Syndrome of the month

Dermal eccrine cylindromatosis

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In 1842 Ansell¹ first described an entity characterised by a striking clinical picture of multiple disfiguring tumours located on the face and scalp, which rapidly recurred after excision, had a distinctive histology, and showed familial occurrence. Differences of opinion as to the pathogenesis of the lesion and especially the various names used (including epithelioma adenoides cysticum, multiple benign cystic epithelioma, multiple trichoepithelioma, turban tumour, tomato tumour, Spiegler's cylindroma, or dermal cylindroma) have led to considerable confusion. An extensive study by Cotton and Braye² strongly supported earlier reports³⁻⁴ of evidence for an eccrine intradermal origin. Therefore, we have adopted the term "dermal eccrine cylindroma" to include the origin of the tumours. A rare subtype of dermal eccrine cylindroma is called turban tumour, a highly descriptive label for the classical total involvement of the scalp with tumours covering the head and causing gross disfigurement.⁵⁻¹⁰

Incidence

The frequency of (multiple) eccrine dermal cylindroma is still uncertain, although most authors consider it rare. In the Netherlands reports of two families have been published^{11,12} and two others are known to us; in total they have 45 affected members. Some studies have indicated a higher incidence in females.^{7,13-15} One study even mentions a female preponderance of 10:1,² while others have reported equal sex distribution. Anderson and Howell¹⁶ suggested that this higher incidence in females may be explained by reduced penetrance in males.

Dermal eccrine cylindromata are mostly reported in white races, but may be found in other ethnic groups as well.¹⁷

Clinical features

The majority of dermal eccrine cylindroma arise as small, solitary lesions on the head or neck^{2,3,18} (fig 1). The mean age of first appearance of lesions in published and personally known cases was 23.2 years (range 1.5 to 69 years). The locations of the cylindromata are shown according to their frequency in the table. Approximately 10 to 15% occur on sites other than the head or neck, such as the trunk and extremities.^{3,5} Six percent are reported to be related to the ear.¹⁹ The giant forms of

Figure 1 Small dermal eccrine cylindromata around the nose and on the nasal bridge in an adult male.

dermal eccrine cylindroma develop chiefly in the frontal and tempoparietal regions of the scalp² (fig 2). The larger dermal eccrine cylindromata are hairless, firm, and nodular, resistant to the touch and mobile on the underlying galea, while being firmly attached to the skin. They may occur in such numbers as to cover the scalp more or less completely^{3,6,7,10,11} which are called turban tumours.

Tumours usually become apparent during adolescence and initially grow slowly.^{6,11} As they continue to develop and grow during life the disfigurement worsens with progression of the disease.^{20,43} Individual tumours may vary in size from a few millimetres to 4 or 5 centimetres, the latter size probably representing coalescences of smaller lesions.^{6,16} Internal tumours of the parotid gland³⁵ and lung¹⁹ have been reported.

Crain and Helwig³ reported five patients in which injury preceded the development of the tumour. However, the significance of this finding is doubtful.³ The lesions do not usually seem to be associated with pain, although the patient reported by Evans⁶ did complain of intense irritation at night, Sherman *et al*¹⁸

Locations of dermal eccrine cylindromata described in published reports and in personally known patients, according to frequency (n = 74)

Site	%
Scalp	96
Nasolabial area	70
Back	43
Chest	42
Forehead	29
Eyelids	18
Extremities	15
Chin	11
Abdomen	9
External genitalia	9
Ears	6

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Figure 2 Large dermal eccrine cylindromata on the scalp of an affected female.

Figure 3 Nearly complete occlusion of the auditory canal by coalescing dermal eccrine cylindromata.

reported pain in a patient during rapid growth, and Blandy *et al*⁵ reported stinging in the lesions.

Complications

Deafness may occur owing either to tumours in the external ear or to occlusion of the auditory canal^{13 14 18 21 22 44} (fig 3). Growth of the tumours may be so extensive as to cover both eyes and ears necessitating a total resection of tumour bearing skin.^{6 8 9 23} If tumours reach this size, the risk of infection increases because the patients have difficulty in keeping their head clean.¹⁴

In late presentations ulceration and maceration of the tumour or tumours may occur, leading to unpleasant fetor and anaemia.^{7 12 18 22 24} Episodes of depression related to the disfigurement caused by the tumours have been reported in three instances.^{10 20 24} Multiple eccrine cylindromata are known to be associated with both trichoepitheliomata and milia,^{19 38 39 42} pointing to a common histogenesis (see Histopathology). Possibly this is a separate entity.

Malignant transformation of multiple or solitary dermal eccrine cylindroma is considered to be rare. One report described dermal cylindromata of the parotid glands in a patient without malignant degeneration during 18 years of follow up.²⁵ However, Lin *et al*²⁶ and Tsamboas *et al*²⁷ reported histological changes, consisting of loss of hyaline sheath and atypical mitotic figures, indicative of possible malignant transformation. Lin *et al*²⁶ also reported a greater tendency towards malignant transformation in multiple dermal eccrine cylindromata compared to solitary lesions, but no well documented evidence to support this view was given. Crain and Helwig³ stated that dermal eccrine cylindromata seldom undergo malignant transformation: Urbanski *et al*⁴¹ encountered 11 cases with a malignancy. Crain and Helwig³ caution that in the case described by Luger²⁸ the picture could have been complicated by repeated and massive radiation therapy over a period of years before the malignant transformation occurred. Bourland *et al*²⁹ described the transformation to a basocellular epithelioma of a previously diagnosed solitary cylindroma in a 90 year old male. Blandy *et al*⁵ suggested that until long term results are known and documented it would be wise to consider the lesions to be potentially malignant.

Differential diagnosis

Dermal eccrine cylindroma should be differentiated from malignant syndromes such as basal naevoid cell carcinoma or metastases from a distant primary tumour, to which a close resemblance may exist.^{5 16} Sometimes dermal eccrine cylindromata are confused with neurofibromata, even necessitating a biopsy for reliable differentiation.³⁰ Cylindromata may also occur as solitary, non-hereditary lesions.^{3 31}

Histopathology

The origin of dermal eccrine cylindromata has long been controversial. Fusaro and Goltz³² and Hashimoto and Lever³³ favoured an apocrine differentiation because their electron microscopic findings showed two types of granules similar to the secretory cells of apocrine glands. In addition, these authors felt that this view was supported by the common association of trichoepithelioma and dermal eccrine cylindroma, both originating from cells of the primary epithelial germ, and by the fact that no dermal cylindroma has been reported on the palm or sole where tumours of eccrine origin would be expected.

However, studies by Crain and Helwig,³ Munger *et al.*,⁴ and especially Cotton and Braye² supplied evidence that the dermal cylindroma is derived from the eccrine sweat gland. Cotton and Braye² studied 10 examples of cylindromata taken from their routine histopathology files, using histological, ultrastructural, and immunocytochemical techniques. The eccrine origin of the cylindromata was supported mainly by their derivation from the coiled segment of intradermal eccrine ducts.² Further evidence has been provided by the coexistence of cylindromata and eccrine spiradenomata in the same patients^{20 23 24 34 35 45} and the coexistence of dermal eccrine cylindromata and multiple trichoepitheliomata of the face (rarely in the same clinical lesion), suggesting a common histogenesis from a pluripotent stem cell.^{4 20 23 34–36} Recently, it was shown that both dermal eccrine cylindromata and trichoepitheliomata stained positively with type IV and type VII collagen antibodies, which constitutes further evidence of a common origin.³⁷

The primary histological features of cylindromata are cystic and duct-like structures with cords of basophilic cells and a prominent acidophilic hyaline basement membrane. Microscopic examination shows multiple foci of closely clustered epithelial cells with uniform size and shape and a palisading arrangement within nodules surrounded by a hyaline wall.¹³ The oval to round islands of basophilic cells may have the appearance of an assembled jigsaw puzzle.^{2 7 12 26 34} The cystic spaces in almost all cases are lined by squamous, cuboidal, or columnar epithelium and in some instances resemble sweat ducts.^{3 4 38} Small units of tumour are invariably present at the margins and may account for the high recurrence rate after excision.

Genetics

A decal eccrine cylindroma may occur either in a solitary or a multiple form. The more frequent solitary form is a sporadic event,³ but multiple dermal eccrine cylindromata are inherited as an autosomal dominant trait with incomplete penetrance which has been estimated to be 60% to 75%.^{14 39} Welch *et al.*¹⁹ reported a higher percentage approaching 100% in a family with both cylindromata and trichoepitheliomata. There is no clue whatsoever available about a chromosomal location as no patient has been reported with a chromo-

some anomaly. A remarkable finding has been that dermal eccrine cylindromata overexpressed type VII collagen, which is the major structural protein of the anchoring fibrils.⁴⁰ However, it is uncertain whether this has any pathogenetic relevance.

As mentioned before, a preponderance of affected females has been reported.² Anderson and Howell,¹⁶ however, reported in their extensive analysis of 19 previously published pedigrees and one newly ascertained pedigree (in total 175 cases) that there was no indication of an excess of affected females, but, rather, a marked deficit of affected males. They found a high penetrance level when the males belonged to the proband's sibship, a small sibship, or had early birth order but found a reduced disease frequency in males when sibship or pedigree size was large, birth order late, or when the males belonged to a sibship not containing the proband. Furthermore, they found no evidence of reduced viability in males or of sex linkage, suggesting that the differences in affected rates between males and females can be best explained by a combination of a different penetrance and detection rate. Less overt expression and diminished penetrance in males may imply that generally the disorder is more variable and less expressed in males compared to females, resulting in fewer and smaller tumours, later development of multiple tumours, or location of tumours in unobtrusive areas. Anderson and Howell¹⁶ concluded that endocrine influences could be a factor in the different expression in both sexes.

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