Bowen-Armstrong Syndrome

Synonyms (probable differing phenotypic manifestations of the same/similar genetic abnormality):[1]

- AEC syndrome (A nkyloblepharon, E ctodermal defects, C left lip/palate).
- Hay-Wells syndrome.
- Rapp-Hodgkin syndrome.
- CHAND syndrome (C urly H air A nd N ail D ystrophy - no craniofacial abnormalities).
- Rosselli-Gulienetti syndrome (sometimes also known as Zlotogora-Ogur syndrome).

This is an extremely rare congenital disease that shares overlapping features with several conditions that exhibit congenital ectodermal dysplasia (malformation/disordered growth of external covering tissues derived from embryonic ectodermal layer). It occurs in familial clusters and its defining features are:[2]

- Cleft lip and/or palate.
- General learning disability.
- Features of ectodermal dysplasia affecting development and growth of skin, hair, nails, teeth and sweat glands.

Genetics

Bowen-Armstrong or similar syndromal cases have been observed in sporadic, autosomal recessive and autosomal dominant with incomplete penetrance pedigrees. The locus for Rosselli-Gulienetti and Bowen-Armstrong syndromes is on the long arm of chromosome 11.[3] This disease and its syndromal associates are thought to be caused by mutation of the p63/p73 or associated genes. p63/p73 are protein transcription factors that play a role in tumour suppression and tissue growth.

Recent molecular biological insights show that p63 products are needed for the up-regulation of glyoxalase II (GLX2), an enzyme that breaks down a by-product of glycolysis, methylglyoxal.[4] The failure to remove this by-product of aerobic metabolism may have an effect on tissues with high-protein production and turnover such as hair follicles, nailbeds and epidermis.

The gene locus for AEC syndrome and Hay-Wells syndrome is on the long arm of chromosome 3.[5]

Epidemiology

These are exceedingly rare conditions with only a handful of reported cases. The subdivision of the congenital ectodermal dysplasias into syndromal eponymous entities probably makes them appear rarer than they truly are but they are undoubtedly unusual diseases.

Presentation

Antenatal course and birth is usually uncomplicated but antenatal ultrasound may detect abnormalities such as cleft lip/palate. The child appears abnormal from birth and there is an array of potential abnormalities which overlap with other syndromal congenital ectodermal dysplasias.[6]

Ectodermal dysplastic features:

- Fused eyelids at birth (ankyloblepharon)
- Dermatoses (erosions, erythematous patches, pustules, oozing with crusts), affecting the scalp (little or no hair, which appears abnormal), face, eyebrows (may be absent), eyelashes (may be absent), ears, perineum/genitalia.
- Patchy skin pigmentation/café-au-lait spots.
- Abnormalities of growth and development of nails (thickened, yellow/brown discolouration) and teeth, including their absence or reduction in number (oligo-onychia/oligodontia).
- Urogenital abnormalities such as hypospadias and fused labia.
- Abnormal sweat ducts causing hypohidrosis.
- Absent/dysfunctional tear ducts.
- Syndactyly.
- Abnormal structure and function of middle and outer ear.
Other possible features of Bowen-Armstrong syndrome and associated conditions include:

- Cleft lip and/or palate ± other facial dysmorphic features.
- Learning disabilities.
- Delayed bone age.

**Differential diagnosis**

There is a wide range of inherited conditions that may cause cleft lip and/or palate, learning difficulties and ectodermal dysplasia in isolation. The three occurring in conjunction suggests one of the ectodermal dysplastic eponymous syndromes discussed in this article.

**Investigations**

Specialist investigation by paediatric/genetic services may be appropriate to try to establish a correct diagnosis when one or more of these congenital features is present.

Clinical, molecular, chromosomal and genetic analysis will be used to try to diagnose the condition formally. This will aid in determining the best source and method of ongoing specialist management.

**Associated diseases**

See ‘Synonyms’, above.

**Management**

**General points**

- Multidisciplinary team management is required with specialist dermatological, paediatric and paediatric-surgical input.
- Patients may need to have a temperature-controlled environment, wear light clothing and maintain hydration with cool fluids to avoid hyperthermia if they suffer from hypohidrosis.
- It is clear from looking at online support groups that families have benefited a great deal from these groups and contact with other affected families. It is worth making this a distinct part of the management plan.

**Medical management**

- Dermatoses are treated with keratolytic shampoos ± topical corticosteroids.
- Systemic or topical antibiotics/antifungals may be used to treat suspected superinfection of skin or other infective complications.

**Surgical management**

- Ankyloblepharosis may lyse spontaneously in some cases but it can be treated by surgical repair.
- Other surgical input may be needed to address cleft lip/palate, lacrimal duct hypoplasia and urogenital deformities.
- Skin lesions need to be managed attentively and debridement may be required in severe cases.
- Specialist dental input is likely to be needed.

**Complications**

- Long-term psychological and learning difficulties.
- Chronic suppurative otitis media.
- Hearing loss.
- Lacrimal dysfunction leading to chronic conjunctivitis.
- Urogenital dysfunction.
- Tendency to hyperthermia due to impaired sweating.
- Dental disease.
- Disordered bone growth.
- Chronic dermatoses.

**Prognosis**

This syndrome is rare and has only recently been delineated, so it is difficult to find any reliable information on long-term outlook. Patients who are adequately managed seem to do well in the medium term. Other causes of ectodermal dysplasia seem to be associated with a good outlook, provided that dangerous complications such as hypohidrosis/hyperthermia and infection are addressed and treated correctly.

**Prevention**

Prenatal diagnosis may be able to help some families who have already had an affected child.
Further reading & references

- Dianzani I et al; Rapp-Hodgkin and AEC syndromes due to a new frameshift mutation in the TP63 gene; J Med Genet On-line Mutation Report 2003;40:e133 [Full Text]; Free registration required
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