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Case Report

MULTIPLE FAMILIAL TRICHOEPITHELIOMA: A CASE REPORT AND REVIEW OF LITERATURE.

***SJ Yiltok, **GO Echejoh, *AM Mohammad, *AM Ituen, *MI Igoche, *OT Dades**
*Departments of *Surgery and **Histopathology, Jos University Teaching Hospital, Jos, Nigeria.*

ABSTRACT

Objective: Multiple familial trichoepitheliomas are rare autosomal dominant skin disease that is rarely reported from this part of the world. The lesions resemble other types of skin diseases that present with papules and nodules.

Patient and Method: This is case report of a patient who presented with multiple facial papules and nodules. He wanted treatment to improve his facial (cosmetic) appearance.

Results: A 36 year old single male with a 25 years history of multiple facial papules and nodules. Similar lesions were present in other members of the family. He had several treatments including that for leprosy. Histologically the lesions showed keratinized stratified squamous epithelium overlying proliferating packets of basoloid cells with hyper chromatic nuclei, along with several keratin horn cysts and moderate stromal infiltrate of chronic inflammatory cells. Based on the history and the histology a diagnosis of multiple familial trichoepithelioma was made.

Conclusion: For a diagnosis of multiple familial trichoepithelioma to be made in patients presenting with multiple facial papules and nodules a high index of suspicion is needed. This is more so if there is a history of similar lesions in the family.

Key Words: Multiple Trichoepithelioma, Familial, Cosmetic appearance, Diagnosis

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INTRODUCTION

Trichoepitheliomas (TE) are benign cutaneous tumours that originate from hair follicles and occur either as solitary non-familial or multiple familial [1, 2].
The multiple familial trichoepithelioma (MFT) is an uncommon autosomal dominant disease skin tumour, characterized by multiple facial papules and nodules located around the nasolabial area, nose, forehead, upper lip and occasionally the scalp, neck and upper trunk [2-6].
Histological examination usually shows the typical horn cysts, tumour islands composed of basophilic cells arranged in a lace liked network, foreign body giant cell reaction and some differentiation towards hair structures [1].
This is case report of a patient that presented with multiple facial papules and nodules with a family history of similar lesions who had histological diagnosis of Trichoepithelioma (TE).

CASE REPORT

A 36years single male presented with a 25years history of painless, non-puritic multiple nodular facial lesions which were cosmetically unacceptable to him. There was no information to suggest reaction to any substance or trauma. He had no associated areas of hypopigmentations; neither was there any ocular nor skeletal problem. His mother and younger sister have similar lesions. He had consulted several clinics including a leprosy clinic where he was treated for leprosy with dapsone, a drug he took for 6 months without improvement. The main findings were multiple facial papules and nodules distributed on the nose, forehead and malar, with the nodules mainly on the midline (Figure1).

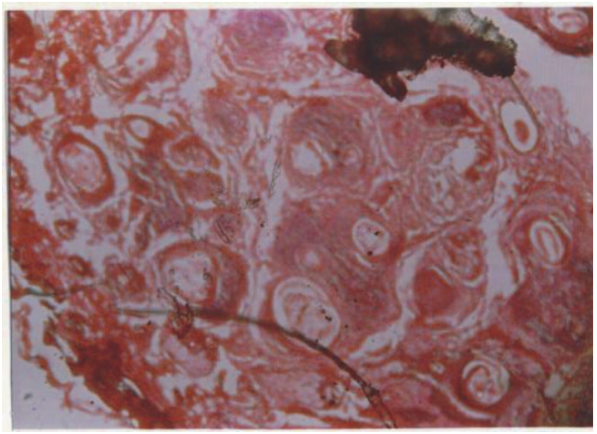
Figure1: **Photograph of Patient with Multiple Facial Papules and Nodules.**

Correspondence: Dr S J Yiltok
Email: simyiltok@yahoo.com

Histological sections of one of the lesions showed keratinized stratified squamous epithelium overlying proliferating packets of basoloid cells with hyper chromatic nuclei. Several keratin horn cysts in addition to moderate stromal infiltrate of chronic inflammatory cells (Figure 2) were seen. Based on these findings a diagnosis of trichoepithelioma (TE) was made.

No treatment was offered, as surgical excision will lead to multiple scars and the effective non surgical treatment is currently not available in our centre.

Figure 2: **Photomicrograph of Papules Showing the Typical Features of Trichoepithelioma with the Presence of Keratinized Horn Cells and Islands of Proliferating Basaloid Cells.**



DISCUSSION

Patients with MFT most often present to the hospital for cosmetic reason [7] and usually want treatment to improve their outlook. The lesions are usually dense and are disfiguring[2,4] a cause of psycho-social problem in patients, as seen in our patient who was not happy with his face even though the lesions were asymptomatic.

It is an uncommon pathology with a dermatopathology laboratory in the US reporting about 2.14 to 2.75 cases per year [4] and most of them are females even though both sexes receive equal genes (autosomal dominant). Females are most affected because of the lessened penetrance [4, 6].

The lesions are skin coloured, firm papules or nodules of 2-8mm in diameter (fig.1), slow growing and commonly seen in childhood and adulthood [3, 4, 8]. It shares similar features with Basal Cell Carcinoma (BCC) and their distinction may be difficult in small biopsies [9]. However, this difficulty is mainly in the solitary TE than in MFT as the family history as well as the multiple lesions tends to distinguish it clinically. The main histological features that distinguish BCC from TE are stroma, clefting and the absence of papillary mesenchymal branches[4]. In addition to this, there are histochemical staining techniques that can also differentiate the two[9]. antibodies against bcl-2 CD34 that are expressed by TE are stained by histochemical method according to their distribution.

Reports have shown that TE can undergo malignant transformation to BCC [3]. This is a rare occurrence but it tells the clinician to remain vigilant and to examine patients carefully as a seemingly benign lesion might be malignant. This is more so that the lesions tend to reoccur after surgical treatment [3].

It has been shown that familial cylindromatosis (FC) and MFT can occur within one family and a single person[10], which suggest that the two types of dermatosis may be caused by a dysfunction of the same gene. Based on these facts it has been suggested that there are two forms of MFT: one that occurs in isolation is determined by a gene in the region at 9p and another that co-occurs with FC is determined by a gene on chromosome 16 the *CYLD* gene [2]. The *CYLD* has been mapped out by Biggs et al [11] and is located at chromosome 16q12-13. In a study by Leonard et al [12] they were able to demonstrate loss of heterozygosity (LOH) in a patient with sporadic TE at 16q, based on this Zhang et al [2] and Zheng et al [6] studied the region of *CYLD* and they were able to demonstrate that the gene was the genetic basis for MFT in their patients.

The pattern of LOH is characteristic of a tumour suppressor gene (recessive oncogene), that follows the classic two-hit model[2,13]. If the germline mutations are loss of function mutations and the second hit (somatic mutation) occurs with equal chance in eccrine (or apocrine) and hair follicle cells equally, we expect to see both TE and cylindromatosis in patients carrying *CYLD* germline mutation[6]. One hypothesis says that germline mutation displays tissue specific function loss which is dependent or independent of the genome background [13]. Germline mutation may determine the tissues where the second hit occurred, with cylindromatosis developing if it happens in eccrine (or apoccrine) cells and TE when it happens to hair follicle cells.

Inactivation of the *CYLD* protein may contribute to oncogenesis by enhancing the degradation of proteins that suppress cell proliferation or promote apoptosis[2]. MFT and FC are caused by a gene encoding the *CYLD* protein. This protein has been shown to be a deubiquitinating enzyme that negatively regulates activation of the transcription factor NF-κB (nuclear factor- κB) by specific tumour necrosis factor receptors (TNFRs)[14] that are implicated in the proper development of skin appendages[15]. The NF-κB transcription factor has key role in inflammation, immune response, oncogenesis and protection against apoptosis[16]. Inhibition of *CYLD* increases resistance to apoptosis (which prevents cell death), a mechanism that has been suggested to cause tumourogenesis.

NF-kB can be inhibited by a number of pharmacological agents, mainly anti-inflammatory agents such as steroids and non- steroidal anti-inflammatory drugs[8,17]. Studies have shown that salicylates and prostaglandins inhibit the enzyme IkB kinase an enzyme involved in the NF-kB pathway[17]. This principle has been applied with encouraging result by Fisher and Geronemus [8] who reported a case of MFT that was treated with adalimumab (a neutralizing antibody to TNF) and aspirin. With more successful trials this may replace the traditional modes of treatment amongst which include laser resurfacing[4,8], electrosurgery[7], and dermabrasion [4].

MFT though a relatively uncommon disease can be diagnosed clinically by the pattern of distribution of the papules and nodules (usually centro-facial), family history of similar lesions and confirmation by histology. It remains a difficult lesion to be treated with the current treatment modalities. Studies have shown that the use of anti-inflammatory agents like the salicylates can reduce the sizes of lesions in MFT. With further research it is hoped that medical treatment will become the choice of treatment rather than surgical treatment.

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