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Multiple Nonfamilial Trichoepitheliomas: A Rare Case with Review of the Literature

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Abstract **Case Report**

Trichoepitheliomas are benign tumors of follicular origin and often appear in childhood or early adolescence. They present as small, firm papulonodular lesions of normal skin color or translucent. The lesions gradually increase in size and then stabilize. They sit electively on the face, mainly in the nasolabial folds, on the forehead, chin, and cheeks, and sometimes on the scalp and neck. Trichoepitheliomas can be divided into three subgroups: multiple familial Trichoepitheliomas, solitary non-hereditary Trichoepitheliomas, and desmoplastic Trichoepitheliomas. Nonfamilial multiple trichoepitheliomas are rarely described. We report a case of a 12-year-old child whose clinical history and clinicopathologic correlation allowed us to retain the diagnosis of multiple non-familial trichoepitheliomas.

Keywords: Trichoepitheliomas, Sporadic, Genodermatosis, the CYLD gene.

INTRODUCTION

Trichoepitheliomas (TE) are benign tumors of follicular origin. They were first described by Brooke in England in 1892 as "cystic adenoid epithelioma" and in the United States by Fordyce as "multiple benign cystic epithelioma" [1, 2]. These are papules, measuring a few mm, mainly located on the face, scalp, and neck, which appear in childhood and increase in number with age. They can be isolated or multiple and occur sporadically or in families [3]. Although rare, the malignant transformation of TE into trichoblastic carcinoma or basal cell carcinoma has been described [4]. We report a case of multiple non-familial TE in a 12-year-old child.

CASE REPORT

This is a 12-year-old male child, with no particular pathological history, and no notion of consanguinity, who presented for asymptomatic skin lesions on the face that had been evolving for 1 year, gradually increasing in size and number, without any similar case in the family and other associated cutaneous or extra-cutaneous signs.

The general examination found a patient hemodynamically and respiratory stable. Dermatological examination showed translucent, flattened, and globular papules, 2mm to 4 mm, pink and fleshy, painless sitting on healthy skin, electively on the face (nose, nasolabial folds, eyelids, cheeks, forehead, chin) (Figs. 1a and 1b). The rest of the dermatological and somatic examination was unremarkable.

The histopathological study of the papules confirmed the diagnosis of TE by showing a well-limited benign tumoral proliferation localized in the reticular dermis, made up of lobules and islands of basaloid cells arranged in anastomosed spans and developed around horny cysts (Fig. 2). The diagnosis of multiple non-familial TE was retained given the absence of similar cases in the family, the clinical and histological aspects. We cared to offer the CO2 laser with regular clinical monitoring after having informed parents about the risk of malignant transformation of the disease.

DISCUSSION

Trichoepitheliomas are benign hamartomas of pilosebaceous follicles and often appear in childhood or early adolescence [5]. Various synonyms, trichoepithelioma papulosum multiplex, cystic adenoid epithelioma, cystic adenoid acanthoma, multiple benign cystic epithelioma, Brooke's tumor or Brooke Fordyce's trichoepithelioma have been used for TE [6]. Clinically, TE presents as small, firm, papulonodular lesions of normal or translucent color, sometimes covered with telangiectasias. The lesions gradually increase in size and then stabilize. They sit electively on the face, mainly in the nasolabial folds, on the forehead, chin, and cheeks, and sometimes on the scalp and neck [7]. Their prevalence is unknown. However, a dermatopathology laboratory in the United States found 2.14 to 2.75 cases of TE out of 9,000 biopsies per year [8].

TE can be divided into three subgroups: Multiple Familial TE, Solitary Non-Hereditary TE, and Desmoplastic TE. Non-familial multiple TE is rarely described, Sehrawat and al published the 1st case in 2016 [9]. Our case had multiple TE with no similar family history.

Multiple familial trichoepitheliomas (MFT) is an autosomal dominant hereditary genodermatosis associated with mutations in chromosome 9p21 or the cylindromatosis (CYLD) tumor suppressor gene, located on chromosome 16q12-113 [10, 11]. The CYLD gene encodes a protein of 956 amino acids with a molecular weight of 120 kDa belonging to the family of deubiquitinases. In the normal state, the CYLD protein acts primarily as an inhibitor of nuclear factor B in the TNF signaling pathway. In the majority of cases, the mutations lead to the formation of an abnormal truncated protein, leading to an increase in NF-kB activity induced by TNF and a defect in apoptosis at the origin of tumor proliferation [12, 13]. MFT can be seen in Brooke-Spiegler syndrome, in which inherited adnexal tumors are combined, including multiple trichoepitheliomas, cylindromas, and spiradenomas [5]. Moreover, it can also be seen in other syndromes such as Rombo syndrome (vermicular atrophoderma, milia, trichoepithelioma, hypotrichosis, basal cell carcinomas, and hypohidrosis) and Bazex syndrome (follicular atrophoderma, trichoepithelioma, hypotrichosis, basal cell carcinomas, and hypohidrosis) [14]. MFT has also been found associated with multiple renal and pulmonary cysts, basal cell adenoma of the parotid gland, ovarian cancer, breast cancer, steatocystomas, alopecia, and myasthenia gravis [15].

The differential diagnosis of TE includes the juvenile colloid milium, cylindroma, syringoma, milium, eccrine poroma, eccrine nevus, nevus comedonicus, multiple trichoblastoma, sebaceous adenoma, trichofolliculoma, the basal cell carcinoma and molluscum contagiosum, [14] Histological examination of a TE confirms the diagnosis. It shows a well-defined lesion made up of epithelial bands and small cords of basophilic cells, often centered or terminated by horny cysts taking on a characteristic “tadpole tail” appearance. The basaloid cells can assume a palisade arrangement around the periphery of the lobules and islets. The perilesional stroma is dense and fibrous [16].

Multiple nonfamilial TE are rare and the diagnosis is usually made by clinicopathologic correlation in the absence of a family history of similar cases and, if necessary, a genetic study. Our original case represents the 4th case of multiple non-familial TE reported in the literature. For the 3 other cases, one presented multiple non-segmental unilateral grouped papules on the truck [8], the other had extensive and disfiguring TE in the face [9], and the 3rd had multiple segmental TE along Blaschko lines on the right shoulder [17].

The evolution of nonfamilial multiple TE is marked by the multiplication of lesions. The damage is essentially aesthetic, as was the case with our patient. However, rare cases of associated malignant tumors have been described (basal cell carcinoma, trichoblastic carcinoma), justifying regular monitoring [18, 19].

Therapeutic methods are based on surgical excision or destructive methods (cryotherapy, electrocoagulation, CO2 laser, or Erbium YAG) but the latter does not prevent the occurrence of new lesions [20, 21].

Topical Sirolimus at 1%, Imiquimod at 5%, and Tretinoin at 1% were also used. In an 11-year-old girl with multiple TE, the application of Imiquimod initially alone and then in combination with Tretinoin resulted in an 80% improvement in the lesions after three years [22, 23].

A better knowledge of the pathophysiological mechanisms of the CYLD protein, in particular concerning its inhibitory activity on nuclear factor B induced by TNF, could make consider other therapeutic alternatives such as NF-B antagonists (Aspirin or Non-Steroidal Anti-inflammatory drugs) or anti-TNF (adalimumab). But as the lesions are asymptomatic and have a very low malignant potential; treatment is usually not necessary unless there is disfigurement [7, 24].

CONCLUSION

We have reported a rare case of sporadic multiple TE with no family history. To our knowledge, our case represents the 4th case described to date in the literature.

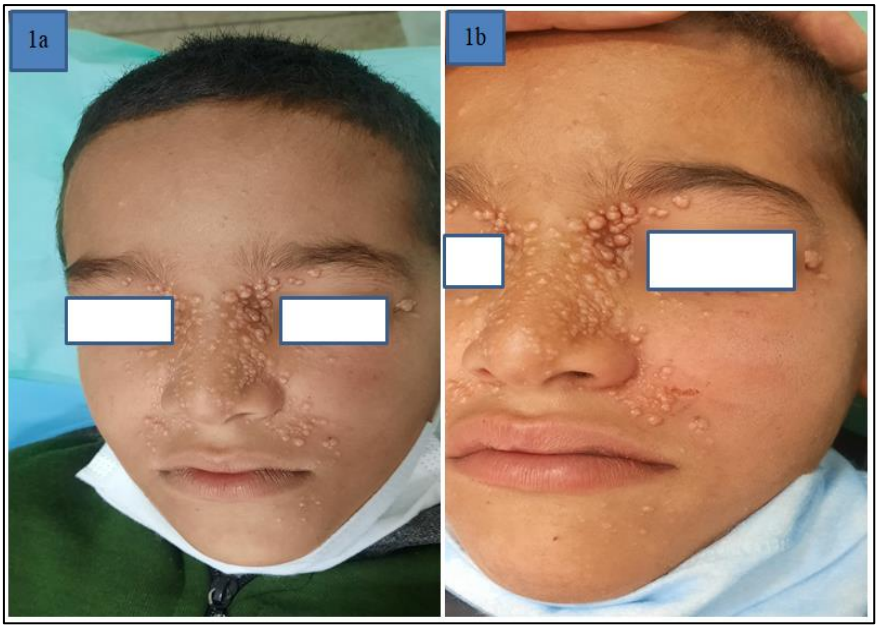

Figure 1a & 1b: Translucent, flattened, and globular papules, 2 to 4 mm, pink and fleshy, located on healthy skin on the face

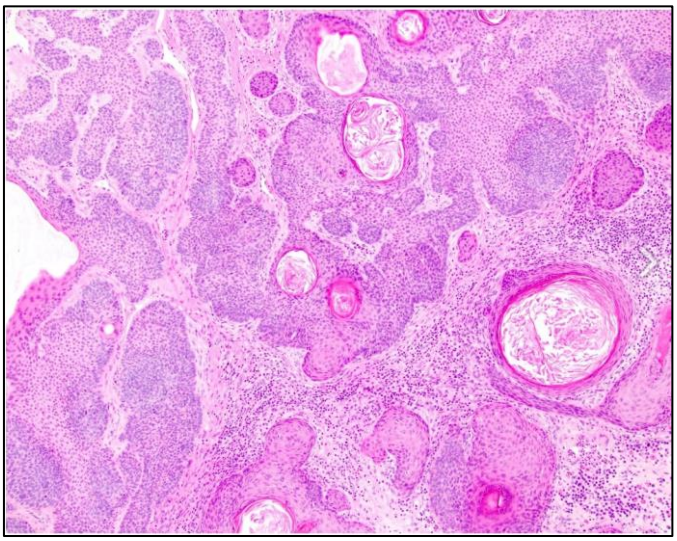

Figure 2: Horny cysts of trichoepithelioma of the face (HE X 100)

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