Washington University School of Medicine

Digital Commons@Becker

Open Access Publications

7-1-2009

Amniotic constriction band: A multidisciplinary assessment of etiology and clinical presentation

Charles A. Goldfarb

Washington University School of Medicine in St. Louis

Achara Sathienkijkanchai

University of Alabama - Birmingham

Nathaniel H. Robin

University of Alabama - Birmingham

Follow this and additional works at: https://digitalcommons.wustl.edu/open_access_pubs

Part of the [Medicine and Health Sciences Commons](#)

Please let us know how this document benefits you.

Recommended Citation

Goldfarb, Charles A.; Sathienkijkanchai, Achara; and Robin, Nathaniel H., "Amniotic constriction band: A multidisciplinary assessment of etiology and clinical presentation." *The Journal of Bone and Joint Surgery*. 91, Supplement 4. 68-75. (2009).

https://digitalcommons.wustl.edu/open_access_pubs/834

This Open Access Publication is brought to you for free and open access by Digital Commons@Becker. It has been accepted for inclusion in Open Access Publications by an authorized administrator of Digital Commons@Becker. For more information, please contact vanam@wustl.edu.

Amniotic Constriction Band: A Multidisciplinary Assessment of Etiology and Clinical Presentation

By Charles A. Goldfarb, MD, Achara Sathienkijkanchai, MD, and Nathaniel H. Robin, MD

A *amniotic constriction band*, first described in 1832 by Montgomery¹, is one term used to describe a wide range of associated congenital anomalies, including anular constrictions of multiple extremities, oligodactyly, acrosyndactyly, talipes equinovarus, cleft lip and cleft palate, and hemangiomas. Additional, less common clinical manifestations include complete absence of the limb, short umbilical cord, craniofacial disruptions, neural tube defects, cranial defects, scoliosis, and body-wall defects, such as gastroschisis and extrathoracic heart. Some of these manifestations are uncommonly noted at birth because they result in spontaneous abortion²⁻⁵.

The prevalence of amniotic constriction band is approximately one in 1200 to one in 15,000 live births^{6,7}. The prevalence rate for male infants has been reported to be 0.91 and, for female infants, 1.44. These defects are reported to occur 1.76 times more frequently among African-Americans as compared with Caucasians⁶. Evidence of familial involvement is extremely rare. Although temporal and geographic clustering has been reported, this phenomenon is not well understood⁸.

The variability of presentation between patients, the unusual nature of this constellation of findings, and the lack of a consensus on etiology are all reflected in the fact that thirty-four different names have been used to describe this entity in the literature⁹. Most of the descriptive terminology used to describe this entity relates to the extremity manifestations; the central manifestations affecting the face and body have not typically been considered for nomenclature. The various names include amnion rupture sequence, aberrant tissue band syndrome, ADAM (amniotic deformity, adhesions, mutilations) complex², constriction band syndrome, constriction ring syndrome, amnion disruption sequence, and Streeter dysplasia, among others⁹. The use of the word "syndrome" is controversial because there are no classic, consistently present and defining features of amniotic constriction band as are seen in other syndromes. Rayan⁹ evaluated the nomenclature and concluded that amniotic constriction band was the most appropriate terminology that is reflective of both etiology and description; we have chosen to employ this same terminology while understanding its limita-

tions related to both etiology and manifestations. The purpose of this review is to describe the clinical presentation of patients with amniotic constriction band and to critically evaluate the various theories of etiology.

Clinical Manifestations

A *amniotic constriction band* is associated with three general types of anomalies: disruptions, deformations, and malformations. Consideration of the manifestations of amniotic constriction band in this context is helpful both for discussion and for assessing theories of etiology. Disruptions are the breakdown of normal tissue from any cause. No two affected fetuses with tissue disruption will have exactly the same features, and there is no single feature that consistently occurs². The classic disruptive findings in amniotic constriction band are constriction bands, amputations, and acrosyndactyly. Deformations result from abnormal forces on an otherwise normal fetus. Classically, and not simply in amniotic constriction band, deformations may result from oligohydramnios, associated with a resultant direct pressure phenomenon and decreased fetal movement. Talipes equinovarus, scoliosis, and various joint contractures may result^{2,5}. An insult early in gestation results in malformation, or abnormal development, of an organ. Classic malformations associated with amniotic constriction band include body-wall defects, internal organ abnormalities, and craniofacial abnormalities.

There have been several reports of additional anomalies, most of which are consistent with malformations, in patients with amniotic constriction band¹⁰⁻¹³. In one series, constriction rings were seen together with cleft lip (with or without cleft palate), anal atresia, and ventricular septal defect in 15%, 13%, and 7% of subjects, respectively¹⁴. If these facial and organ abnormalities are indeed malformations rather than disruptions or deformations, then this study demonstrates either that malformations are associated with amniotic constriction band or that amniotic constriction band anomalies may have more than one etiology.

The classic phenotype of amniotic constriction band includes the involvement of multiple extremities to varying

Disclosure: The authors did not receive any outside funding or grants in support of their research for or preparation of this work. Neither they nor a member of their immediate families received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity.

Fig. 1
Several classic features of amniotic constriction band are demonstrated. There is a fenestrated syndactyly involving the index and long fingers, a marked constriction ring of the ring (and little) finger with edema distally, and a partial loss of the thumb.

degrees and a variety of abnormalities in each patient. The three most common abnormalities include limb or digit amputations, constriction rings, and acrosyndactyly, each of which is discussed below (Figs. 1, 2, and 3). Additional findings

may include talipes equinovarus and, less commonly, scoliosis. Even rarer are craniofacial abnormalities, such as cleft lip or cleft palate, body-wall defects, and internal organ abnormalities. These abnormalities require evaluation by specialist physicians in addition to the orthopaedic surgeon, as they may be life-threatening. An evaluation by a clinical geneticist should be performed to comprehensively evaluate the child for uncommon findings and to explore possible etiologies.

There is no widely accepted classification scheme for amniotic constriction band. Patterson classified the common extremity manifestations¹⁵; this is perhaps the most helpful classification for clinicians. Type 1 includes extremities with simple constriction rings. There may be deficient subcutaneous tissue at the level of the ring, but the extremity distal to the ring is normal. Type 2 is a constriction ring with distal deformity, including atrophy and lymphedema. These findings are thought to represent lymphatic or neurovascular disruption caused by the ring. There may be sensory deficits, especially when rings occur at the proximal aspect of the extremity¹⁶⁻¹⁹. Type 3 is acrosyndactyly, or fenestrated syndactyly, which is a distal cutaneous fusion of the skin with separation of the digits proximally. This differs from typical or developmental syndactyly, which results when normal interdigital cell death does not occur during hand development and which always involves the proximal web. Short digits are commonly noted in infants with acrosyndactyly, in contrast to the normal-length digits that are seen in most infants with developmental syndactyly. Finally, Type 4 includes amputation at any level of the extremity or digit.

Three reports²⁰⁻²² of large series of children with amniotic constriction band provide information about the common manifestations of this disorder. There was a high prevalence of prematurity in each study, ranging from 35% to 50%, with an

Fig. 2
This hand is more severely involved and has a more complicated fenestrated syndactyly involving all digits, with shortening of all digits.

Fig. 3

A classic constriction ring of the distal part of the calf.

assortment of other gestational issues, including maternal hemorrhage and amniotic fluid leakage. Two of the three studies demonstrated a greater involvement of the upper extremities, while the third study showed nearly equal involvement of the upper and lower extremities. One of the studies reported an average of three involved extremities²¹. Upper extremities most commonly demonstrated constriction rings, acrosyndactyly, and absence of the terminal aspect of the digit (typically affecting the central digits). Constriction rings were seen at all levels of the extremity. Talipes equinovarus was prominent in all three reports.

Risk factors for amniotic constriction band are not well defined. An epidemiological analysis of a case-control study of birth defects demonstrated that mothers of patients with amniotic constriction band and body-wall defects are more likely to be young and African-American and less likely to be educated, although there were no clear-cut associations with age or race for mothers of patients with limb abnormalities alone. The authors suggested that these differences may indicate different etiologies²³.

Body-Wall Defects

Body-wall defects represent a variety of abnormalities of the ventral body wall; while their exact etiology is unknown, these defects likely represent disruptions or malformations. Body-wall defects have been considered a severe manifestation of amniotic constriction band on the basis of the presumption that body-wall

defects represent an earlier rupture of the amniotic sac and/or a more severe presentation than isolated limb abnormalities do²⁴. The relationship between body-wall defects and the extremity findings of amniotic constriction band has been established solely through a common presentation in patients, as noted below. Definitive evidence of a causal relationship is lacking.

In one series of twenty-five fetuses with limb and body-wall defects²⁵, while 95% of the fetuses had limb defects, “the majority . . . were not typical of ‘amniotic bands’ but nevertheless appeared disruptive in nature . . .” Less than half (ten of twenty-five fetuses) actually had amniotic bands of any variety. In another review, fifty-four subjects with limb and body-wall defects and a variety of internal organ anomalies were reported as having lower-limb lesions (amelia in seven subjects; limb hypoplasia in five; rotational abnormality in three; split foot in two; and a complex defect in one), but no upper-extremity abnormalities were reported²⁶. On the basis of a series of eighteen fetuses with amniotic constriction band, twelve of whom were also diagnosed with limb and body-wall defects²⁷, the authors noted that the nine amputations in that series were not typical of amniotic constriction band (one amputation involved an absent radius and several involved “rudimentary” arms), and they concluded that amniotic constriction band and limb and body-wall defects were likely from separate etiologies with a phenotype overlap.

If considered to be malformation-type anomalies rather than disruption-type anomalies, craniofacial clefting and se-

vere body-wall defects would be expected to be predictable in presentation due to the timing and pattern of organ development and the embryonic planes of closure. However, the anomalies seen in children with amniotic constriction band do not follow the usual embryonic planes of fusion and are not predictable in presentation. For example, craniofacial clefting in patients with amniotic constriction band is usually asymmetrical and bizarre, in contrast to the typical presentations of meningoencephaloceles resulting from abnormal closure of the neural tube. The defects of the body wall in patients with amniotic constriction band also do not correspond with the normal planes of ventral closure²⁸. Since these defects do not follow the typical planes of fusion, the defects may not be representative of malformations and may instead represent a disruptive etiology that would be compatible with the etiologic spectrum of other findings of amniotic constriction band.

Differential Diagnosis

A mniotic constriction band has become a default diagnosis in the child born with limb deficiency. This is, in part, due to the fact that amniotic constriction band may mimic other conditions, especially the ones presenting with limb-reduction defects. The fact that different insults can cause a similar limb abnormality makes the diagnosis of patients with these defects particularly challenging.

In assessing a child with limb abnormalities that are consistent with a diagnosis of amniotic constriction band, specific gestational risk factors must be considered. There are multiple different human teratogens that may affect limb morphogenesis, including thalidomide, warfarin, phenytoin, valproic acid, and cocaine. Phenytoin and several others, including misoprostol, may cause vascular disruption in a limb that had formed normally²⁹. Diagnostic or therapeutic procedures during pregnancy, such as chorionic villi sampling and dilatation and curettage, can also cause vascular disruption and result in limb anomalies³⁰.

Ideally, before making the diagnosis of amniotic constriction band, the geneticist constructs a three-generation family tree, with a detailed enquiry regarding limb defects and other potentially associated anomalies, and obtains a detailed history of the pregnancy from five to eleven weeks of gestation, including such issues as drug exposure, trauma, and invasive procedures. Physical examination of the infant at the time of delivery is very helpful; if fibrous bands are attached to the affected limb at delivery, the diagnosis of amniotic constriction band may be made with greater confidence. Unfortunately, this level of detailed information is rarely available.

Symbrachydactyly is commonly misdiagnosed as amniotic constriction band. While both disorders can affect the extremity at the level of the forearm, wrist, or hand, several features distinguish these diagnoses. First, symbrachydactyly affects only one extremity, whereas amniotic constriction band usually affects multiple extremities. Second, with digit loss or transverse failure of formation associated with symbrachydactyly, the distal end of the extremity typically has nubbins with fingernails and there are invaginations at the end of the stump (representing muscle attachment to the skin)³¹; these

findings are not usually seen in amputations associated with amniotic constriction band. Finally, while syndactyly may be present in both abnormalities, it manifests as acrosyndactyly in amniotic constriction band and as developmental syndactyly, usually short digits, in symbrachydactyly.

Other conditions that should be considered in the differential diagnosis of amniotic constriction band include Adams-Oliver syndrome (autosomal dominant inheritance of heterogeneous defects, including multiple transverse limb or digit deficiencies, a scalp anomaly called cutis aplasia, and cardiac malformations)²⁹ and a very rare condition characterized by autosomal dominant inheritance of unilateral distal transverse deficiency with nubbins^{32,33}. Another differential diagnosis is ectrodactyly, ectodermal dysplasia, and cleft lip/palate (EEC) syndrome, an autosomal dominant condition caused by mutations in p63 on 7q21-22 with variable deficiency of the central rays of the hands and feet, cleft lip and/or cleft palate, dry skin with variable hypohidrosis, sparse fair dry hair, hypodontia, and thin brittle nails²⁹.

Recently, several genes causing cleft lip and/or cleft palate have been identified; subjects with these genetic profiles may also have oral or facial fibrous bands. The Van der Woude and popliteal pterygia syndromes have been associated with the IRF6 mutation. Similar findings are noted in the Hay-Wells syndrome, caused by mutations in p63. Furthermore, p63 mutations are also known to be associated with limb anomalies. Therefore, the finding of cleft lip and/or cleft palate in a patient with amniotic constriction band-like anomalies may represent a previously unrecognized syndrome with a genetic basis⁴.

The majority of cases of amniotic constriction band are sporadic; therefore, the recurrence risk for this condition seems to be negligible³⁴ in contrast to the risk associated with other inherited genetic disorders that can cause clinically similar anomalies with higher recurrence risk, such as EEC syndrome. This highlights the importance of establishing the diagnosis of amniotic constriction band.

Etiology

The debate on the etiology of amniotic constriction band has been waged in the literature for the last eighty years with no firm conclusions. Each theory has limitations; some explain certain findings in a convincing fashion while others may provide a more acceptable generalized explanation but inadequately explain specific abnormalities. As the debate has continued, some authors have begun to accept the idea that no single theory can explain all possible manifestations^{27,35}. We will summarize and evaluate the various theories (intrinsic, extrinsic, vascular, and others), with respect to extremity abnormalities (constriction rings, acrosyndactyly, and amputation) and central abnormalities (craniofacial and body-wall abnormalities).

Intrinsic Theory

The intrinsic theory, as described by Streeter in 1930³⁶, holds that an intrinsic, germline developmental abnormality is responsible for the development of amniotic con-

striction band. This theory is often used to explain major craniofacial abnormalities, body-wall defects, and internal organ abnormalities. While other theories may be more convincing in their ability to explain the extremity abnormalities, the intrinsic theory remains a popular means of explaining the central abnormalities.

Bamforth found support for the intrinsic theory in five previous comprehensive investigations on body-wall defects²⁶. He concluded that a discrete lesion could cause multiple limb and body-wall defects if it occurred at twenty-six days after fertilization and that the typical “pattern of defects bear more resemblance to the embryonic proximity of the affected structures than to their proximity in the mature body pattern.” This suggests, of course, that other theories that attempt to explain the body-wall defects through a pressure phenomenon or through amniotic band-related pressure are inaccurate. Bamforth does not suggest, however, that this single theory explains all findings of amniotic constriction band.

An evaluation of four fetuses that had limb and body-wall malformations²⁴ showed that three had internal organ abnormalities and two had separation of the amnion and chorionic cavities; however, the timing of the amnion rupture in each fetus was later than the timing that would explain the malformations that were present in these fetuses. These authors believed that these findings were most suggestive of a germline defect; they dismissed the vascular and banding theories.

The exact nature of a germline defect that may lead to amniotic constriction band is unknown and could be multifactorial. A teratogenic insult that damages germline cells has been proposed, but there is little evidence to support this theory. One report relates the ingestion of misoprostol at nine weeks gestation to a nonviable fetus with an amniotic constriction band-like presentation of upper-limb amputation, bilateral talipes equinovarus, and cerebellar atrophy. The authors of this report did not conclude that there was a definitive link and acknowledged that the defect may have been the result of premature rupture of the amnion³⁷.

There are several important critiques of the intrinsic theory. First, this theory does not sufficiently explain the development of banding abnormalities. The argument for a mechanical etiology of the band-related abnormalities is more convincing, as noted below. Second, a germline defect, affecting a defined portion of the developing embryo, would be expected to lead to a more reproducible abnormality. However, children with amniotic constriction band and body-wall defects have a combination of abnormalities that is unique to each child. By this rationale, a disruptive etiology may have more credence than the malformation concept²⁷. Finally, as Kino states, “if this syndrome arose from abnormal constitution of the germ plasm, neither fenestrated syndactyly nor constriction rings could possibly result.”²²

Extrinsic Theory

Background

The developing embryo sits within two cavities: the inner amniotic cavity, and the outer chorionic cavity. The am-

niotic cavity (lined by embryonic ectoderm cells) gradually expands and, by twelve weeks, the outer chorionic space is obliterated³⁸. It has been suggested that if this space does not undergo obliteration, the chorion does not support the amnion and the amniotic sac may rupture³⁵. If the amniotic sac ruptures, amniotic fluid may be lost and the fetus may pass in part or in total into the chorionic cavity; amniotic bands potentially occur as the result of premature rupture of the amniotic sac, and bands and fragments from torn amnion together with mesodermic fibrous strings (which form on both the outer surface of the amniotic membrane and the inner surface of the chorion) may encircle various fetal parts^{8,39}. The amniotic bands are composed of either acellular fibrous tissue or fibrous tissue containing fibroblasts covered by squamous cells. The fibrous nature of these amniotic bands makes them inelastic and produces a ligature effect³⁹.

The Theory

The extrinsic theory, as described by Torpin in 1965⁴⁰, holds that a rupture of the amniotic sac leads to the formation of amniochorionic mesodermal bands leading to the development of amniotic constriction band. Torpin reviewed only three cases and discussed a total of eleven, arguing that the asymmetry of the digital amputations and other findings, and the associations with constriction rings and clubfoot, point away from a genetic or an intrinsic cause. The etiology of such findings as limb and body-wall defects and craniofacial abnormalities was not discussed. The cause of early amniotic rupture remains unknown, although trauma has been reported in a few cases²⁸.

The gestational age at which the amniotic sac ruptures is believed to be the major factor determining the range and severity of amniotic constriction-band deformities. The rupture can occur at any time during gestation; however, it most likely occurs before twelve weeks. Theoretically, early rupture could decrease amniotic fluid, causing the compressive consequences of early constraint, such as scoliosis and clubfoot². Additionally, and more severely, a vascular disruption could result from the early rupture, leading to facial clefts and limb reduction with body-wall defects¹⁰.

An examination of eighteen stillborn fetuses with amniotic constriction band revealed that eleven had bands comprised of amniotic epithelium encircling one or more limbs²⁷. In two fetuses, the bands encircled the umbilical cords, a known cause of fetal death. The authors concluded that “incomplete amniochorionic fusion with partial persistence of the extra embryonic coelom explains the accidental character of most cases . . .” In contrast to Torpin’s assertion that the bands are mesodermal, the bands examined in this study consisted of amnion. The authors also described another lesion—the broad amniotic adhesion—as being the result of a distinct pathological process. They believed that raw surfaces resulting from “fetal defects associated with the disruption of the ectodermal integrity” were responsible for facial abnormalities. They could not relate limb and body-wall defects to the extrinsic theory and thought these were a separate entity entirely.

An evaluation of seventy-nine patients with amniotic constriction band, including banding and/or major deficiencies⁴¹, resulted in the conclusion that the timing of the amnion rupture and the nature of the entanglement and subsequent banding determine the pattern of presentation. Later rupture primarily affects the limbs, whereas earlier rupture can lead to multiple malformations and limb and body-wall defects. Another review of twenty-seven cases of limb and body-wall defects resulted in the conclusion that these represent the most severe manifestation of early amnion rupture⁴²; amniotic bands were noted in 41% of these subjects. The authors concluded that, according to the extrinsic theory, early amnion rupture (and resulting loss of amniotic fluid and subsequent pressure phenomenon) causes the severe “non band-related defects in limb/body wall deficiency.” They also cited animal studies (see below) supporting the crucial nature of sufficient amniotic fluid to normal development, and concluded that defects depend on the timing and extent of the amnion rupture, the extent of compression, and the presence or absence of banding.

Others have performed amniotic sac puncture in rats and found that this caused hemorrhagic lesions, tissue necrosis, limb reduction, and cephalic changes⁴³. They attributed these findings to intrauterine compression related to lost amniotic fluid and uterine pressure and subsequent obstruction of circulation.

Do Tight Bands Cause Constriction Rings?

Scientific investigations including animal and human studies have supported the extrinsic theory. In one study, researchers used silk ligature to simulate amniotic bands in forty rats⁴⁴. In Group 1, the limb was placed through the amniotic sac and uterine wall and the uterus was allowed to constrict around the limb. In Groups 2 through 4, the limbs were exteriorized through a small hysterotomy and a single suture was tied around the extremity prior to placing the limb back into the uterus and closing the hysterotomy. Group 2 had a loose ligature; in Group 3, it was tight proximally; and, in Group 4, it was tight distally. Late examination in Group 1 demonstrated classic constriction rings with changes distally. Group 2 had constriction rings without distal edema. In Group 3, 40% of the rats died but all survivors had rings with infarction distally. Finally, in Group 4, nine of the ten had deep rings and distal infarction.

Other investigations with similar findings include animal and human studies of fetoscopy⁴⁵. In a fetal lamb model, a constrictive band was applied at 100 days gestation, and typical amniotic constriction-band findings were demonstrated at birth, including distal deformity, pitting edema, and venous congestion⁴⁶. Much milder findings with a near normal limb appearance were noted when the band was released fetoscopically twenty-five days later. Others⁴⁷⁻⁴⁹ reported fetoscopic release at approximately twenty weeks gestation in humans, with improvement in the appearance of the extremities. These reports do not advocate isolated fetoscopic release, as the risks of such intervention are high. However, these investigations do

lend credence to the concept of a defined band causing the extremity manifestations of amniotic constriction band.

Prenatal ultrasound examination of one subject resulted in the detection of constriction rings at twenty-one weeks gestation, with a subsequent loss of blood flow and auto-amputation⁵⁰; the authors concluded that this case supported the extrinsic theory. Other ultrasound investigations have also provided similar findings in the upper extremity⁵¹. At birth, constriction of the arm with band formation was noted after the insertion of a soft and flexible pleuro-amniotic shunt into a twenty-three-week-old fetus⁵², providing evidence that a compressive band can cause constriction bands in humans.

Critique of Extrinsic Theory

There are several important limitations to the extrinsic theory. First, the internal visceral abnormalities and limb and body-wall defects are difficult to explain by the concept of band-applied pressure. Facial anomalies, such as cleft lip or cleft palate, are also difficult to explain by the extrinsic theory, although band pressure has been argued to cause such defects. Oligohydramnios from an early amnion rupture has been cited as a link between banding and these more severe deficiencies^{41,42}. The consequences of very early amnion rupture may include compressive consequences of early constraint, such as scoliosis and clubfoot, as well as vascular disruption leading to facial clefts and limb reduction with body-wall defects¹⁰. Yet it is difficult to understand how the array of limb and body-wall findings could be caused by pressure on one area of the fetus.

Second, this theory depends in part on the concept of amnion rupture leading to decreased amniotic fluid². However, despite some reports of amniotic fluid leakage²⁰, oligohydramnios is not consistently noted and the presence of the chorion may prevent amnion rupture from causing oligohydramnios.

Vascular Theory

Van Allen suggested that vascular disruption can lead to both internal and external defects²⁵. In her report of twenty-five children with limb and body-wall defects, twenty-four had a limb deficiency, twenty-four had internal organ abnormalities, eighteen had a cephalic deficit, fourteen had craniofacial defects, and ten had amniotic bands. The author related the various abnormalities, especially the internal organ deficiency, to vascular disruption causing a systemic alteration of the embryonic blood supply. The author theorized that a traumatic event, such as amnion rupture, amniocentesis, direct trauma, or exposure to a teratogen at four to six weeks of gestation, may disrupt development by interrupting the blood supply to the fetus, causing hemorrhagic necrosis and embryonic circulatory collapse. The timing of the insult determines the presenting abnormality⁴¹.

A similar theory, based on the effects of uterine blood-flow disruption in rat embryos, was tested in a study designed to replicate the effects of maternal uterine trauma⁵³. Amputation and digit hypoplasia resulted; constrictions were seen but were not particularly common.

Another theory of vascular disruption holds that a specific intrauterine traumatic event, as may be simulated in an animal model by an intra-adnexal injection of glucose, leads to the development of amniotic constriction band⁵⁴. In this rabbit experiment, injections into the uterine adnexa performed between eleven and twenty days of gestation (corresponding to two to three months in humans) led to cellular destruction and hemorrhage, causing amniotic constriction band-like transverse limb amputations at different levels and facial anomalies, including cleft lip, ulcerations, syndactyly, and clubfoot. Amniotic bands, not previously produced in a laboratory setting, were infrequent. The authors concluded that neither amniotic sac rupture nor amniotic bands play a role in human disease.

A rat amniocentesis study demonstrated that hemorrhage preceded limb constriction, amputation, talipes equinovarus, and cleft palate. Early amniocentesis caused a higher rate of both limb malformation and cleft palate and was more lethal than amniocentesis performed later. There are no strong data suggesting that amniocentesis in humans leads to amniotic constriction band, but reduction defects similar to amniotic constriction band have been documented after chorionic villus sampling⁵⁵.

Critique of Vascular Theory

Bamforth evaluated the vascular hypothesis in terms of embryonic organization and did not find this theory credible as he did not believe that the abnormalities followed the known embryonic vascular patterns²⁶. He believed that the embryonic anatomical proximity was more “striking” than the vascular relationships.

Other Theories

None of the above theories can explain all findings in patients with amniotic constriction band, especially the non-extremity findings. Ds (short for “disorganization”) is an au-

tosomal dominant mouse mutant that produces a wide variety of birth defects with markedly reduced penetrance; it has been suggested as a model for an amniotic constriction band-like phenotype^{56,57}. The Ds gene has yet to be identified, but much has been inferred through murine breeding studies. This gene is a candidate for the intrinsic factor proposed by Streeter³⁶.

Conclusions

Based on an assimilation of historical and current research, the findings in amniotic constriction band can be grouped as classic, which can be explained by disruptions and deformations (constriction rings, amputation defects, and talipes equinovarus), and nonclassic, which result from malformations (cleft lip and/or cleft palate, imperforate anus, and body-wall defects). These two groups of findings have different etiologies that cannot be reconciled on the basis of our current understanding. The phenotypic overlap between classic and nonclassic findings in amniotic constriction band confounds scientists and clinicians, and the search for a unifying theory of causation continues. ■

Charles A. Goldfarb, MD
Department of Orthopaedic Surgery,
Washington University School of Medicine,
660 South Euclid Avenue,
Campus Box 8233, St. Louis, MO 63110.
E-mail address: goldfarbc@wustl.edu

Achara Sathienkijkanhai, MD
Nathaniel H. Robin, MD
Division of Medical Genetics, Department of Pediatrics,
University of Alabama at Birmingham, Kaul 210,
1530 3rd Avenue South, Birmingham, AL 35294

References

- Montgomery WF. Observations on the spontaneous amputations of the limbs of the foetus in utero, with an attempt to explain the occasional cause of its production. *Dublin J Med Chem Science*. 1832;1:140-4.
- Jones K. Smith's recognizable patterns of human malformation. 6th ed. Philadelphia: WB Saunders; 2005.
- Kiehn M, Leshem D, Zuker R. Constriction rings: the missing link. *Eplasty*. 2007;8:e4.
- Robin NH, Franklin J, Prucka S, Ryan AB, Grant JH. Clefting, amniotic bands, and polydactyly: a distinct phenotype that supports an intrinsic mechanism for amniotic band sequence. *Am J Med Genet A*. 2005;137:298-301.
- Gorlin RJ, Cohen MM Jr, Hennekam RCM. Syndromes of the head and neck. 4th ed. New York: Oxford University Press; 2001. Amnion rupture sequence; p 10-3.
- Garza A, Cordero JF, Mulinare J. Epidemiology of the early amnion rupture spectrum of defects. *Am J Dis Child*. 1988;142:541-4.
- Lindenau KF, Evers G. [An unusual case of bilateral and symmetric amniogenic indentations]. *Pediatr Grenzgeb*. 1974;13:61-5. German.
- Lockwood C, Ghidini A, Romero R, Hobbins JC. Amniotic band syndrome: reevaluation of its pathogenesis. *Am J Obstet Gynecol*. 1989;160(5 Pt 1):1030-3.
- Rayan GM. Amniotic constriction band. *J Hand Surg [Am]*. 2002;27:1110-1.
- Graham JM Jr, Higginbottom MC, Smith DW. Preaxial polydactyly of the foot associated with early amnion rupture: evidence for mechanical teratogenesis? *J Pediatr*. 1981;98:943-5.
- Carey JC, Greenbaum B, Hall BD. The OEIS complex (omphalocele, exstrophy, imperforate anus, spinal defects). *Birth Defects Orig Artic Ser*. 1978;14:253-63.
- Harrison IM, Brosnahan D, Phelan E, Fitzgerald RJ, Reardon W. Septo-optic dysplasia with digital anomalies—a recurrent pattern syndrome. *Am J Med Genet A*. 2004;131:82-5.
- Jabor MA, Cronin ED. Bilateral cleft lip and palate and limb deformities: a presentation of amniotic band sequence? *J Craniofac Surg*. 2000;11:388-93.
- Orioli IM, Ribeiro MG, Castilla EE. Clinical and epidemiological studies of amniotic deformity, adhesion, and mutilation (ADAM) sequence in a South American (ECLAMC) population. *Am J Med Genet A*. 2003;118A:135-45.
- Patterson TJ. Congenital ring-constrictions. *Br J Plast Surg*. 1961;14:1-31.
- Moses JM, Flatt AE, Cooper RR. Annular constricting bands. *J Bone Joint Surg Am*. 1979;61:562-5.
- Uchida Y, Sugioka Y. Peripheral nerve palsy associated with congenital constriction band syndrome. *J Hand Surg [Br]*. 1991;16:109-12.
- Tada K, Yonenobu K, Swanson AB. Congenital constriction band syndrome. *J Pediatr Orthop*. 1984;4:726-30.
- Weeks PM. Radial, median, and ulnar nerve dysfunction associated with a congenital constricting band of the arm. *Plast Reconstr Surg*. 1982;69:333-6.
- Askins G, Ger E. Congenital constriction band syndrome. *J Pediatr Orthop*. 1988;8:461-6.

21. Foulkes GD, Reinker K. Congenital constriction band syndrome: a seventy-year experience. *J Pediatr Orthop*. 1994;14:242-8.
22. Kino Y. Clinical and experimental studies of the congenital constriction band syndrome, with an emphasis on its etiology. *J Bone Joint Surg Am*. 1975;57:636-43.
23. Werler MM, Louik C, Mitchell AA. Epidemiologic analysis of maternal factors and amniotic band defects. *Birth Defects Res A Clin Mol Teratol*. 2003;67:68-72.
24. Hartwig NG, Vermeij-Keers C, De Vries HE, Kagie M, Kragt H. Limb body wall malformation complex: an embryologic etiology? *Hum Pathol*. 1989;20:1071-7.
25. Van Allen MI. Fetal vascular disruptions: mechanisms and some resulting birth defects. *Pediatr Ann*. 1981;10:219-33.
26. Bamforth JS. Amniotic band sequence: Streeter's hypothesis reexamined. *Am J Med Genet*. 1992;44:280-7.
27. Moerman P, Fryns JP, Vandenbergh K, Lauweryns JM. Constrictive amniotic bands, amniotic adhesions, and limb-body wall complex: discrete disruption sequences with pathogenetic overlap. *Am J Med Genet*. 1992;42:470-9.
28. Aase JM. *Diagnostic dysmorphism*. New York: Plenum; 1990. p 283-5.
29. Firth HV, Hurst JA. *Oxford desk reference: clinical genetics*. New York: Oxford University Press; 2005.
30. Holmes LB. Teratogen-induced limb defects. *Am J Med Genet*. 2002;112:297-303.
31. Kallemeier PM, Manske PR, Davis B, Goldfarb CA. An assessment of the relationship between congenital transverse deficiency of the forearm and symbrachydactyly. *J Hand Surg [Am]*. 2007;32:1408-12.
32. Graham JM, Jr., Brown FE, Struckmeyer CL, Hallowell C. Dominantly inherited unilateral terminal transverse defects of the hand (adactylia) in twin sisters and one daughter. *Pediatrics*. 1986;78:103-6.
33. Neumann L, Pelz J, Kunze J. Unilateral terminal aphalangia in father and daughter—exogenous or genetic cause? *Am J Med Genet*. 1998;78:366-70.
34. Czeizel AE, Vitez M, Kodaj I, Lenz W. Study of isolated apparent amniogenic limb deficiency in Hungary, 1975-1984. *Am J Med Genet*. 1993;46:372-8.
35. Levy PA. Amniotic bands. *Pediatr Rev*. 1998;19:249.
36. Streeter G. Focal deficiencies in fetal tissues and their relation to intrauterine amputations. *Contrib Embryol Carnegie Inst*. 1930;22:1-46.
37. Sentilhes L, Patrier S, Chouchene S, Diguët A, Berthier A, Marpeau L, Verspyck E. Amniotic band syndrome with limb amputation after exposure to mifepristone in early pregnancy. *Fetal Diagn Ther*. 2007;22:51-4.
38. Boyd J, Hamilton W. *The human placenta*. Cambridge: Heffer; 1970.
39. Kim JB, Berry MG, Watson JS. Abdominal constriction band: A rare location for amniotic band syndrome. *J Plast Reconstr Aesthet Surg*. 2007;60:1241-3.
40. Torpin R. Amniochorionic mesoblastic fibrous strings and amnionic bands: associated constricting fetal malformations or fetal death. *Am J Obstet Gynecol*. 1965;91:65-75.
41. Higginbottom MC, Jones KL, Hall BD, Smith DW. The amniotic band disruption complex: timing of amniotic rupture and variable spectra of consequent defects. *J Pediatr*. 1979;95:544-9.
42. Miller ME, Graham JM Jr, Higginbottom MC, Smith DW. Compression-related defects from early amnion rupture: evidence for mechanical teratogenesis. *J Pediatr*. 1981;98:292-7.
43. Kennedy LA, Persaud TV. Pathogenesis of developmental defects induced in the rat by amniotic sac puncture. *Acta Anat (Basel)*. 1977;97:23-35.
44. Rowsell AR. The amniotic band disruption complex. The pathogenesis of congenital limb ring-constrictions; an experimental study in the foetal rat. *Br J Plast Surg*. 1988;41:45-51.
45. Soldado F, Peiró JL, Aguirre M, Moll X, García-Fontecha C, Giné C, Martínez-Ibáñez V. Extremity amniotic band syndrome in fetal lamb. I: An experimental model of limb amputation. *Am J Obstet Gynecol*. 2006;195:1607-10.
46. Crombleholme TM, Dirkes K, Whitney TM, Alman B, Garmel S, Connelly RJ. Amniotic band syndrome in fetal lambs. I: Fetoscopic release and morphometric outcome. *J Pediatr Surg*. 1995;30:974-8.
47. Ronderos-Dumit D, Briceno F, Navarro H, Sanchez N. Endoscopic release of limb constriction rings in utero. *Fetal Diagn Ther*. 2006;21:255-8.
48. Quintero WJ, Morales WJ, Phillips J, Kalter CS, Angel JL. In utero lysis of amniotic bands. *Ultrasound Obstet Gynecol*. 1997;10:316-20.
49. Keswani SG, Johnson MP, Adzick NS, Hori S, Howell LJ, Wilson RD, Hedrick H, Flake AW, Crombleholme TM. In utero limb salvage: fetoscopic release of amniotic bands for threatened limb amputation. *J Pediatr Surg*. 2003;38:848-51.
50. Tadmor OP, Kreisberg GA, Achiron R, Porat S, Yagel S. Limb amputation in amniotic band syndrome: serial ultrasonographic and Doppler observations. *Ultrasound Obstet Gynecol*. 1997;10:312-5.
51. Hill LM, Kislak S, Jones N. Prenatal ultrasound diagnosis of a forearm constriction band. *J Ultrasound Med*. 1988;7:293-5.
52. Brown R, Nicolaidis K. Constriction band of the arm following insertion of a pleuro-amniotic shunt. *Ultrasound Obstet Gynecol*. 2000;15:439-40.
53. Webster WS, Lipson AH, Brown-Woodman PD. Uterine trauma and limb defects. *Teratology*. 1987;35:253-60.
54. Clavert JM, Clavert A, Berlizon A, Buck P. Abnormalities resulting from intra-adnexal injection of glucose in the rabbit embryo—an experimental model of "amniotic disease". *Prog Pediatr Surg*. 1978;12:143-64.
55. Firth HV, Boyd PA, Chamberlain P, MacKenzie IZ, Lindenbaum RH, Huson SM. Severe limb abnormalities after chorion villus sampling at 56-66 days' gestation. *Lancet*. 1991;337:762-3.
56. Donnai D, Winter RM. Disorganization: a model for 'early amnion rupture'? *J Med Genet*. 1989;26:421-5.
57. Robin NH, Nadeau JH. Disorganization in mice and humans. *Am J Med Genet*. 2001;101:334-8.