

The prenatal diagnosis of Binder syndrome before 24 weeks of gestation: case report

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ABSTRACT

A case of Binder syndrome was diagnosed at 21 weeks of gestation using two-dimensional and three-dimensional ultrasound. The first indication of any abnormality was a flattened fetal nose demonstrated in the mid-sagittal plane. Further ultrasound imaging showed the virtual absence of the naso-frontal angle, giving the impression of a flat forehead and small fetal nose. Suspected mild hypertelorism was also seen using transverse and coronal planes. Differential diagnosis of this condition is discussed.

INTRODUCTION

Maxillonasal dysplasia (incomplete development) was first reported by Noyes in 1939¹, while Binder, in 1962, described a condition called maxillonasal dysostosis (defective ossification), characterized by a short nose with a flat bridge, a short columella, an acute nasolabial angle, perialar flatness, a convex upper lip and a tendency to angle class III malocclusion². Since then there have been many reported cases of Binder syndrome, but no such diagnosis has been made antenatally.

Binder syndrome, as it is seen in newborns, children or adolescents, is characterized by the naso-frontal angle being absent with the nose being hypoplastic with a small tip. The nostrils are usually half moon shaped and the upper lip is convex with a high arched palate. Mild hypertelorism is usually present as well as malocclusion and a lower overbite. The frontal sinuses are often hypoplastic or absent. There are various anomalies of the cervical spine which may be seen, such as separate odontoid process, spina bifida occulta, short posterior arch and block vertebrae³. Strabismus and mild mental retardation have been occasionally described^{3–5}. When maxillonasal dysplasia is observed at birth it is usually not thought to be important if it presents as a single finding. Individuals may also be seen as children or adolescents by orthodontists or plastic surgeons, and their facial features are then diagnosed as Binder syndrome⁶.

To our knowledge, Binder syndrome has not been diagnosed antenatally and therefore we now report the first antenatal diagnosis of Binder syndrome using ultrasound imaging at a routine second trimester anomaly scan.

CASE REPORT

A 30-year-old para 2 gravida 1 attended for a routine screening examination at 21 weeks of gestation. She had no relevant past medical, obstetric or family history of note, in particular there was no history of warfarin exposure, alcohol abuse or vitamin K deficiency. Gestational age had been previously confirmed during the first trimester by crown rump length measurement. A 12 week nuchal translucency scan adjusted the maternal risk for trisomy 21 from 1 : 596 to 1 : 2528.

The examination was performed using a High Definition Imaging (HDI) 3000 (Advanced Technical Laboratories, ATL, Letchworth, Herts, UK) two-dimensional ultrasound (2D US) machine with a multifrequency 2–4 MHz transducer, using a decibel range of 35–60 dB.

Nasal hypoplasia with reduced naso-frontal angle was identified with suspected mild hypertelorism (Figures 1 and 2). No other structural abnormalities were seen.

The biometry was found to be normal for 21 week gestation, including the intraorbital diameter (IOD) and the external orbital diameter (EOD). The facial findings were confirmed using a Kretz Technik Voluson 530D (Crawley, W. Sussex, UK) 3D ultrasound machine (Figure 3).

As a chromosomal abnormality could not be excluded, an amniocentesis was performed. A normal male karyotype was obtained. Discussions with the geneticists concluded that Binder syndrome was the most likely diagnosis but we could not confidently exclude a more serious underlying syndrome. In the light of this uncertainty the parents made the difficult decision to terminate the pregnancy. The postmortem findings documented that the fetal measurements were consistent with gestational age. The congenital abnormalities found were facial dysmorphism, flat mid-face and mild hypertelorism. A

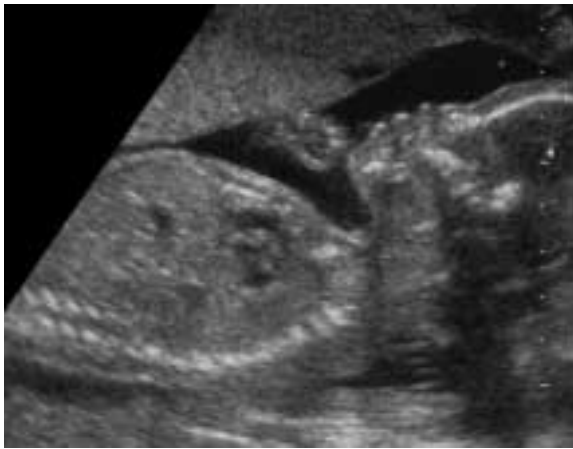


Figure 1 Sagittal section of the fetal face at 21 weeks' gestation demonstrating an abnormal profile with flattened nose and abnormally positioned maxilla.

high intact arched palate was present. Atresia of the right choanus and stenosis of the left choanus were also identified. No other malformation could be identified and no other pathology seen in the internal organs.

DISCUSSION

Identifying a normal fetal profile by ultrasound during second trimester screening is important in the exclusion of facial abnormalities such as micrognathia, flat face, macroglossia (associated with trisomy 21), sloping forehead (associated with microcephaly) and clefting.

A summary of common facial and related ultrasound findings in relation to the most common genetic syndromes is shown in Table 1.

We describe here a case of Binder syndrome diagnosed at 21 weeks of gestation. The overall incidence of fetal nasal malformations is reported as approximately 1 : 1600¹⁰. This figure takes into account all nasal malformations that are isolated or associated with other anomalies. Bronshtein and colleagues detected 15 cases of nasal malformations from

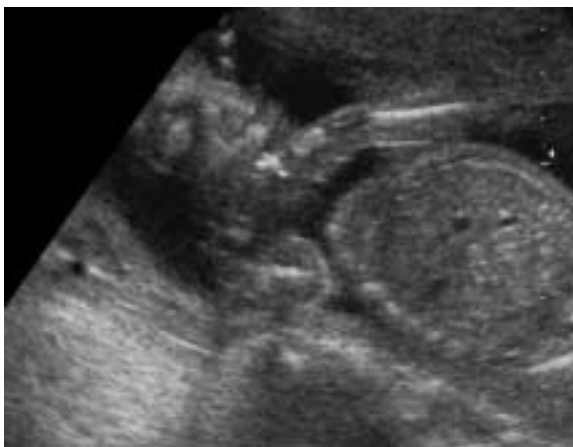


Figure 2. Coronal section of the fetal face at 21 weeks' gestation suggesting a flattened, broad nose and possible hypertelorism.



Figure 3. 3D surface rendered image of the fetal face at 21 weeks' gestation suggesting hypertelorism and flat mid-face.

25 114 fetal examinations¹⁰. There were three cases of flat nasal bridge, all diagnosed at 15 weeks of gestation. One was associated with increased nuchal edema: karyotyping revealed trisomy 21. In the other two cases the flat nasal bridge was an isolated abnormality: in one case tetrasomy 12p was present, while in the second, the karyotype was not available following a missed abortion.

In the series of Nicolaides and colleagues¹¹ all the 19 cases of nasal defects (nasal hypoplasia, proboscis or single nostril) were observed in association with holoprosencephaly.

A low flat nasal bridge is described as being associated with more than 50 neonatal syndromes⁷. However, associated abnormalities are present in most of these syndromes. Teratogens such as warfarin, vitamin K deficiency and alcohol have also been implicated in such facial abnormalities⁵.

In the case described here, the flat fetal nose was found as the only abnormality, and fetal karyotype was normal. The most likely diagnosis was Binder syndrome. The postmortem findings were consistent with this diagnosis, even if the classical criteria for diagnosing Binder syndrome usually apply to neonates/infants and children.

The range of normal familial appearances must be considered when deciding whether the observed findings are normal or abnormal. Such subtle features may be beyond the capabilities of the available ultrasound equipment and/or expertise of the operator, compounding the ability to identify the condition.

Binder syndrome is unique in the group of diagnosable facial abnormalities, the naso-frontal defect appearing in isolation (i.e. no other anomaly seen). Its incidence is

Table 1 Common facial and other ultrasound findings in relation to their most common syndrome^{3-4,7,8-9}

	<i>Common facial ultrasound features</i>	<i>Other ultrasound features</i>	<i>Inheritance</i>	<i>Karyotype</i>
Binder syndrome	Flat mid-face, nasal hypoplasia, hypertelorism		Autosomal recessive Autosomal dominant	Normal
Chondrodysplasia punctata (CDP), X linked	Nasal hypoplasia	Scoliosis, asymmetrical shortening of the limbs	X-linked dominant	Deletion/translocation of chromosome Xp22.3
CDP, rhizomelic type	Flat face	Epiphyseal stippling, talipes, short limbs	Autosomal recessive	Normal
Robinow syndrome	Flat face, hypertelorism	Short forearms, clinodactyly, macrocephaly	Autosomal dominant	Normal
Aarskog syndrome	Flat nose, hypertelorism	Brachydactyly, clinodactyly of the 5th fingers	X-linked recessive	Normal
Crouzon syndrome	Maxillary hypoplasia, hypertelorism	Craniosynostosis, short occipital-frontal diameter	Autosomal dominant	Normal
Apert syndrome	Flat nose, maxillary hypoplasia, hypertelorism	Irregular craniosynostosis, short occipital-frontal diameter, flat occiput, ventriculomegaly, syndactyly	Autosomal dominant	Normal
Achondroplasia	Mid-face hypoplasia low nasal bridge	Short tubular bones, megaloccephaly	Autosomal dominant	Normal
Fetal warfarin syndrome	Flat face	Stippling (mild)	(Teratogen)	Normal
Rudiger syndrome	Flat nasal bridge	Short digits	Autosomal recessive	Normal
Stickler syndrome	Facial cleft, micrognathia, flat face	Osteo-chondrodysplasia, talipes	Autosomal dominant	Normal

unknown in either the pre- or postnatal population as it could often be misdiagnosed, with the facial markers being very similar to chondrodysplasia punctata (CDP). Furthermore, the similarities of the features of Binder syndrome with the facial markers of CDP would suggest that there is an underlying link between Binder syndrome and CDP.

The prognosis of a fetus with a case of isolated maxillonasal dysostosis is excellent. The facies can be surgically improved and orthodontics used to help establish a relatively normal bite. As the child grows towards adulthood, the natural development of the facial features will show a more normal profile.

The sense of smell is completely normal. Five per cent of affected individuals have been found to have hearing loss and 5% nonspecific congenital heart defects³. Decreased intelligence does not seem to be a significant feature of Binder syndrome. Mental retardation was reported in seven out of 108 patients described in four series¹²⁻¹⁵. Four of them had additional features (Down syndrome, cleft palate, strabismus), while the other three had poor school performances.

The mode of inheritance of Binder syndrome has not been clearly defined. These cases will usually be sporadic. Families with a dominant pattern of inheritance have been described with a small number of cases showing a familial recurrence^{12-13,16-18}. For this reason the majority will be detected on the 20-week anomaly scan.

The parents in this case had a familial profile that was not consistent with the findings on ultrasound in terms of the expected phenotype. This caused extreme emotional distress; furthermore, the small risk of mental retardation was unacceptable to them and they requested and were granted a termination of pregnancy on the basis of the UK

Abortion Act 1967, on the grounds of injury to the physical mental health of the pregnant woman.

This case demonstrates some of the management and ethical problems that occur as a result of the 20-week anomaly scan. It also raises the dilemma of diagnosing abnormalities by ultrasound for which there are no confirmatory tests. The diagnosis of Binder syndrome is clinical, the differential diagnosis of a flat mid-face is large and although many of the diagnoses can be excluded, a number of others cannot. Hence the parents will be left with a degree of uncertainty which may not be acceptable to some couples.

Despite these factors, it is important to examine the facial features as they may well give an indication of an underlying severe fetal abnormality (for example a flat mid-face in autosomal recessive CDP). However, the finding of a small flattened nose with no other abnormal features, in a fetus with a normal karyotype, is likely to carry a good prognosis with the possibility of satisfactory surgical correction.

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