Syndrome of the month

Edited by D Donnai and R Winter

Aarskog syndrome

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Aarskog syndrome (facio-digital-genital syndrome) was first described in 1970 by Dagfin Aarskog[1] who presented seven males from one family with a growth disorder and associated anomalies. A year later Scott[2] reported three brothers with similar features and since then there have been over 100 cases published.[3–20] We are aware of 12 subjects with Aarskog syndrome living in the west of Scotland (population 1·6 million). However, owing to the benign nature of the condition, it is underdiagnosed and the true incidence must be higher than this.

Inheritance

Aarskog syndrome has been assigned to the X chromosome on the basis of pedigree analysis but this interpretation remains open to doubt. The importance of shawl scrotum as a clinical feature produces a diagnostic bias in favour of males. The facial features are often as obvious in female carriers as in male carriers, and in two large pedigrees male to male transmission has been found.[11 20]

In 1984, Bawle *et al*[3] described a mother and son with Aarskog syndrome and an X;autosomal translocation (Xq13;8p21.2). In the absence of linkage data to clarify the issue, the disorder is as likely to be a partially sex limited autosomal dominant localised by the autosomal element of the translocation.

Clinical features

The table summarises the main clinical features found in Aarskog syndrome and compares the 17 males in the Glasgow series with those published previously.

Clinical features in Aarskog syndrome.

Clinical features	Glasgow series	Published cases
Hypertelorism	16/17	73/83
Ptosis	8/17	33/64
Downward slanting palpebral fissures	10/17	33/64
Short nose	12/17	30/45
Wide philtrum	12/17	76/87
Maxillary hypoplasia	12/17	72/87
Anteverted nares	14/17	28/36
Abnormal auricles	9/17	76/86
Broad nasal bridge	17/17	33/58
Crease below lower lip	8/17	72/82
Widow's peak	8/17	44/51
Short/broad hands	14/17	49/60
Brachydactyly	13/17	50/60
Syndactyly	9/17	36/56
Clinodactyly	15/17	42/65
Short 5th finger	15/17	22/28
Joint laxity	10/17	36/47
Single palmar crease	13/17	25/38
Broad, short, bulbous toes	12/17	21/28
Short stature (3rd centile)	15/17	71/81
Shawl scrotum	9/17	65/79
Cryptorchidism	6/17	54/77
Inguinal herniae	11/17	47/77
Prominent umbilicus	10/17	6/7
Pectus excavatum	3/17	31/57

Female carriers of the Aarskog gene often exhibit some of the features of the syndrome. They are usually short; all 13 women in our series were below the 10th centile for height, and many exhibit hand or facial anomalies making clinical diagnosis of carrier status possible.

FACIES

Boys with Aarskog syndrome are strikingly similar in facial appearance. Fig 1 shows two unrelated boys with Aarskog syndrome and fig 2 shows three brothers with the syndrome. Carrier females may exhibit many of the facial features (fig 3).

The cardinal features are hypertelorism, a widow's

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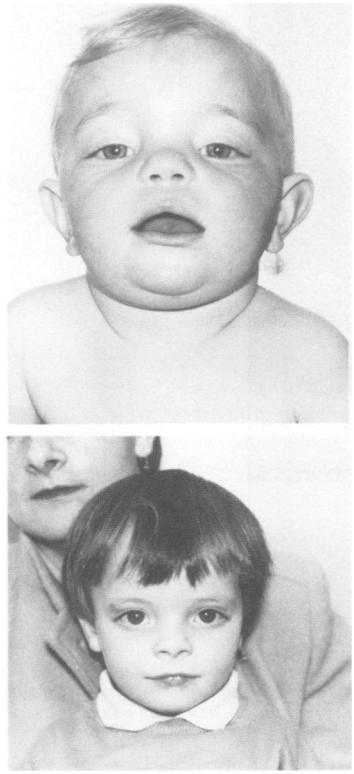

Figure 1 Two unrelated boys with Aarskog syndrome.

Figure 3 Female obligate gene carrier.

peak, ptosis, downward slanting palpebral fissures, small, short nose with anteverted nares, a broad nasal bridge, maxillary hypoplasia, abnormal auricles, a wide philtrum, and a crease below the lower lip. Fig 4 shows the evolution of the facial phenotype through time.

SKELETAL

Short stature in Aarskog syndrome is disproportionate, with an increased upper to lower segment ratio. The hands are short and broad with brachydactyly, syndactyly, clinodactyly, particularly short fifth fingers with single creases, single palmar creases, and striking joint laxity particularly evident in the phalanges (fig 5).

Other skeletal abnormalities which have been documented are odontoid hypoplasia with cervical

Figure 2 Three brothers with Aarskog syndrome.

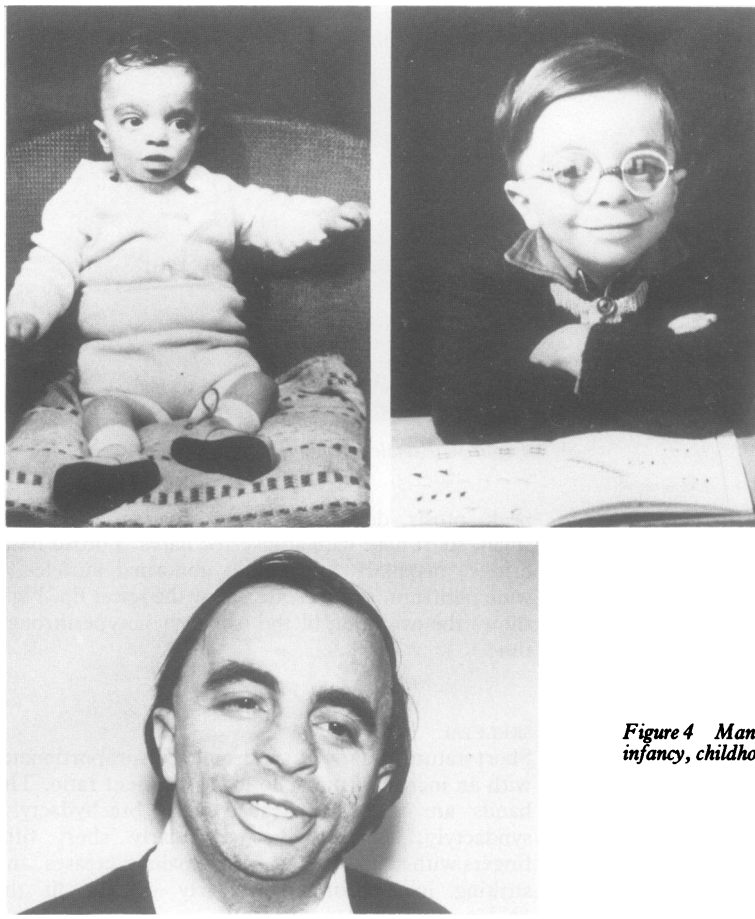

Figure 4 Man with Aarskog syndrome pictured in infancy, childhood, and as an adult.

ligamentous laxity, scoliosis, metatarsus adductus, and splayed toes with bulbous tips.

GENITAL

The characteristic abnormality in Aarskog syndrome is the shawl or overriding scrotum, though this need not be a constant feature. It becomes much less obvious with age. Cryptorchidism is common as are inguinal herniae. If the cryptorchidism is corrected early, fertility is unimpaired.

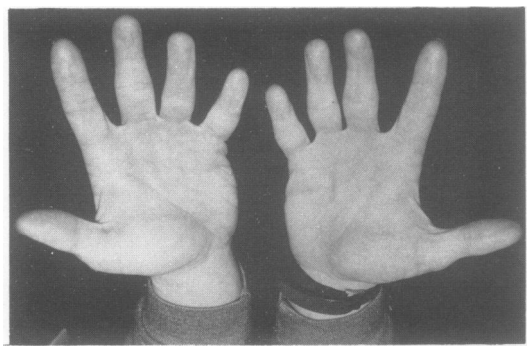

Figure 5 The hands in Aarskog syndrome.

GROWTH

The majority of males with Aarskog syndrome are short, usually below the 10th centile and often below the 3rd. Infants have a normal birth weight but growth falls away across the centiles over the first year. Children remain very small until they enter puberty. Puberty is often delayed but inevitably occurs bringing with it a prolonged growth spurt.

INTELLIGENCE

Subjects with Aarskog syndrome can be expected to have normal intelligence when allowance is made for the ascertainment bias associated with recognition and reporting of handicap in dysmorphic syndromes, and the fact that a number of reported cases with mental

handicap do not satisfy the diagnostic dysmorphic criteria. The proportion of mentally handicapped persons does not show a statistically significant excess over that in the general population, although the sample size is too small to exclude positively an association with mild learning difficulties.

VISION

There is an increased incidence of hypermetropia in persons carrying the gene for Aarskog syndrome.

LIFE EXPECTANCY

Aarskog syndrome is associated with a normal life span.

Differential diagnosis

The differential diagnosis of Aarskog syndrome includes Noonan syndrome and Robinow syndrome. Aarskog syndrome is not associated with heart defects or major genital abnormalities and caution should be exercised before making a diagnosis of Aarskog syndrome if they are present.

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