Ectodermal dysplasia associated with autoimmune disease

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SUMMARY A case is reported of hereditary ectodermal dysplasia with corneal involvement associated with polyendocrinopathy and pernicious anaemia. The presence of autoantibodies to various endocrine organs and ocular tissues is confirmed. This suggests that ectodermal dysplasia may be an autoimmune disease.

Ectodermal dysplasia is known to affect various tissues of embryonic ectodermal origin. The main abnormality affects skin and its appendages and teeth. There are various forms of ocular manifestation, principally involving ectodermal structures such as the cornea, lacrimal systems, lens, and retina. Related disorders of skeletal abnormality and cleft palate have been described. This paper reports an association of ectodermal dysplasia with autoimmune diseases.

Case report

The patient, a male aged 22 years, was born at full term following normal pregnancy. At the age of 18 months he was seen by dermatologist for loss of hair, eyebrows, and eyelashes together with nail dystrophy. At the age of 10 years he presented to a paediatrician with pallor and anorexia; pernicious anaemia was diagnosed. Four years later he developed symptoms of excessive water drinking, salt craving, nocturia, and enuresis. A water deprivation test confirmed the diagnosis of cranial diabetes insipidus. He was first seen by an ophthalmologist at the age of 14 years with symptoms of photophobia and chronic irritation of the eyes. The initial sign was superficial punctate keratitis, which did not respond to various topical antibiotics and steroids. He was followed up in the eye clinic for 2 years, during which his vision remained good at 6/6 in each eye. He was then lost to follow-up in the eye clinic because of his poor general health. At the age of 17 years Addison's disease was diagnosed. Two years later he developed attacks of tetany and was found to have hypoparathyroidism. He was seen again by an ophthalmologist at the age of 18 years, when upper-third corneal pannus was noted

in both eyes; since then the corneal pannus had progressed very slowly.

The parents are normal, but an elder brother had Addison's disease and diabetes insipidus and died at the age of 15 years after fulminating chicken pox.

General examination showed total alopecia (Fig. 1). The skin was smooth and soft; the nails were thick

Fig. 1 *Alopecia totalis*.

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Fig. 2 Nail dystrophy.

and malformed (Fig. 2). The teeth were fragile and malarranged (Fig. 3). The patient was of short stature and had bilateral cryptochidism. His intelligence was normal.

Ocular examination revealed total loss of eyebrows and only 2 to 3 rudimentary eyelashes remained on the upper lids. The lacrimal puncta were present and patent. The Meibomian gland openings were present. Visual acuities were right 6/9 with +0.50 DS and left 6/12 with +0.50 DS. Corneal pannus was present in each eye covering the upper third of the cornea with superficial blood vessels invading sup epithelium and superficial corneal stroma. The deep stroma was not involved (Fig. 4). Schirmer's test gave right 9 mm, left 19 mm, of wetting in 5 minutes. No abnormalities of iris, lens or retina were evident. Laboratory studies showed normal immunoglobulins but defective T lymphocyte function. There were positive autoantibodies to gastric parietal cells, intrinsic factor, adrenal cortex, and Leydig cells. There were also autoantibodies to cornea, iris, and ciliary body (Table 1).

Fig. 3 Malarranged teeth; note chipped central incisor.

Fig. 4 Corneal pannus.

Discussion

Ectodermal dysplasia is a genetically determined syndrome with widespread abnormalities of ectodermal structures characterised by a triad of hypohydrosis, hypotrichosis, and hypodontia.¹ It was first described as early as 1792 by Danz,² later by Widderburn³ in 1838 and Thurnam⁴ in 1848. The mode of inheritance of this syndrome is not fully resolved. Cockayne⁵ considered 2 types of inheritance—autosomal dominant and sex-linked recessive. The latter may explain the preponderance of males being affected.⁶ Kline⁷ suggested that ectodermal dysplasia was transmitted as a dominant trait with sex-affected expressivity. Ectodermal dysplasia may present with various degrees of severity; in the severe form it may be associated with gross skeletal deformities—for example, ectrodactyly, ectodermal dysplasia, and cleft lip and

Table 1 Autoantibodies

Anti-nuclear	negative
Anti-nucleolar	negative
Anti-mitochondrial	negative
Anti-smooth muscle	negative
Anti-salivary gland	negative
Anti-neural	negative
Anti-reticulin	negative
Skin	negative
Thyroid	negative
Gastric parietal cells	positive
Intrinsic factor	positive
Adrenal cortex	positive
Leydig cells	positive
Pancreatic islet cells	negative
Pituitary	negative
Parathyroid	negative
Cornea	positive
Iris	positive
Ciliary body	positive

palate.⁸⁻¹⁰ Ectodermal dysplasia is associated with Friedrich's ataxia and Horner's syndrome of the central type together with nystagmus.¹¹ However, the association with autoimmune disease has not been reported hitherto.

Disordered structures derived from embryonic ectoderm cause various ocular symptoms. Corneal changes with pannus formation,¹² as in this case, and Groenouw type I granular dystrophy⁷ have been described. Lacrimal system anomalies with lacrimal punctal atresia,^{8,13,14} cataracts,^{13,15} and chorioretinal atrophy¹⁵ have also been reported.

Wilson *et al.*¹² recorded the histopathology of the corneal pannus removed at superficial keratectomy: eosinophils and plasma cells were found in the pannus. They suggested that immune mechanisms may be a factor in the corneal changes. Alopecia areata had been found to be associated with a high incidence of autoantibodies to smooth muscle,¹⁶ indicating its association with autoimmunity. It is interesting that the present case has demonstrated the association of alopecia totalis and corneal pannus with autoimmune polyendocrine disease and pernicious anaemia. Indeed, the presence of autoantibodies to gastric parietal cells, intrinsic factor, adrenal cortex, Leydig cells, cornea, iris, and ciliary body were confirmed. Thus ectodermal dysplasia may be an autoimmune disease affecting structures developed from embryonic ectodermal cells.

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