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Original Research Article

Malignancy in Porokeratosis: Chance or Choice?

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Abstract:

Porokeratosis is a disorder of epidermal keratinization characterized by annular plaques with an atrophic center and hyperkeratotic edges and includes a heterogeneous group of disorders that are mostly inherited in an autosomal dominant form. The ethiopathogenesis of this process is complex and it has been speculated that it comes from the proliferation of abnormal clones of epidermal keratinocytes, which may be triggered by stimuli like sunlight exposure, radiation therapy, or immunosuppression, in genetically predisposed patients. Development of carcinoma within the classic type of Porokeratosis of Mibelli is well-documented but there are only a few cases of malignancy being reported with other forms of Porokeratosis.

Keywords: Epidermal Keratinisation, Carcinoma, Malignancy.

Introduction

Porokeratosis is a rare, autosomal dominant, clonal disorder of keratinization with sporadic cases known to occur frequently. There are five classical clinical variants of porokeratosis: classic porokeratosis of Mibelli, porokeratosis palmaris et plantaris disseminate (PPPD), linear porokeratosis, disseminated superficial porokeratosis and disseminated superficial actinic porokeratosis (DASP). Apart from these five clinical variants, a number of atypical morphological forms such as facial, giant, punched-out, hypertrophic, verrucous, and reticulate porokeratosis have also been reported in literature [1].

All these variants are associated with the presence of a cornoid lamella; a column of keratotic cells in an area of epidermal invagination seen through histopathology. A mutant clone of epidermal cells is thought to be the cause for cornoid lamella, predisposing affected patients to malignancy [2]. Porokeratosis may be considered a premalignant lesion, with a risk of change at around 7.5% [3].

Development of squamous cell carcinoma within the classic type of porokeratosis of Mibelli is well-documented [4]. Classic porokeratosis or porokeratosis of Mibelli is a chronic, progressive dermatosis that may rarely evolve with spontaneous remission [5]. Classic porokeratosis, the most common variant, was first described in 1893 by Vittorio Mibelli, hence the name porokeratosis of Mibelli [6]. It is common in Caucasians particularly Italians and is rarely observed in dark skinned individuals [7].

Aim

The aim of our study is to evaluate all cases of porokeratosis for any remote possibility of development of carcinoma within the lesion by virtue of long term follow up and thereby calculate the percentage chances of change to a pre-malignant or malignant lesion.

Material and Method

The study was carried out in all established cases of porokeratosis attending our outpatient department of Jawaharlal Nehru medical college and hospital, Bhagalpur, Bihar for a period of 2 years from April 2017 to March 2019.

The patients were categorised into 5 groups depending upon the five classical clinical variants of porokeratosis described as classic porokeratosis of Mibelli, porokeratosis palmaris et plantaris disseminate (PPPD), linear porokeratosis, disseminated superficial porokeratosis and disseminated superficial actinic porokeratosis (DASP). Thereafter all the patients were kept on long term follow up at intervals of 3 months and were assessed for any morphological changes in the existing lesions suggestive of malignancy which was confirmed further with the help of biopsy and histopathology.

Result

A total of 14 cases became a part of our study out of which 1 case of classic type of porokeratosis of Mibelli developed squamous cell carcinoma within the lesion giving the risk of change to malignancy of 7.14 %.

Discussion

Porokeratosis of Mebelli consists of one or more plaques which may occur anywhere in the body, more frequently in extremities, especially hands and feet, with unilateral distribution. Other areas, such as neck, shoulders and genitals may also be affected.

Clinically it is characterized by annular brownish macules or hyperkeratotic plaques with an atrophic or depressed center and a raised, sharply marginated keratotic border.

The occurrence of facial and mucosal lesions is rare. It starts, in general, during childhood or adolescence, being more prevalent in males (ratio of 23:1) [8].

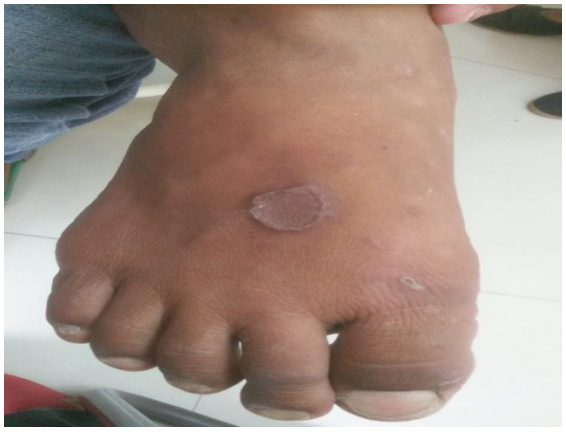

Figure 1: Hyperpigmented, solitary, annular plaque on dorsum of right foot

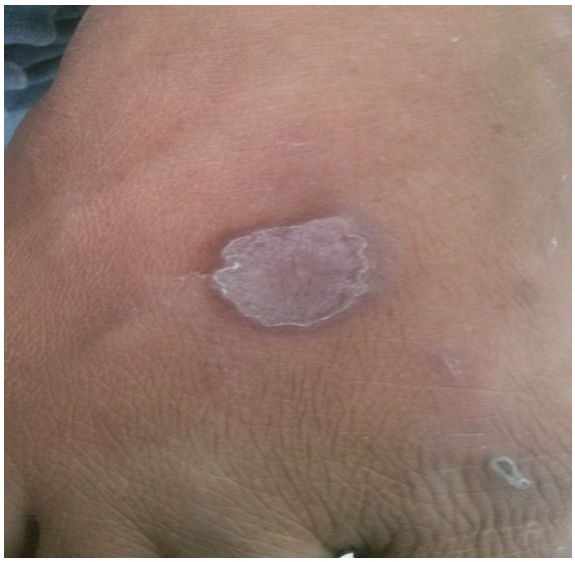

Figure 2: Close up of same lesion showing central atrophy and keratotic ridge

Pathogenesis

It has been found to have an autosomal dominant inheritance with variable penetrance. In addition, various triggers such as immunosuppression, infection, drugs, ultraviolet radiation and mechanical trauma have been incriminated [9].

Pathological Manifestations and Diagnosis

Diagnostic confirmation is achieved through histopathological examination with the finding of the cornoid lamella. The cornoid lamella, a column of parakeratotic cells that occupies the small epidermal invaginations, constitutes a characteristic histopathological finding confirming its diagnosis. Histopathology from the ridge showes keratin-filled epidermal invaginations [10].

Differential Diagnosis

Differential diagnosis of Porokeratosis must address mainly Bowen's disease, squamous cell carcinoma and melanoma.

Less commonly and depending on different presentations and locations of various other forms of porokeratosis, differentials include lichen striatus, lichen planus annulare, lichen sclerosus et atrophicus, inflammatory linear verrucous epidermal nevus (ILVEN), pityriasis rubra pilaris, acrokeratosis verruciformis, elastosis perforans serpiginosa, linear scleroderma, actinic keratosis, basal cell epithelioma and porokeratosis eccrine ostial [11].

Treatment

There are various modalities of treatment like topical 5-fluorouracil, oral retinoid, CO2 laser ablation, 585-nm pulsed dye laser radiation, Grenz ray radiation, Nd:YAG laser radiation, cryotherapy, dermabrasion, surgical excision and electrodessication [12]. Other forms of therapy include keratolytic agents, topical retinoids, topical imiquimod and photodynamic therapy [13].

Since no recurrence of porokeratosis is observed following surgical excision, this suggests that surgical excisions may completely cure porokeratosis. Therefore, it is suggested that surgical excisions should be performed for the treatment of porokeratotic lesions if possible and regular follow-up is required, given that malignancy is possible in porokeratosis.

Causal Association with Malignancy

Although, porokeratosis was first reported more than a century ago, the etiology and pathogenesis remains unclear and the results from different studies are contradictory. Certain mutations that are associated with porokeratosis, including frame shift mutations, have been identified. Clinical and molecular evidence has demonstrated that porokeratosis can be considered to be a premalignant skin condition in view of the over expression of p53 gene in porokeratosis and it is possible that malignant transformation is likely in long-standing lesions with prolonged sun exposure irrespective of the type of porokeratosis.

Chromosomal instability and reduced immune surveillance along with overexpression of p53 are hypothesized to play a role in the development of cutaneous malignancies within porokeratosis [14]. Gene expression profiles reveal an up regulation of mRNAs of hyper proliferative keratins, calcium-binding proteins, connexin 26 and 30 and involucrin in the cornoid lamellae [15].

Associated Malignancies

Development of squamous or basal cell carcinomas has been reported in all forms of porokeratosis [3]. Metastasis although rare, has occurred in a giant lesion along with hypercalcemia. There are reports of epithelioma and basal cell carcinoma arising from porokeratosis of Mibelli, DSAP, as well as in PPPD, and linear porokeratosis possibly from the mutant clone of cells [16,17]. Premalignant lesions such as Bowen's disease [18], cutaneous horns [19,20] and dysplasia at the base of cutaneous horn [21,22] may arise from porokeratosis, which may progress to malignancy.

Conclusion

P53 gene has a wide spectrum of mutations, which are present in half of all tumors [23]. In view of the overexpression of p53 gene in porokeratosis and likely malignant transformation in long-standing lesions with prolonged sun exposure, education regarding photo protection and the long-term follow-up of these patients is of great importance.

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