Syndrome of the month

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Maxillonasal dysplasia (Binder's syndrome)

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Binder's 'syndrome' or maxillonasal 'dysplasia' is a congenital malformation which has been well described in publications on oral surgery, but few references occur in genetics publications.^{1,2} Although the first case was described by Noyes,³ the 'syndrome' was not recognised until Binder's comprehensive report of three unrelated children in 1962.⁴ Since

then, well over 200 cases have been reported; males and females are affected equally. However, the aetiology, pattern of inheritance, and prevalence still remain obscure.

Clinical features

FACE

The most striking facial features are maxillary hypoplasia and a flat, vertical nose (fig 1a). The columella is short and the nostrils have a semilunar shape when viewed from below.⁵ If the columellar hypoplasia is severe, the nostrils may have a triangular shape (fig 1b).⁶ The upper lip is convex with an acute nasolabial angle (fig 1a). Cephalometric studies have confirmed that the major skeletal abnormality is a small maxilla

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(a)

(b)

Figure 1 (a) Lateral view of face showing flat nose, maxillary hypoplasia, and acute nasolabial angle. (b) AP view of the face. Note the short columella and triangular nostrils.

positioned posteriorly on a short anterior cranial base.⁷⁻¹⁰ Horswell *et al*⁸ noted that the maxilla was hypoplastic in both anteroposterior and vertical directions in early childhood; the latter showed some improvement with age. Maxillary hypoplasia leads to relative prognathism and Angle type III malocclusion. In some cases, mandibular length may be greater than normal, thus suggesting true prognathism.⁶⁻⁹

TEETH

Descriptions of significant dental abnormalities are few, apart from those secondary to malocclusion. Delaire *et al*⁶ reported that many of their patients had small central upper incisors. In addition, one of their patients had amelogenesis imperfecta. Hopkin¹¹ noted one patient with congenitally absent maxillary incisors and small central incisors. The patient of Noyes³ had absent molars.

PALATE

Seven patients have been noted to have an associated cleft palate.^{6 10 12 13} Two of these patients were stated

to be mentally retarded but no further details were given^{12 13}; a third patient was noted to have bilateral hearing loss.¹³ The presence or absence of a highly arched palate has received little comment, which is surprising given the known maxillary abnormality.

INTELLIGENCE

Most authors have not commented directly on intelligence. Four reports,^{6 12-14} describing a total of 108 patients, mention seven with mental retardation. Four of these patients had additional features: one had Down's syndrome, two had cleft palate (as noted above), and one had strabismus. A further three patients were noted to be performing poorly at school.¹² It therefore seems that decreased intelligence is not a significant feature in this condition.

SKULL X RAY

The anatomical basis for some of the facial abnormalities can be appreciated from reviewing the lateral skull x ray (fig 2). The normal crest dividing the floor of the nasal cavity from the anterior aspect of the maxilla is missing and the anterior nasal spine is either

Figure 2 (a) Facial bones shown in a normal lateral skull x ray. The anterior nasal spine is arrowed. (b) Lateral skull x ray of the child from fig 1; note the absence of the anterior nasal spine, maxillary hypoplasia, and the sloping of the alveolar bone into the nasal cavity.

absent or hypoplastic. The absence of the nasal spine can be detected clinically by palpating between the upper lip and gum. In a careful anatomical study during the surgical dissection of 50 patients, Holstrom¹⁵ noted a small scaphoid depression in the anterior nasal floor, which cannot be observed radiologically.

In his original description Binder⁴ noted that two patients had hypoplastic frontal sinuses; this finding has been noted by subsequent authors.^{6 12 16}

VERTEBRAL ANOMALIES

Three surveys^{12 14 17} showed that approximately 50% of patients had single or multiple anomalies of the cervical spine which were not associated with neurological complications. Frequently, but not exclusively, the malformations affected C1 or C2 and included hypoplastic arches or abnormal ossification patterns. Delaire *et al*⁶ suggested that cervical abnormalities were associated with true prognathism. However, Olow-Nordenram and Radberg¹⁴ found no correlation between the presence of cervical spinal abnormalities and the severity of malocclusion. Holstrom¹⁵ reported that three of 50 patients had thoracolumbar scoliosis that required orthopaedic treatment. Unfortunately, systematic skeletal surveys were not undertaken in this group.

Treatment

After assessment of the degree of facial bone abnormality, orthodontic and surgical procedures can be planned.^{10 18} The more severe cases require a Le Fort I or II osteotomy with nasal grafting.^{5 7 19}

Differential diagnosis

Similar facial features may be seen in other well defined conditions, including warfarin embryopathy, acrodysostosis, and Stickler's syndrome. It should be possible to distinguish each of these syndromes on the basis of additional historical and clinical features. The phenotypic overlap with one form of chondrodysplasia punctata is described below.

Aetiology

Binder⁴ believed that his patients had a mild form of arhinencephaly but there have been no reports of difficulties with the sense of smell to support this hypothesis. Noyes³ considered that his patient's abnormalities resulted from birth trauma but did not comment on how this could account for the absent anterior nasal spine. Hopkin¹¹ reported five cases, none of whom had any birth trauma. He was able to contrast the facial features with a sixth case with undoubted trauma to the anterior nasal spine and concluded that Binder's 'syndrome' was the result of a

developmental insult. This hypothesis was strengthened by the observation that these patients frequently have vertebral abnormalities.

Narcy *et al*²⁰ reported a case of Binder's 'syndrome' in association with achalasia of the cardia and abnormal autonomic reflexes (pupillary, cardiac, and axonal), suggesting that in this patient the phenotype might be caused by abnormal neural crest migration.

Horswell *et al*¹² reported that six of their patients had full skeletal surveys before the age of 1 year; two had punctate calcaneal epiphyses and a third had an abnormal calcaneum. These authors suggested a phenotypic overlap with a mild form of chondrodysplasia punctata described by Sheffield *et al*,²¹ which they distinguished from the more usual rhizomelic and X linked forms. The patients of Sheffield *et al*²¹ had a facial appearance which showed maxillary and nasal flattening; they all had punctate epiphyses (which was the clinical feature determining ascertainment) and 11 of 23 had vertebral clefting. In addition, these patients had moderate short stature and mild mental retardation.

Inheritance

Although the majority of cases of this malformation are sporadic, familial recurrence has been noted by a number of authors. In six pedigrees the recurrence was in second or third degree relatives.^{12 13 15} Recurrence in sibs with unaffected parents has been noted seven times and an affected parent and child (or sibship) has been noted 10 times.^{12 15 22} In the cases of vertical transmission, detailed pedigrees were not always given; it is, therefore, not possible to comment on male to male transmission, except to say that it has not been documented unequivocally.

Horswell *et al*¹² suggested that dominant inheritance with reduced penetrance could account for their pedigrees. Olow-Nordenram and Valentin²² undertook a formal genetic analysis and found low segregation ratios. They suggested that recurrence in their pedigrees could be explained by either autosomal recessive inheritance with reduced penetrance or by multifactorial inheritance. The latter hypothesis could not be tested further since the prevalence of the malformation in any population is unknown. In conclusion, the Binder phenotype may be heterogeneous (see below); no reliable recurrence risks are available for genetic counselling purposes.

Nosology

It is clear from the above that the pattern of abnormalities seen in this condition does not represent a causally defined entity; therefore, the use of the word 'syndrome' is inappropriate. Histological abnormalities have not been reported in any one tissue, so

the use of the word 'dysplasia' is also incorrect. We therefore suggest that the phenotype be considered as an 'association', which principally affects the maxilla and vertebrae; other features such as strabismus, deafness, or autonomic neuropathy may be seen occasionally. This designation does not prejudice thinking about the predisposing mechanisms and allows adequate clinical delineation for consideration of clinical management, prognosis, and recurrence.

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