Preventing misdiagnosis in amniotic band sequence: a case report

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ABSTRACT

Amniotic band sequence (ABS) is an uncommon and heterogeneous congenital disorder caused by entrapment of fetal parts by fibrous amniotic bands, causing distinctive structural abnormalities involving limbs, trunk, and craniofacial regions. The incidence ranges between 1/1200 and 1/15,000 live births, but is higher in stillbirths and preivable fetuses. The intrinsic theory attributes the constringtion band syndrome as an inherent development defect of embryogenesis while the extrinsic theory proposes that an early amnion rupture is responsible for the adherent bands. It is also suggested that amputations and constringtion rings might be due to vascular disturbances. Anomalies resulting from amniotic bands are quite variable and sometimes may simulate chromosomal abnormalities. The authors report a case of a 36-week-gestation male neonate who lived for 29 hours after a vaginal delivery with an Apgar score of 8/9/9. The mother was primipara, and the prenatal was uneventful except for two episodes of urinary tract infections. The newborn examination depicted multiple anomalies characterized by exencephaly, bilateral labial cleft with distorted nostrils and palate cleft. There was also facial skin tag band, exophthalmus with hypoplasia of the eyelids. The limbs showed distal amputation of the fingers in both hands and feet, oligodactyly associated with syndactyly in the left foot, ring constringtion in the right leg, the presence of right hyperextension, and clubfoot. The upper limbs showed length discrepancies. Karyotype analysis was normal at 46 XY. The authors conclude that the recognition of the malformations secondary to ABS is important in genetic counseling to prevent misdiagnosis between chromosomal and secondary disruption disorders.

Keywords: Amniotic Band Sequence; Cleft Palate; Congenital Abnormalities; Neural Tube Defects.

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CASE REPORT

A 36-week-gestation male neonate weighing 2230 g was born to a 29-year-old female patient, primipara, by vaginal labor induced with oxytocin. The mother’s medical history was unremarkable, except for two episodes of urinary tract infection and a morphologic ultrasound examination at 19 weeks’ gestation showing exencephaly, medial labial cleft, and edema. After a breech delivery with a laceration of the umbilical cord during birth, a neonate with multiple malformations was born, with an Apgar score of 8/9/9. The neonate was referred to the neonatal ICU for palliative care. The parents were aware of the prognosis, with the malformations being incompatible with life. The karyotype analysis was normal, 46 XY (20 cells analyzed). During the ICU stay, the neonate was placed in a heated crib, prescribed serum, analgesic, fentanyl, and midazolam. The physical examination presented heart rate of 180 beats per minute and room air oximetry of 100%. The newborn evolved with grunting and died with 29 hours. An autopsy was performed.

Autopsy Findings

The ectoscopic examination showed a male neonate with multiple malformations (Figure 1). Multiple craniofacial abnormalities were observed: central nervous system and skull defects were represented by asymmetric and anteriorly placed exencephaly in fronto-parietal topography; bilateral labial cleft with distorted nostrils; and palate cleft. There was also a facial skin tag band from the right nasal ala to the edge of the skin with the exencephaly. The exophthalmos was more prominent in the right eye with hypoplasia of the eyelids and a cutaneous appendix on the temporal scalp topography was also present (Figure 2).

A thin winy-yellowish-colored membrane and areas with fibrinous material deposition coated the exposed surface of the brain. The brain showed multiple malformations with a lobulated appearance. The microscopic examination showed arachnoid-to-amnion membrane adhesions, which showed signs of acute inflammation (Figure 3).

The limbs showed predominantly distal deformities such as distal amputation of the fingers in both hands and feet, oligodactyly associated to syndactyly in the left foot with evident amniotic band, ring constriction in the right leg, presence of right hyperextension and clubfoot. Upper limbs showed length discrepancies (Figure 4).

At the opening thoracic and abdominal cavities there was no abnormality in the organic topography neither in their gross examination. The weight of the organs is showed in Table 1. The heart showed foramen oval and a patent duct arteriosus. The lungs showed multiple petechiae scattered on the pleural surface and in the parenchyma (Figure 5). The microscopic examination depicted the lungs in the alveolar stage of development with multiple areas of alveolar hemorrhage. Hepatic extra medullary hematopoiesis was observed with no evidence of conspicuous nephrogenic zone in the kidneys—findings that are consistent with the 36th gestational week.

Figure 1 – Panoramic pictures of the neonate. A - Ventral sight showing multiple craniofacial malformations, mammary hypertelorism, limbs with distal deformities, and upper limb length discrepancy; B - Back view.
two umbilical arteries and one vein. Over the fetal face, the blood vessels were prominent and turgid. The maternal face was complete, showing a winy staining with opalescent areas. At the histological examination, chronic infarction areas, an increased number of syncytial knots, slight villous immaturity, foci of dystrophic calcification, and foci of chronic villitis with lymphocytes, histiocytes and focal granuloma were observed (Figure 6).

**Table 1 – Weight of organs**

| Organ            | Weight (g) | RV (g) 36th gestational week | Organ            | Weight (g) | RV (g) 36th gestational week |
|------------------|------------|------------------------------|------------------|------------|------------------------------|
| Thymus           | 13.2       | 7.7 ± 5.0                    | Spleen           | 5.3        | 8.1 ± 3.1                    |
| Right & left lungs | 12.8/15.0 | 36.9 ± 17.5*                 | Right & left kidneys | 12.6/11.7 | 21.7 ± 6.8*                 |
| Liver            | 73.1       | 96.3 ± 33.7                  | Pancreas         | 2.8        | 2.6 ± 0.7                    |
| Heart            | 14.0       | 15.0 ± 5.1                   |                  |            |                              |

* RV = reference value; *weight for both left and right organs.

We concluded that all malformations described above were caused by an amnion band disruption sequence.

The placenta measured 16.0 × 13.0 × 2.5 cm and weighted 343.0 g. The marginal insertion of the membranes showed up opalescent. The umbilical cord had a central insertion and measured 40.0 cm in length and 1.0 cm in diameter, with three vases: A - Exencephaly in fronto-parietal topography, bilateral labial cleft with distorted nostrils, and palate cleft; B - Facial skin tag band from the right nasal ala to the edge of the skin with the exencephaly (arrow) and right exophthalmia with hypoplasia of the eyelids; C - Bilateral labial cleft in continuity with palate cleft; D - Exencephaly with winy-yellowish-coated membranes and a skin tag on the scalp.
terms have been used as synonyms for this complex anomaly, namely: amniotic band disruption sequence, amniotic band syndrome, amniotic deformity adhesions and mutilation complex (ADAM), and limb body wall complex (LBWC).

ABS occurs in approximately 1/1200-1/15,000 live births. There is a higher prevalence of ADS between previable fetuses and stillbirths, with 11.4 per 10,000 previable fetuses of less than 28 weeks' gestation and 178.2 per 10,000 in fetuses from spontaneous miscarriages and induced abortions of 9-18 weeks' gestation.

The etiology of ABS remains debatable, and its physio pathogeny still remains unknown. The amniotic cavity is generated by epiblastic cells, which differentiate into amnioblasts during the second week post conception. This cavity enlarges relative to the extraembryonic coelomic cavity until the amnion fuses with the chorionic plate by 12 weeks post conception. Amniotic bands occur when the amniotic membrane fails to fuse with the
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represents an inherent development defect in embryogenesis. The second is the extrinsic theory, and was described by Torpin in 1965.\textsuperscript{11,13}

There are two main theories that explain the development of ABS. The first is the intrinsic theory, proposed by Streeter in 1930,\textsuperscript{11,12} which suggests that the constriction band syndrome

chorionic plate, or when the amnion epithelium and stroma become detached from the deeper chorionic structures of the extraplacental membrane and chorionic plate.\textsuperscript{10} This theory proposes that an early amnion rupture is responsible for the formation of adherent bands that can constrict, entangle, and amputate limbs. As the amnion ruptures, it slips off the chorion to form the

Figure 4 – Gross examination of the limbs. \textbf{A} and \textbf{B} - Distal finger amputations in both hands; \textbf{C} - Lower right limb ring constriction (arrow) and the presence of hyperextended right clubfoot, medial sight of the syndactyly in the left foot with evident amniotic band; \textbf{D} - Details of the oligodactyly associated with syndactyly in the left foot with evident amniotic band (arrow).

Figure 5 – \textbf{A} - Gross examination of the intrathoracic organs monoblock showing multiple petechiae on the pleural surfaces; \textbf{B} - Open right cardiac chambers view showing the patent foramen oval.
Although we could not demonstrate fibrous amniotic strands in placenta, we undoubtedly observed evidence of amnion band constrictions on the neonate. The latter were represented by multiple craniofacial malformations with a facial skin tag band, arachnoid-to-amnion membrane adhesion, and ring constriction band in the limbs with distal amputations of the fingers. This finding may be in favor of the extrinsic theory.

The etiology for ABS cannot be found in most pregnancies. According to the literature, ABS has been related to young maternal age, primigravida, use of acetaminophen, abdominal trauma, chorioamnionitis, vaginal bleeding during the first trimester, abortion, intrauterine contraception, chorionic villus sampling, amniocentesis, malformation of the uterus, prematurity, and non-cephalic presentation.\(^4,16,19\) Except for the episodes of urinary tract infection treatment during pregnancy, the maternal history of this case report was unremarkable. The placental examination showed...
foci of chronic villitis near the decidua, which could be related to these infectious episodes.

Nevertheless, ABS has not been linked to chromosomal abnormalities or genetic bases. Some cases have been reported in families with collagen tissue disorders, more specifically Ehler-Danlos syndrome and osteogenesis imperfecta, due to the abnormality of amnion collagen formation. Anomalies resulting from amniotic bands may simulate chromosomal abnormalities especially when neural tube defects (NTD) evolve as the exencephaly observed in this case report. NTD may present as ex- or anencephaly, encephalocele, meningomyelocele, or spina bifida in association with cranioschisis. NTD was observed in 3.6-6.7% of the intact embryos in cases of miscarriage. Most of these cases were chromosomally abnormal. Folic acid deficiency is also part of the pathology of NTD. Moreover, the midline facial defects observed in this case, with labial and palatal clefts, have a differential diagnosis with trisomy 13 and trisomy 18, but the karyotype study was normal.

CONCLUSION

The prognosis of ABS depends on the type, the number of disruptions, and the stage of embryonic development. Newborns with early ABS who have severe neural tube and body-wall defects rarely survive. Surgical treatments for functional and aesthetic restoration may be indicated in some cases. Treatment must be individualized and the timing of surgery is determined by the disease severity and predicted skeletal growth. The possible surgical treatment, described in the literature, encompass cleft lip repair, cleft palate closure, distraction osteogenesis for severe micrognathia, ocular surgery for colobomas, hand surgery, and craniofacial surgery as fronto-orbital remodeling during the first months of life.

Actually, current improvements in prenatal diagnosis and fetoscopic surgical techniques may eventually allow in utero treatment of ABS. Fetal limb abnormality interventions associated with ABS are described in fetuses with abnormal but present arterial Doppler flow to the distal limb. After evaluating the benefits and high risks of in utero therapy, the constriction band could be released and blood flow re-established. However, this “band lysis” surgery remains a high-risk procedure, with the occurrence of premature rupture of membranes in 71% of cases.

The authors describe a case of ABS with multiple malformations with severe craniofacial abnormalities, oligodactyly, syndactyly, and limb distal amputation. The recognition of malformations described herein, secondary to ABS, is important in genetic counseling to prevent misdiagnosis between chromosomal and secondary disruption disorders.

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Conflict of interest: None

Submitted on: 21st December 2012
Accept on: 5th March 2013

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