Eruptive tumor of the follicular infundibulum with unusual clinical presentation: A case report and literature review

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Abstract

Eruptive tumor of the follicular infundibulum (TFI) is an extremely rare benign neoplasm that usually presents as asymptomatic multiple hypopigmented macules symmetrically distributed on the head, neck, and upper trunk. Herein, we report a case of eruptive TFI presenting as hypopigmented macules with central and slightly elevated erythematous papules at rarely involved locations of the four extremities, which has not been reported previously. The pathology showed characteristic features that were conclusive of the diagnosis of eruptive TFI. Because hypopigmentation is a common clinical manifestation and malignant transformation is possible with eruptive TFI, correct early diagnosis, and regular follow-ups are recommended.

Keywords: Eruptive tumor of the follicular infundibulum, hypopigmented macules, macules, tumor of the follicular infundibulum

INTRODUCTION

Tumor of the follicular infundibulum (TFI) is an uncommon benign adnexal neoplasm that was first described in 1961 by Mehregan and Butler.[1] This neoplasm has two distinct variants, namely, solitary and multiple/eruptive TFI. The solitary form is more common than the eruptive form. The reported incidence of all TFIs ranges from about 3 to 20/100,000 skin biopsies.[2-5] Two previous large studies have reported that the eruptive form constitutes about 6%–7.7% of all TFIs.[4,5] Hence far, only a few cases of eruptive variants have been reported. In addition, most cases of eruptive TFI manifest as asymptomatic hypopigmented macules and are usually symmetrically located in the head, neck, and upper trunk.[3-6] Herein, we report a case of an eruptive form of TFI presenting as hypopigmented macules with central slightly elevated erythematous papules on the extremities.

CASE REPORT

A 71-year-old Asian female patient presented with hundreds of whitish macules of approximately 0.5–1 cm each in diameter with central slightly elevated erythematous papules symmetrically distributed over both lower extremities and forearms [Figures 1a-c]. She reported that the lesions initially appeared 30 years ago on both her lower extremities and progressively spread to both the forearms 10 years ago. The lesions gradually increased in number for 30 years. She had no underlying chronic diseases, and she denied having pruritus or skin tenderness. None of the family members had similar skin lesions. The skin lesions became more obvious after

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sun exposure and during summer. She had not received any treatment before. The clinical tentative diagnoses included idiopathic guttate hypomelanosis, pityriasis versicolor, vitiligo, verruca plana, and postinflammatory hypopigmentation. KOH scraping did not show elements of pityriasis versicolor.

The histopathological examination showed irregular acanthosis with basal cell hyperplasia and elongated epidermal ridges with horizontal anastomosis, without dysplasia. Horizontal plate-like proliferation of pale monomorphic keratinocytes was present with multiple thin connections to the epidermis [Figure 2a and b]. There was a loss of melanin pigments in the tumor plates, but these pigments were preserved in the epidermis between the tumor plates [as shown by Fontana–Masson staining, Figure 2c]. The number of basal melanocytes was not changed [as shown by SOX10 and microphthalmia transcription factor staining, Figure 2d]. The increased mucin deposition in the papillary dermis of the central erythematous papule was shown by Alcian Blue stain [Figure 2e and f]. Based on these clinical and histopathological findings, the diagnosis of eruptive TFI was established.

Because cutaneous eruption is asymptomatic, and the current therapy for eruptive TFI shows limited responses and no further intervention was proposed for her. However, long-term regular follow-up was recommended because of the rare but possible malignant transformation into basal cell carcinoma.[7]

**DISCUSSION**

This study presents a case of eruptive TFI with an unusual clinical presentation. Multiple or eruptive form of TFI is extremely rare and often occurs in younger patients compared with solitary form. In addition, among the different presentations of TFIs, only the eruptive variant can be identified clinically. It presents as asymptomatic, irregularly shaped macules, slightly elevated papules, or depressed lesions, which are usually symmetrically distributed on the head, neck, and upper trunk.[3-6] The skin lesions are usually asymptomatic, but pruritus is the most frequent complaint after sun exposure.[5,7,8] The lesions are mostly hypopigmented and can be normochromic or erythematous. Besides, the hypopigmented macules also become more visible after sun exposure, like in our case.[7,9,10] The differential diagnosis of hypopigmented macules includes vitiligo, pityriasis alba, pityriasis versicolor, postinflammatory hypopigmentation, idiopathic guttate hypomelanosis, and tuberculoid leprosy.[5,11,12] The number of eruptive lesions can vary from fewer than 20 to more than 100, and these lesions can show a progressive increase in their numbers over many years.[11] They usually measure from 2 to 10 mm. Lesions are prone to be monomorphic in the same patient.[13]

Extremities are rarely reported as the sites of involvement for these skin lesions.[3,13,14] So far, only four studies have shown eruptive variants in unusual locations, such as the extremities. However, these four previous case reports have revealed cutaneous manifestations different from those seen in our case. Schnitzler *et al.* showed a progressive papular eruption – some of which appeared as prurigo nodularis with photosensitivity – on the face, lips, and vulva in a 38-year-old female patient.[7] Cheng *et al.* reported multiple brown-to-dusky red papulomacules on the face, neck, trunk, both sides of the forearms, inner arms, axillae, and groin in a 64-year-old man.[14] Zhu *et al.* reported hundreds of pruritic, erythematous maculopapules over the arms, shoulders, trunk, buttocks, and legs in a 49-year-old woman.[15] Haddad *et al.*
presented a case of star-shaped hypochromic lesions with hyperchromia on the edges on the posterior side of the right lower limb in a 53-year-old male patient.[13]

TFI has characteristic and consistent histopathological and immunohistochemical features. Therefore, histological diagnosis of TFI is essential. Histopathological analysis of TFI revealed superficial horizontal interanastomosing epithelial plate-like proliferation of pale cells with abundant cytoplasm.[1,2,16] Tumor cells are monomorphous without cytologic atypia and mitotic activity seen in the basal cell carcinoma, and peripheral palisading is occasionally seen.[17] The presence of a dense elastic fiber network beneath the base of the tumor is also a characteristic feature that distinguishes TFI from seborrheic keratosis and basal cell carcinoma, which lack this feature.[10]

Immunohistochemical analysis showed that the cytoplasm of the pale keratinocytes contains abundant glycogen and can be stained with Periodic acid–Schiff stain.[1] The brush-like network of elastic fibers at the base of tumor can also be stained with orcein stain.[10] A loss of melanin pigment from the tumor plates was also noted, whereas the melanin pigments preserved between the altered epidermis were highlighted by the Fontana–Masson stain.[10,11] There was no alteration in the number of the basal melanocytes in these lesions. There is no histopathological difference between solitary and eruptive TFI, except for the loss of melanin pigments in eruptive TFI.[9] It is likely that systemic factor rather than regional factor may contribute to the loss of pigments in the eruptive TFI. The defect might result from melanosome transfer or melanin synthesis, although more evidence are required.[18]

Ackerman et al. described the histological diagnostic criteria as follows: (1) a distinctive silhouette with a horizontal proliferation of keratinocytes, (2) characteristic neoplastic epithelial cells with small monomorphic nuclei and abundant pink cytoplasm, and (3) thin columns of cells and bulkier aggregations, all of which are interconnected.[16]

Additional histopathological feature was also found that the increased mucin deposition was stained by Alcian Blue in the papillary dermis of the central erythematous papule. Cutaneous mucin was composed primarily of glycosaminoglycans, which are secreted by fibroblasts. The pathogenesis why excess mucin produced in the skin is still unclear. Multiple factors can stimulate the synthesis of glycosaminoglycans such as increased level of serum immunoglobulins and cytokines of interleukin-1, the tumor necrosis factors, and transforming growth factor.[10] However, this pathology feature has not been reported previously in eruptive tumor of follicular infundibulum, and the exact mechanism remains to be determined.

Regarding the histogenesis of TFI, there are at least two different hypotheses. One hypothesis initially proposed by many authors, including Mehregan and Butler, who named the tumor, was that TFI originates from the follicular infundibulum because of the topography of the proliferation.[1,5,20] A different hypothesis based on the abundant pink cytoplasm, proposed by other authors including Ackerman et al., was that the tumor usually arises from the infundibulum but differentiates toward the isthmus. They think that “TFI” is a misnomer.[16] This hypothesis is also supported by immunohistochemical analysis with cytokeratin stains in which most cases revealed differentiation comparable to that in the fetal follicular isthmus and only in one case, differentiation in keeping with the fetal follicular infundibulum.[21] Alomari et al. believed that TFI originates from the follicular infundibulum with mostly isthmic differentiation and some degree of infundibular differentiation, wherein some cases presented cysts with keratohyalin granules and lamellar keratin.[5]

Treatments reported for TFI include topical corticosteroids, topical keratolytics, topical retinoic acid, topical imiquimod, and long-term oral etretinate,[7] all of which have limited effects with incomplete resolution. Other more destructive therapies, including cryotherapy, curettage, electrocautery, ablative laser, and surgical excision, have produced unpleasant outcomes and even carries the unacceptable risk of scarring.[17]

TFI can be associated with other cutaneous lesions, and the incidence of the association varies from 11.3% to 25%.[4,5] The most common lesion associated with TFI is basal cell carcinoma.[4,5,16] In addition to basal cell carcinoma, TFI may be associated with other cutaneous neoplasms, such as nevus sebaceous, and trichilemmoma, and with Cowden syndrome.[4,22] Although both solitary and multiple TFIs are benign tumors, transformation into basal cell carcinoma in two tumors has been reported in one case with eruptive variants in 100 lesions.[7] Therefore, it is recommended that patients diagnosed with TFI with numerous lesions be followed up in the long term.

**Conclusion**

We report a case of eruptive TFI with an unusual clinical presentation, which has not been published previously. Eruptive TFI is a rare cause of macular hypopigmentation and is often underdiagnosed. Macular hypopigmentation is a common feature in dermatological cases. Dermatologists should be aware that eruptive TFI could also have unusual clinical manifestations at rarely involved locations at the four extremities that should be added to the clinical differential diagnosis to properly perform skin biopsies. Since TFI has characteristic histopathological and immunohistochemical features, skin biopsy is the key to a definite diagnosis. In addition, due to the possibility of malignancy transformation into basal cell carcinoma, correct early diagnosis and regular follow-ups are advised.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients
understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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