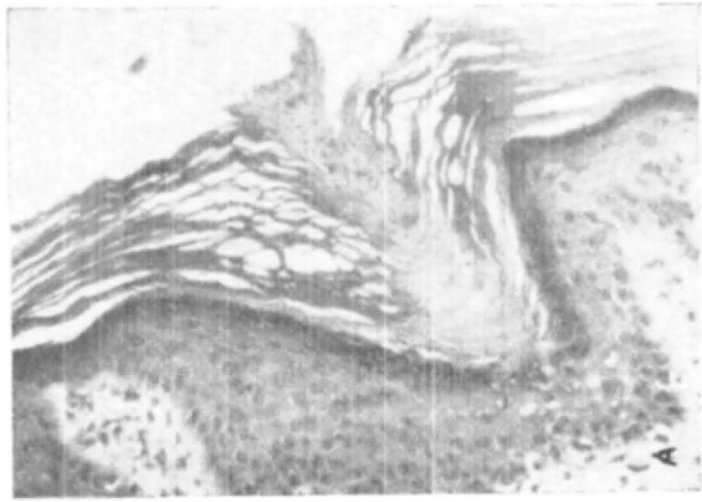

Fig. 2-A
Showing histological features of PM

relation to the cornoid lamella (Fig. 3A). Treatment on the same lines as in case 1 produced similar results.

Case No. 3

30 years old male patient reported with the complaints of itching on the right side of the neck. Examination revealed lesions suggestive of neurodermatitis. He had two asymptomatic, circular, hyperkeratotic discrete lesions, one on the right shoulder and the other on the medial aspect of the thigh. These had typical features of PM There was no family history of similar lesions. The lesions were successfully treated with repeated chemical cauterizations of concentrated trichloroacetic acid (100%) at weekly intervals for a period of 3 months.

Case No. 6

50 years old male patient attended the skin clinic with complaints of generalized skin lesions of 2 years' duration. He had numerous discrete, 3–5 mm circular lesions situated almost on the entire surface of the body. Examination of the lesions with a hand lens revealed hyperkeratotic, circular papules with a depressed centre and a raised border traversed by a linear furrow. There was no famliy history of similar disease. Histology and treatment details were similar to those of other cases.

Discussion

In our series of cases the disease manifested as an autosomal dominant trait in two cases and as isolated forms in the remaining 4 patients,

Fig. 3
Note the lesions in PM simulating tinea corporis, verruca and neurodermatitis respectively

Case No. 4

35 years old female patient presented with asymptomatic skin plaques over the chest and back of 2 years' duration. Examination and histopathology revealed typical lesions of PM over the right breast, back, thighs and legs. There was no family history of similar lesions. Treatment result was similar to that of case No. 1.

Case No. 5

9 years old male child reported with complaints of asymptomatic skin eruption over the face of 1 year's duration. Clinical examination revealed typical lesions of PM over the face, left angle of mouth and extensor aspects of the extremities (Fig. 4). Histology of skin lesions was similar to that of PM and treatment as described earlier had no effect.

suggesting genetic mutation in the latter group.

PM is reported to have a distinct predilection for male sex[14]. Our series confirms this (5 males to 1 female). The onset of lesions in PM is usually in the pubertal age, when sex hormones exert their effect on different target organs. This may have a bearing on the expression of the disease. Variation in the clinical picture may be due to regulation of the gene responsible for the phenotypic expression of the disease by certain factors, like sunlight in DSAP[14]. It is reasonable to presume that female sex-hormones influence the gene responsible for phenotypic expression of the disease and masks the clinical appearance of lesion. DSAP is reported to affect females and males equally but in this

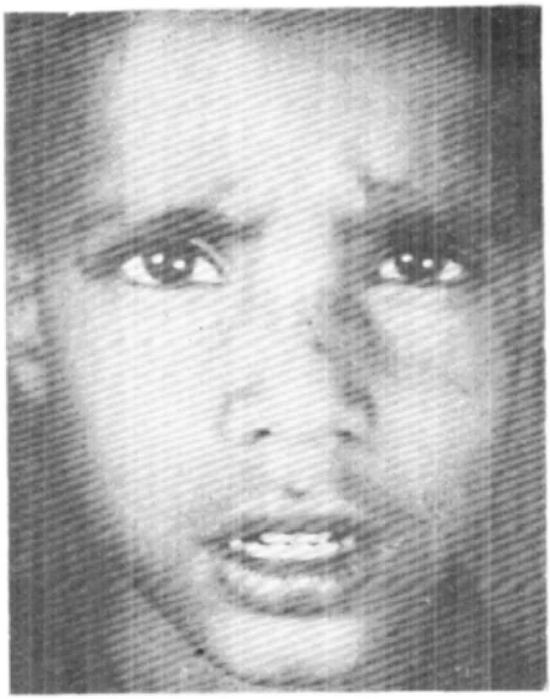

Fig. 4
Note the lesions of PM on the face and left angle of the mouth in a 9 yrs child.

form of the disease, the lesions occur at a later age (3rd and 4th decades of life). It is possible that hormonal changes associated with menopause may affect the phenotypic expression allowing its emergence with greater frequency. In brief it may be postulated that the relative rarity of PM in adolescent females is related to the excess of female sex-hormonal activity present at the time of puberty. Equal expression of DSAP in males and females may be attributed to decreased female sex-hormonal activity in later age groups in women.

The considerable morphological variations in PM is well illustrated in our cases which showed lesions simulating tinea corporis, warts and neurodermatitis.

Several therapeutic remedies have been suggested for this chronic disorder which include electrodesiccation, liquid nitrogen cryotherapy, keratolytics, intralesional steroids[14], topical 5-fluorouracil[37], topical vitamin A acid[38] and oral vit E + A[39]. Two solitary lesions of case 3 in our series were successfully treated with trichloroacetic acid cauterization. Oral Vit A capsules and intralesional triamcinolone acetonide were found to be of no benefit.

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