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ORIGINAL ARTICLE

Placento-Cranial Adhesion: A New Syndromic Association

Bal Chander[1] · Daisy Dwivedi[2] · Sita Thakur[3] · Suman Yadav[2]

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Abstract Cases of placento-cranial adhesion are rare and most of them are incompatible with life. A few case reports in the literature have included such cases under the overarching rubric of amniotic band syndrome. We present autopsy findings of four cases with gestation period ranging from 16 to 21 weeks. All of them displayed placenta-cranial adhesion, low weight for gestation, absence of flat bones of skull, anencephaly, dysmorphic facial features, short umbilical cord and limb/digit amputation with oligohydrambios. Three out of four showed nasal groove. We propose that there are grounds for syndromic association of the features mentioned above. Furthermore, it is important that whenever such cases are identified termination of pregnancy should be considered. The article also underscores the importance of fetal autopsies.

Keywords Fetus · Adhesion · Fatal

Introduction

Direct placental attachment to a part of fetus is generally placed under the rubric of amniotic band syndrome (ABS), which refers to a process wherein a spectrum of congenital malformations is seen resulting from formation of bands composed largely of fibrous tissue. Placental attachment to the fetal head has been reported mostly as case reports since the condition is rare and in almost all these cases the outcome has been fatal. Inclusion of these cases under ABS is perhaps not right since ABS can be compatible with survival whereas placenta-cranial adhesion appears to be incompatible with life. The attachment appears to be accompanied by other features as is illustrated by the cases being presented in this paper. The combination of features appear to qualify for a new syndrome comprising of placento-cranial adhesion, short umbilical cord, absence of some skull bones with underdeveloped or absent cerebral hemispheres, dysmorphic facies, low weight for gestational age and fatal outcome. We propose that this condition be considered as a distinct entity and differentiated from ABS, acrania and acalvaria and present arguments for doing so along with critical review of literature.

Report of Cases

Four pregnant individuals had reported for routine ultrasound in the OPD without any specific complaints and in all cases IUD was declared on the basis of absent fetal heart sounds. None of the pregnant women had any abnormality in prenatal screening tests. Antenatal ultrasound had not diagnosed placenta-cranial adhesion and/or any manifestation of amniotic band syndrome except for oligohydramnios in all the cases. All the cases were admitted and labour was induced.

The common features shared by all the three fetuses delivered were: placental attachment to the head, facial dysmorphism, absence of parts of frontal and bilateral parietal bones along with dura and muscles, bilateral upper

✉ Bal Chander
ssst419@hotmail.com

[1] Department of Pathology, Dr. Rajendra Prasad Government Medical College, Kangra, Tanda, Himachal Pradesh 176001, India

[2] Department of Anatomy, Dr. Rajendra Prasad Government Medical College, Kangra, Tanda, India

[3] Department of Obstetrics and Gynecology, Dr. Rajendra Prasad Government Medical College, Kangra, Tanda, India

and lower limbs flexion deformities, small for gestational age, oligohydramnios. Cerebral hemisphere were rudimentary in two of the cases and not discernible in rest either microscopically or gross examination. Umbilical cord in all cases was short and appeared to be hypocoiled.

Case 1

A 33 years old gravida three at 16 weeks of gestation delivered a female fetus. Bilateral protruding eyes, flattened nose, amputation of digits, right hand and congenital talipes equinus varus. No consanguity present. Other features are described earlier (Further details given in Tables 1 and 2).

Case 2

A 28 years old second gravida at 20 weeks of pregnancy delivered a still born male fetus. Right hand showed absent distal part of thumb along with index and middle finger. All the toes were either completely or partly missing. Nasal cleft was seen. No consanguity present. Other features are described earlier (Further details given in Tables 1 and 2).

Table 1 List of features and corresponding frequency in four cases

S. no.	Feature	No. of cases seen in
1	Placento-cranial adhesion	4/4
2	Absent flat bones of skull	4/4
3	Absent or rudimentary cerebral Hemispheres	4/4
4	Facial dysmorphism	4/4
5	Low weight for gestation	4/4
6	Short umbilical cord	4/4
7	Oligohydramnios	4/4
8	Limb/digits amputation	4/4
9	Nasal cleft	¾
10	Abdominal wall defect	¼
11	Cleft lip	¼

Case 3

A 24 years old primi gravida at 21 weeks of gestation. A still born male fetus was delivered. There was nasal cleft. Left ankle showed constriction ring and left foot displayed gangrenous changes with right club foot. No consanguity present. Other features are described earlier (Further details given in Tables 1 and 2).

Case 4

A 30 years old primigravida at 20 weeks of gestation delivered a still born male fetus. Right upper limb was missing. Left hand showed amputation of four digits. There was cleft lip and palate and amniotic band could be seen extending from left nostril to forehead. Abdominal wall showed defect and loops of small intestine, stomach and liver were outside the cavity. No consanguity present. Other features are described earlier (Further details given in Tables 1 and 2).

Complete autopsy was carried out in all the cases. Similar findings were noted in all. All the thoraco-abdomino-pelvic organs were in normal anatomical locations with no malformations except for one case (Figs. 1, 2, 3, 4).

The sections examined from the tissue covering the skull defect and membrane/ band connecting the heads and main bodies of placenta showed similar features. The membrane/ band was composed largely of collagen and focally lined by cytotrophblastic cells. Focal calcification and bone formation was also noted. In addition, there was tissue rich in thin walled dilated vascular channels sandwiched between immature brain parenchyma and placental membrane covering the skull defect.

Discussion

Placento-cranial adhesions wherein part of placenta is attached to the fetal head has consistently been considered as a part of ABS which fails to communicate the salience of the former. The incidence of placenta-cranial adhesion is

Table 2 Comparison between expected and observed parameters

S. no.	Gestational age weeks (days)	Crown rump (CR) length (cm)	Expected Age corresponding to CR lenghts (days) [1]	Umbilical cord length (cm)	Expected normal mean umbilical cord length (cm) [2]	Weight (Gms)	Expected weight
1	16 (112)	9	97	9.5	19	101	150
2	20 (140)	15	118	13	32	144	350
3	21 (147)	14.5	123	19	32	159	400
4	20 (140)	11.5	118	12	32	135	350

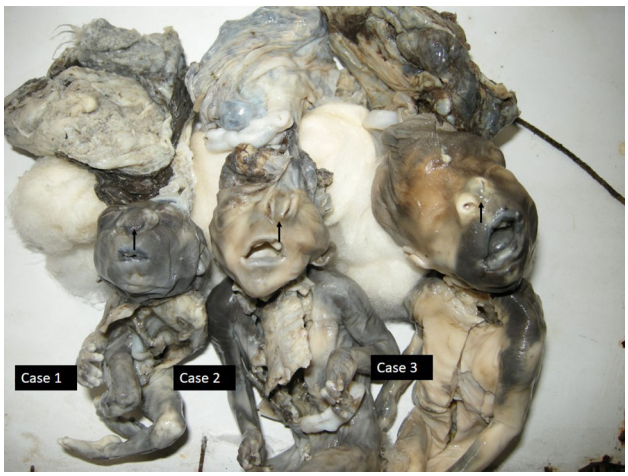

Fig. 1 Photograph showing placenta attached to the head and dysmorphic facial features along with contractures, bilateral limbs

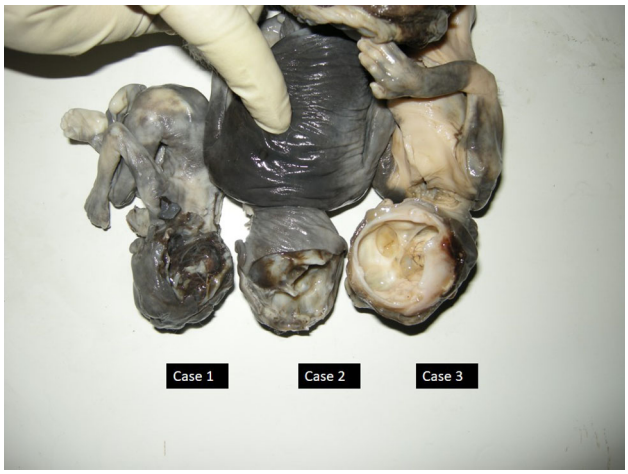

Fig. 2 Cases with similar defects in the skull

not known. However, in our center, we have seen four of such cases over the last eight years and 90,000 pregnancies. Cases similar to the present studies have been published as case reports most of which were incompatible with survival [3–6]. There are occasional reports of live birth who had died shorty or survived however there is no long term follow up of the surviving cases [7].

There is no dearth of literature on ABS. The incidence ranges from 1:1200 to 1:15,000 in live births [8]. In ABS, regardless of etiopathogensis, the fetal malformations/disruptions are mostly consequences of amniotic bands either disrupting normal development for instance of lip/palate resulting in cleft lip/palate or amputating a part of body, mostly limbs or parts of owing to constrictive nature of bands which compromises the blood supply. There is barely any debate about the cause and effect although hypotheses proposed apropos etiopathogenesis of ABS is debatable.

According to the hypothesis propounded by Streeter in 1930, anomalies and fibrous bands are the consequence of early perturbation of germinal disc in early embryo [9]. It appears to go against common sense which dictates that earlier the defect in embryogenesis, higher the chances of associated anomalies. The hypothesis also fails to explain why internal organs defects should be rare with ABS since the germinal disc itself is compromised early on.

The so called 'extrinsic model' proposed by Torpin and Faulkner in 1966 points out that damaged amnion in early pregnancy leads to amnion loss, extrusion of fetal parts into chorionic cavity which in turn leads to formation of fibrotic bands [10]. The hypothesis has been proven by inducing ABS in experimental animals by deliberately rupturing amnion. However, it is not known what causes spontaneous amnion damage in humans. Moreover, it is difficult to explain the preponderance of lower limb involvement as reported by Foulkes and Reinker wherein they found one third of 71 patients with lower limb involvement [11].

In the cases presented here, it is very difficult to speculate regarding the cause and effect. It would be impossible to state that anencephaly is caused by placental attachment to head or vice versa and similarly short umbilical cord is result of placenta attached to head or the opposite of that. Although it is tempting to conclude that skull defect leads to placental attachment however vast majority of anencepahic cases without placental attachment militates against such conclusion. At best it would be safe to state that in these cases anencephaly, placental attachment to head and short umbilical cord are associated with each other. Perhaps it can be stated that in select cases combination of anencephaly, olihydramnios, short umbilical cord facilitate placenta-cranial adhesion or for that matter attachment of placenta to any part of fetal body. It is true that two out of four cases showed evidence of ABS in the form of amputated limb and/or digits which would favor these cases to be included in ABS, however placental attachment of head, anencephaly, short umbilical cord and facial dysmorphism should make a compelling argument to treat such cases as separate from ABS.

Syndrome is group of symptoms which consistently occur together more than chance would allow. There are appreciable reasons to consider placento-cranial adhesions as a syndrome which ought to be recognized as a distinct entity. All of the cases we are presenting displayed no discernible presence of parietal, temporal and majority of frontal bones. Absence of flat bones of fetal skull is observed in either acrania or acalvaria. In the former flat bones are absent and brain is directly exposed to amniotic fluid where as in the latter the skull defect is covered by skin. In both acrania and acalvaria, the base of skull is normal and cerebral hemispheres are present albeit abnormally developed [4]. There are reports of ABS, acrania and

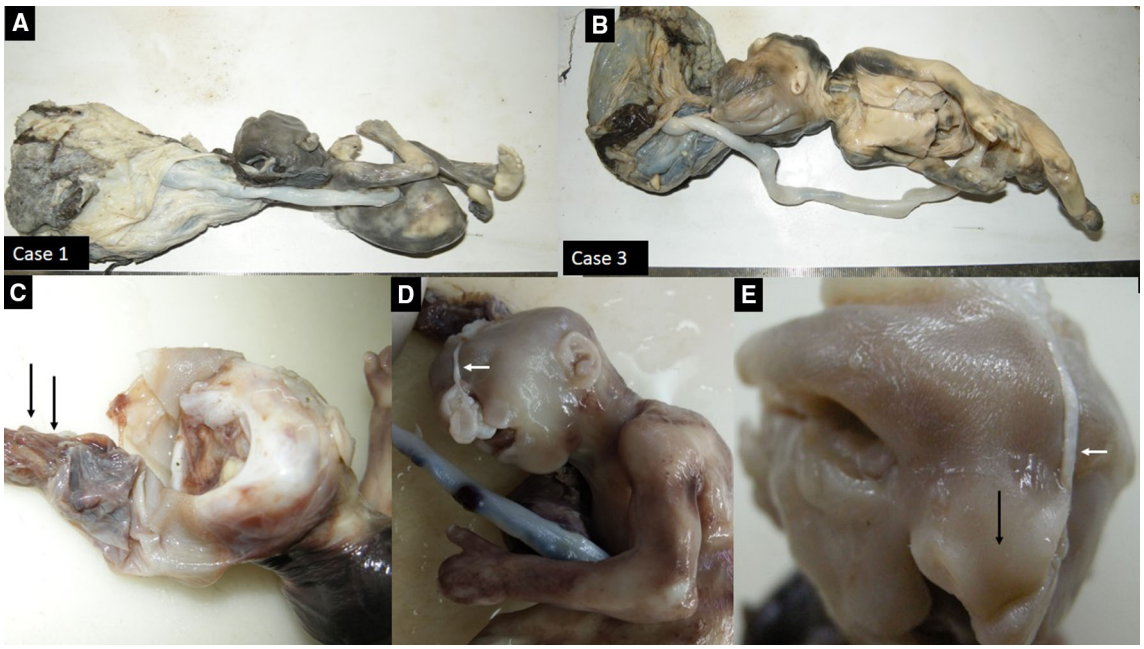

Fig. 3 Presence of short umbilical cords

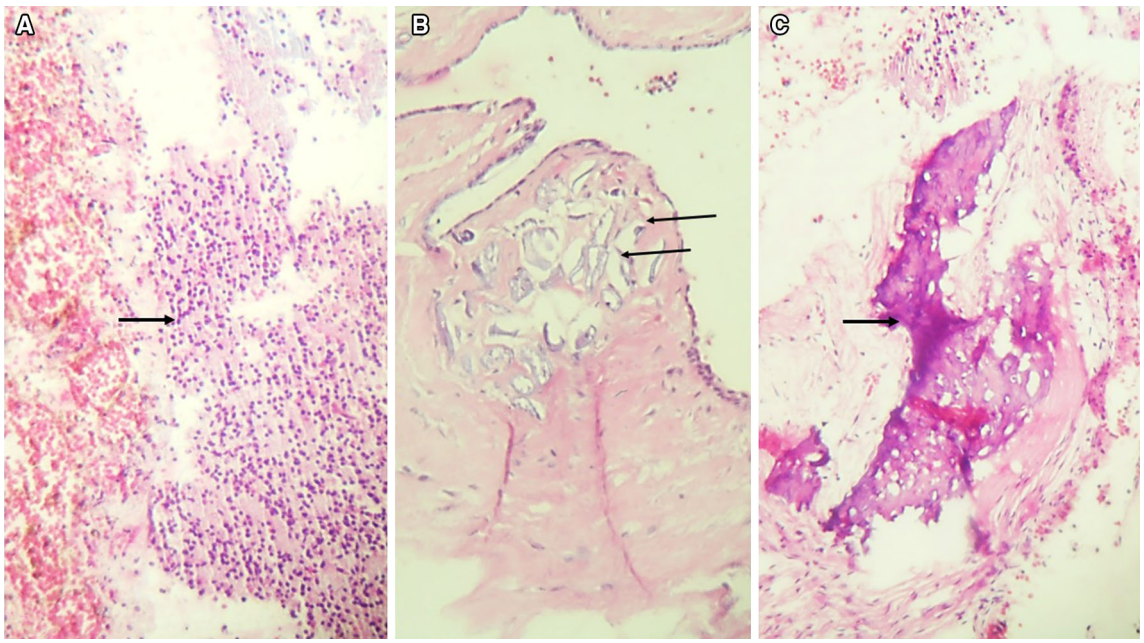

Fig. 4 **a** Section of underlying brain with areas of dilated vascular channels and interstitial hemorrhage. **b** Areas of calcification (arrows) and **c** focal bone formation with underlying brain

acalvaria being compatible with survival but with compromised functionality and need for surgical intervention [12]. In all the cases presented cerebral hemispheres were not seen on gross examination however two of the cases showed presence of immature neural tissue on microscopic examination. The skull defect was covered by amniotic membrane and skin as opposed to just skin in acalvaria and no covering in acrania.

The sequence of acrania, exencephaly and anencephaly is rather well documented which proposes that the primary event is failure of development of flat bones of skull leading to extrusion of brain which is gradually eroded owing to direct exposure to amniotic fluid eventually leading to anencephaly as first described by Wilkings et al. [13].

The sequence is difficult to reconcile with the cases presented here since cranial cavity and contents in all were shielded from amniotic fluid by skin and/or placental membranes however it is quite plausible that 'erosion' of brain was actuated by excessive direct exposure to MMP2 and MMP9 or other related enzymes serving the purpose of parenchymal degradation which are known to be secreted by placenta [14]. There is no published report of direct placental attachment of placenta to the fetal body unaccompanied by defect at the point of attachment.

Facial dysmorphic features and flexion deformities can be attributed to oligohydramnios and tethering of fetal skull as proposed by Higginbottom et al. [15] resulting in constrictive uterine space and shear mechanical forces respectively [15].

Limited fetal movements are also exacerbated by short umbilical cords in all the cases. The same can also facilitate placenta-cranial attachment owing to close physical proximity of head to placenta. Whether amnion rupture as primary event leading to formation of amniotic bands and subsequent entrapment of fetal parts as espoused by Torpin et al. [16] can explain placenta-cranial attachment is a moot question [16].

Similar cases reported by Chandran et al. [4] and Halder [3] have been included in ABS by the authors. Two fetuses with 20 and 28 weeks of gestational age had placenta attached to the head and face along with anencephaly. In addition, there was thoracoabdominoschisis. Umbilical cords were small. The author has not commented on the status of skull bones [3].

Chandran et al. [4] described a 32 weeks fetus with placental attachment to head and absence of flat bones of skull. The brain according to the authors was normal. The fetus died at 6 h post birth. The case was referred to as fetal acalvaria with ABS. There is no comment regarding the length of umbilical cord [4].

In three of the four cases, midline nasal cleft is noticed giving the appearance of minimal bifid nose. Manifestation of bifid nose ranges from minimal grooving of nasal tip to complete bifurcation of osteo-cartilagenous structure [17]. Putative role of incomplete union of maxillary and nasal processes has been proposed that leads to midline facial anomalies including nasal cleft [18]. Failure to fuse might be due to incomplete expression of genes such as BMP 7, SHH, FGF 8, PAX 1 [19].

We have not come across any case of bifid nose in any gestational age apart from the three cases.

All the cases weighed less than expected for the gestational age which might be because of placental insufficiency because of placento-cranial adhesion resulting in compromised functionality of the placenta. Placental insufficiency might also be contributory factor for oligohydramnios. In addition, one of the cases also showed two umbilical cord vessels. Diagnosis of short umbilical cords can be entertained since cord length in all the cases was found to be less than 50% of the expected umbilical cord length.

Therefore in conclusion, we propose that there are grounds for syndromic association between placento-cranial adhesion, facial dysmorphism, low weight for gestational age, anenecephaly, oligohydramnios and short umbilical cord with or without limb malformations/disruptions and other manifestations of amniotic band syndrome.

Further detailed studies are required to conclude whether it has genetic association or it is just stochastic.

Alternatively there may be two separate categories of amniotic band syndrome (ABS) depending on whether the band is attached to the scalp or not. The underlying logic is simple and salient. If the band is attached to the scalp, the fetus invariably dies in utero and if there is no attachment to the scalp the fetus may survive albeit with spectrum of malformations depending on the site of band attachment. Therefore it becomes imperative that all ABS cases must be screened carefully for placento-cranial adhesion and appropriate decision be taken regarding continuation of pregnancy.

Compliance with ethical standards

Conflict of interest There is no conflict of interest. Furthermore the study was not funded by any organization.

Ethical approval Ethical approval was taken from Institutional ethical committee. We in Dr Rajendra Prasad Government Medical College regularly perform fetal autopsies.

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