Abnormal or delayed development of posterior membranous area of the brain: anatomy, ultrasound diagnosis, natural history and outcome of Blake’s pouch cyst in the fetus

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KEYWORDS: Blake’s pouch cyst; cerebellar vermis; fetus; posterior fossa; three-dimensional ultrasound

ABSTRACT

Objectives To review the normal and pathological development of the posterior membranous area (PMA) in the fetal brain, to define sonographic criteria with which to diagnose a Blake’s pouch cyst (BPC) in the fetus and to review the ultrasound features, associations and outcome of 19 cases of BPC seen at our center over the last 5 years.

Methods We conducted a MEDLINE search using the terms ‘Blake’s pouch’, with or without ‘fourth ventricle’, or ‘4th ventricle’, with or without ‘roof’ and identified articles describing normal and/or abnormal development of the PMA, whether or not they were cited in the limited clinical literature on the BPC. A description of the normal and abnormal development of the BPC was derived by collating these articles. The clinical retrospective study included 19 cases of posterior fossa anomalies with a final diagnosis of BPC seen at our institution. The following variables were assessed: referral indication, gestational age at diagnosis, ultrasound and magnetic resonance imaging (MRI) findings, associated anomalies, natural history and pregnancy and neonatal outcome. A transvaginal three-dimensional (3D) ultrasound examination was performed in all cases and 13 cases underwent MRI. To confirm the diagnosis, MRI transfontanellar ultrasound or autopsy were available in all cases.

Results Among the 19 cases reviewed, referral indications were: suspicion of vermian abnormality in 11 (58%) cases and other non-central nervous system anomaly in eight (42%) cases. Sonographically, all cases showed the following three signs: 1) normal anatomy and size of the vermis; 2) mild/moderate anti-clockwise rotation of the vermis; 3) normal size of the cisterna magna. On 3D ultrasound, the upper wall of the cyst was clearly visible in 11/19 cases, with choroid plexuses on the superolateral margin of the cyst roof. On follow-up, the BPC had disappeared by 24–26 gestational weeks in six of the eleven cases which did not undergo termination of pregnancy (TOP), and remained unaltered until birth in the other five cases. There were associated anomalies in eight (42%) cases, in five of which this consisted of or included congenital heart disease. Karyotype was available in 12 cases, two of which were abnormal (both trisomy 21). Regarding pregnancy outcome, there were eight (42%) TOPs, two (10%) neonatal deaths and nine (48%) survivors. One neonate, in whom the BPC had disappeared by the time of birth, had obstructive hydrocephaly confirmed. Another neonate was diagnosed with Down syndrome after birth. Neurodevelopmental outcome was normal at the time of writing in seven of the eight cases (excluding the Down syndrome baby).

Conclusions Based on our analysis of ultrasound features, we propose that for BPC to be diagnosed in a fetus the following three criteria should be fulfilled: 1) normal anatomy and size of the vermis; 2) mild/moderate anti-clockwise rotation of the vermis; 3) normal size of the cisterna magna. Furthermore, we found that BPC can undergo delayed fenestration at 24–26 weeks in more than 50% of cases. Finally, it seems that BPC shows a risk of association with extracardiac anomalies (heart defects in particular) and, to a lesser extent, to trisomy 21. Copyright © 2012 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Blake’s pouch cyst (BPC) has been considered a pathological entity deriving from abnormal development of the posterior membranous area (PMA) of the fetal...
brain\textsuperscript{1–3}. However, while its first description dates back to 1900\textsuperscript{1,2}, there is scant evidence of this anomaly in the literature, with fewer than 10 articles published on the postnatal appearance of BPC in infants and adults\textsuperscript{3–8}. Despite the fact that posterior fossa cystic malformations are one of the most frequently discussed topics in fetal neurology, we found very few series dealing with BPC in the fetus from a diagnostic or clinical standpoint, the only exceptions being a pathology study\textsuperscript{9} and another couple of interesting articles\textsuperscript{10,11}, one of which included an initial diagnostic definition of BPC\textsuperscript{10}. We therefore decided to review the key papers dealing with the normal and abnormal development of the PMA, in order to clarify, as thoroughly as possible, the origin of BPC. Having done so, we aimed to identify sonographically adoptable criteria for its diagnosis and to review our experience with the diagnosis of BPC in the fetus.

Specifically, the objectives of this study were: 1) to review the normal development and pathogenesis of the PMA in the fetal brain, as evident from the literature published to date; 2) to define sonographic criteria with which to diagnose BPC in the fetus; 3) to review the ultrasound features, associated anomalies and outcome of 19 cases of BPC seen at our center over the last 5 years.

METHODS

All articles describing the normal and/or abnormal development of the PMA, whether or not cited in the limited clinical literature on the BPC, were consulted. In particular, a MEDLINE search with the terms ‘Blake’s pouch’, with or without ‘fourth ventricle’ or • ‘4th ventricle’, with or without ‘roof’ was made, and all pertinent articles\textsuperscript{1–3,12–16} reviewed. A description of steps leading to the normal or abnormal development of the posterior fossa and the fourth ventricle was created collating the evidence reported in these articles.

Regarding our retrospective clinical and sonographic study, all 19 cases with posterior fossa anomalies and a final diagnosis of BPC\textsuperscript{•} were retrieved from our database. The following variables were assessed: indication for referral for expert targeted ultrasound\textsuperscript{17}, gestational age at diagnosis, ultrasound findings, magnetic resonance imaging (MRI) findings, associated anomalies, karyotype, natural history and pregnancy and neonatal outcome. In all cases, a transvaginal 3D ultrasound examination had been performed using an E8 (General Electrics, Milwauke, IL, USA) ultrasound machine equipped with a conventional 5–9-MHz or high-frequency 6–12-MHz endovaginal volumetric transducer. The ultrasound criteria adopted to diagnose a BPC were as follows: 1) normal anatomy (including normal appearing fastigium) and size of the vermis (median section of fetal brain); 2) mild to moderate anti-clockwise rotation of the vermis (median section of fetal brain); 3) normal size of the cisterna magna (median and axial sections of fetal brain); 4) evidence of the BPC roof within the cisterna magna (median section of fetal brain), which was observed inconsistently. The nomograms published by Vinals et al.\textsuperscript{18} were used to assess vermic size. Follow-up scans were scheduled at 3-week intervals, until 35 weeks. Fifteen cases also underwent prenatal MRI at diagnosis or on follow-up. To confirm the BPC diagnosis, follow-up transfontanellar sonography or MRI were performed in cases in which the pregnancy reached term. In cases of TOP, only the normal aspect of the vermis on the median section could be assessed, due to the fact that the fluid collection often disappears as soon as the posterior fossa is dissected at necropsy.

RESULTS

Development of the posterior membranous area (PMA) of the fetal brain

Normal PMA development: Blake’s pouch\textsuperscript{1–2,12–16}

Blake’s pouch represents an evagination of the PMA, one of the two components of the rhomboencephalic roof (the other being the anterior membranous area, AMA), which develops at Carnegie stage 14 of embryonic development. These two components, AMA and PMA, are separated by a transverse vascular fold, the plica choroidea, which invaginates into the fourth ventricle and represents the first evidence of the choroid plexus, which eventually appears in the fourth ventricular roof by Carnegie stage 19 (48–51 days postovulation, gestational week 7, crown–rump length, 18–20 mm). In the meantime, the cerebellar vermis starts developing from the rhombic lips of the AMA due to intense cell proliferation, and this leads to the forming choroid plexus being displaced caudally, cranially to the PMA. Until this time, it is assumed that there are no communications between the fourth ventricle and the cisterna magna. In fact, it seems that in most cases the lateral apertures of Luschka appear much later: between the 14\textsuperscript{th} and 17\textsuperscript{th} weeks of gestation, according to some authors\textsuperscript{12–15}, or even not before the 26\textsuperscript{th} week according to others\textsuperscript{16}; in some 20% of cases they do not open at all\textsuperscript{12–15}. The median Magendie foramen seems to open between the 9\textsuperscript{th} and 10\textsuperscript{th} gestational weeks (see below\textsuperscript{1,2,16}). If this is the case, then the only way to explain the presence of cerebrospinal fluid in the subdural spaces is through cavitation. At 7 weeks postovulation (9 gestational weeks), an evagination begins to appear on the roof of the fourth ventricle. This developmental event, which eventually leads to the formation of the Magendie foramen, was described at the beginning of the 20\textsuperscript{th} century for the first time by Blake\textsuperscript{1} and confirmed after a few years by Wilson\textsuperscript{2}. This structure, which is essentially formed of extremely thin ependyma, is referred to by most authors as ‘Blake’s pouch’, after the person who initially described it; similarly, the abnormal or delayed development of this structure is referred to as ‘Blake’s pacy cyst’ (BPC) (or Blake’s pouch persistence)\textsuperscript{1–7,9–11,14}, although others have applied the term ‘Blake’s pouch’ directly to the abnormal development of this structure, when perforation does not occur\textsuperscript{5}. For the purposes of our present study, we will adopt the former terminology.
Blake’s pouch cyst in the fetus

If further development of the posterior fossa is normal, the Blake’s pouch grows and eventually perforates, at the latest by the end of the 10th gestational week, forming the midline aperture of the Magendie foramen. It seems that, at approximately the same time, the cisterna magna, which represents a sub-arachnoid space, develops by cavitation from the primitive meninx. As already mentioned, the Luschka foramina opens much later, at 14–17 weeks; or even later (around 26 weeks); it has been also reported that in one fifth of cases the lateral recesses of the fourth ventricle may fail to perforate.

Abnormal PMA development: Blake’s pouch cyst (BPC)/persistence

If Blake’s pouch does not perforate to form the midline aperture of the Magendie foramen, it enlarges to become a cyst-like structure (BPC) protruding into the cisterna magna and acting as a wedge below the developing cerebellar vermis, which is located just cranial to the unruptured Blake’s pouch. As a result, the vermis is lifted and passively rotated anti-clockwise due to the increasing volume of the unruptured Blake’s pouch, which has in the meantime become a cyst (BPC). In this condition, the vermis itself is unremarkable, since the BPC derives from the PMA and not from the AMA, as confirmed by the fact that its walls contain ependymal cells but not neurons.

The fourth ventricular choroid plexus is displaced within the initial tract of the upper wall of the cyst. The cyst itself is located in the cisterna magna, but it is an expansion of the neuraxis (fourth ventricle) not in contact with the sub-arachnoid space represented by the cisterna magna.

Ultrasound and clinical data

Our study population consisted of 19 cases of BPC. The median gestational age at diagnosis was 22 weeks, with only two cases referred in the third trimester (Table 1). Eleven (58%) cases were referred for suspicion of vermis abnormality; eight (42%) were referred for other, non-central nervous system, anomalies; four of these were referred for fetal echocardiography due to suspicion of congenital heart disease.

With respect to the ultrasound features of BPC, on the median view of the posterior fossa the upper wall of the cyst was clearly visible in 11/19 cases (Figure 1e–1l); on the coronal view, choroid plexus tufts were evident in most cases on the superolateral borders of the cyst roof (Figure 2). The axial transverse view was abnormal in all cases, showing the classic keyhole sign (Figure 2c).

Table 1 Characteristics, associated anomalies and outcome in 19 cases of Blake’s pouch cyst

<table>
<thead>
<tr>
<th>Case</th>
<th>Indication to US</th>
<th>GA (weeks)</th>
<th>Associated anomalies</th>
<th>Karyotype</th>
<th>Fenestration (GA)</th>
<th>Outcome (age at follow-up)</th>
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<tr>
<td>1</td>
<td>Vermian abn.?</td>
<td>24</td>
<td>No</td>
<td>Normal</td>
<td>No*</td>
<td>NND*</td>
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<td>2</td>
<td>Vermian abn.?</td>
<td>22</td>
<td>NF</td>
<td>Normal</td>
<td>—</td>
<td>TOP</td>
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<tr>
<td>3</td>
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<td>18</td>
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<tr>
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<td>Normal†</td>
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<td>A&amp;W (24 months)</td>
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<tr>
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<td>13</td>
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<td>Normal†</td>
<td>Yes (25 weeks)</td>
<td>A&amp;W (1 month)</td>
</tr>
<tr>
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<td>23</td>
<td>Clubfeet + Micronathia</td>
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<td>—</td>
<td>TOP</td>
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<tr>
<td>19</td>
<td>ECA?</td>
<td>19</td>
<td>pAVSD + NF + absent NB</td>
<td>Trisomy 21</td>
<td>—</td>
<td>TOP</td>
</tr>
</tbody>
</table>

*Preterm delivery for placental abruption at 28 weeks; severe cerebral hemorrhage. †On postnatal examination. ‡Dichorionic twin pregnancy; co-twin was alive and well at time of writing; affected neonate weighed 1090 g at birth (38 weeks) and died soon after due to severe IUGR and multiple anomalies. ?, suspected; Abn., abnormality; A&W, alive and well; CHD, congenital heart disease; DISV, double inlet single ventricle; DV, ducus venosus; ECA, extracardiac anomaly; GA, gestational age at diagnosis; IUGR, intrauterine growth restriction; LSVC, left superior vena cava; NA, not available; NB, nasal bone; NF, nuchal fold > 5 mm; NND, neonatal death; PA, pulmonary atresia; pACC, partial agenesis of the corpus callosum; pAVSD, partial atrioventricular septal defect; TOF, tetralogy of Fallot; TOP, termination of pregnancy; US, ultrasound; VSD, ventricular septal defect.

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Figure 1 Cystic anomalies of the posterior fossa, as seen on median view of the fetal head, approached transvaginally from the posterior fontanelle. (a) Normal aspect at 22 weeks of gestation: the vermis is very close to the pons and the fastigium, the fourth ventricle and the cisterna magna are clearly visible. (b) Megacisterna magna at 32 weeks. In this case, the fluid collection in the posterior fossa is rather large, displacing the tentorium (usually this finding is not seen at midtrimester); the position of the vermis is similar to that in (a). (c) Inferior vermian hypoplasia at 21 weeks. The fastigium cannot be recognized, the lowermost portion of the vermis is absent and the vermis itself shows pronounced anti-clockwise rotation. (d) Dandy–Walker malformation at 28 weeks. The tiny hyperechoic vermis is barely visible and is surrounded by a large fluid cystic collection in the posterior fossa; the insertion of the tentorium is displaced cephalad. (e–l) Blake’s pouch cyst in eight fetuses in our series during the second (e,f,g,i,j,k) and third (h,l) trimesters of pregnancy. Note the normal aspect of the vermis, with normal folia, and the variable degree of anti-clockwise rotation (maximum in (f) and (g); minimal in (k)). In all, the vermis appears detached from the pons (compare with (a)). Cases with respect to Table 1 are as follows: (e) Case 15, (f) Case 11, (g) Case 10, (h) Case 4, (i) Case 13, (j) Case 5, (k) Case 9 and (l) Case 6.
Blake’s pouch cyst in the fetus

Figure 2 Blake’s pouch cyst at 22 weeks’ gestation. Three-dimensional ultrasound with multiplanar and volume contrast imaging. In the median view (plane A), the anti-clockwise rotation of the normal vermis (V) and the roof of the Blake’s pouch cyst (arrowhead) are evident. In the corresponding coronal view (plane B), two tufts of choroid plexus (arrowheads) can be seen on the superolateral margins of the cyst wall, just below the vermis (V). The occipital horns of the lateral ventricles are indicated (OH). In the axial plane (plane C), the classic ‘keyhole sign’ (arrow) is seen, with non-visualization of the vermis between the two cerebellar hemispheres. This sign leads to referral for expert opinion and final diagnosis. The lateral walls of the cyst are evident (arrowheads).

Figure 3 Three-dimensional ultrasound with surface rendering at 24 weeks’ gestation. (a) To render the outer surface of the Blake’s pouch cyst, the region of interest box should be in the posterior fossa, with the green bar slightly curved on the upper surface of the cerebellum. In this way, it is possible to demonstrate the digit-like expansion of the cyst protruding into the cisterna magna (arrows), just below the cerebellar vermis (V). (b) In comparison, in a normal posterior fossa, the same technique shows only the area corresponding to the empty cisterna magna (CM), with no evidence of any cystic structure below the vermis (V). In both images, arrowheads identify the occipital bone.

Occipital bone in the majority of cases. In most cases, it was noted that the echogenicity of the fluid content of the cisterna magna was hypechoic, with tiny strands, and not completely translucent as it was within the Blake’s cyst (Figure 4).

On ultrasound follow-up, the BPC had disappeared, with the vermis returning to its normal position, in six of the ten cases which reached term (excluding Case 1 (Table 1), delivered at 28 weeks due to placental abruption), likely due to late fenestration (Figure 5).
the five of these cases which had been followed up at our center, this event took place between 24 and 26 weeks of gestation; in the remaining case (Case 16), we could only gather postnatal information (MRI) after initial diagnosis at 23 weeks. In Case 6, the neonate (a dichorionic twin) died soon after birth; at the time of demise, the BPC was still in place according to transfontanellar ultrasound examination. In the other three cases (Cases 4, 10 and 15) the moderate anti-clockwise rotation of the vermis persisted until neonatal follow-up.

MRI was performed in 15/19 cases at diagnosis or follow-up, but in no case did it add anything to the ultrasound diagnosis; in the five cases in which it was performed on follow-up, after sonographic evidence of late fenestration of the BPC, it confirmed the normal position and anatomy of the vermis and the absence of cysts in the posterior fossa.

Associated major anomalies were present in eight (42%) cases, five of these consisting of or including congenital heart disease (Table 1). The karyotype was normal in 12 cases (five from amniocentesis and seven postnatal observations) and abnormal in normal to both trisomy 21; it was not performed in the remaining five cases, all of which underwent TOP.

With respect to pregnancy outcome (Table 1), there were eight (42%) TOPs, two (10%) neonatal deaths, and the remaining nine (48%) survived. One neonate (Case 16, Table 1) had obstructive hydrocephaly confirmed (the BPC had disappeared) and is being followed up closely; another (Case 13) was diagnosed with Down syndrome after birth. Neurodevelopmental outcome was normal in eight of nine cases (with the exception of the Down syndrome baby), according to the pediatricians following them, at a mean follow-up time of 16 (range, 1–42) months.

DISCUSSION

From the initial description of BPC by Blake in 19001, publications on this anomaly have been scant in the neonatal1–8 and prenatal9–11 literature and no criteria have been set for its diagnosis in the fetus. We propose that for a fetal BPC to be diagnosed, the following three criteria should be observed, on the median view of the posterior fossa: 1) normal anatomy (including normal appearing fastigium) and size of the vermis; 2) mild to moderate anti-clockwise rotation of the vermis; 3) normal size of the cisterna magna. There may also be visualization of the BPC roof within the cisterna magna (Figures 1–3) and a more translucent echogenicity of the cyst content in comparison with the cisterna magna fluid (Figure 4). The normal size of the cisterna magna can also be confirmed on the axial view.

Our criteria, a slightly expanded version of those proposed by Malinger et al.10, would allow in most cases a differential diagnosis of BPC vs Dandy–Walker Malformation (DVM), inferior vermis hypoplasia (IVH) and megacisterna magna (MCM)3,19–22. Both DVM and IVH represent abnormal development of the AMA. DVM is characterized by moderately severe/severe hypoplasia and anti-clockwise rotation of the vermis, an elevated insertion of the tentorium, and a large fluid collection in the cisterna magna communicating with the fourth ventricle10,19 (Figure 1d). IVH is characterized by moderate to severe hypoplasia of the inferior vermis portion, moderate/moderately severe anti-clockwise rotation of the vermis and moderate increase of the fluid collection in the posterior fossa communicating with the fourth ventricle19 (Figure 1c). This represents the most challenging differential diagnosis for BPC, because it is based only on the normal vs abnormal aspect/size of the inferior vermis, both demonstrating moderate anti-clockwise rotation of the vermis and moderate increase of the fluid collection in the posterior fossa. Furthermore, it is possible to observe a cystic expansion of the fourth ventricle in the cisterna magna in some cases of IVH. In our experience, prenatal MRI cannot differentiate between these two in most cases, especially if performed at 20–23 weeks of gestation. MCM (Figure 1b), like BPC, is an abnormality of the lateral ventricles.

Figure 4 Three-dimensional ultrasound with multiplanar and volume contrast imaging at 22 weeks’ gestation: median (a) and coronal (b) views. Using a high frequency (6–12 MHz) transvaginal transducer, the fluid content of the Blake’s pouch cyst (BPC) appears completely sonolucent, whereas the contents of the cisterna magna (arrows) appear grainy in texture, with thin vertical strands. OH, occipital horns of the lateral ventricles.
Figure 5 Blake’s pouch cyst (BPC) in the fetus can undergo delayed fenestration (a,b) or persist until birth (c,d); median views, showing BPC (•) and its roof (arrow) when visible, and rotation of the vermis (V). (a) BPC at 20 weeks of gestation; the classic aspect of BPC is seen, with an anatomically normal vermis showing anti-clockwise rotation. The BPC and its roof are visible. (b) The same case at 28 weeks; the vermis is no longer rotated anti-clockwise, having returned to its normal position close to the pons. A normal fourth ventricle is visible (which was not before), and there is no longer any sign of the former BPC. (c) Another case of BPC detected at 22 weeks of gestation. As in (a), there is an anatomically normal vermis showing anti-clockwise rotation and the BPC and its roof are visible. (d) At 33 weeks, the situation remains the same, with anti-clockwise rotation of the vermis. A similar appearance was observed on magnetic resonance imaging performed 1 month postnatally.

PMA. It is characterized by a wide collection of fluid in the posterior fossa freely communicating with the arachnoid space and the fourth ventricle, with a vermis of normal size and showing no rotation.

It is interesting to note that the fluid content of the BPC showed a more translucent echogenicity than did that of the cisterna magna (Figure 4). Considering that the cisterna magna apparently forms from cavitation of the meninges and that the Luschka apertures are probably still absent (they may open as late as 26 weeks16), it can be speculated that the different echogenicity may reflect the different origins of the fluid content: the BPC fluid content was completely anechoic, consisting of cerebrospinal fluid produced from the choroid plexuses; the cisterna magna fluid content was less translucent, this structure representing only a hollow space, deriving from cavitation, which would eventually fill with cerebrospinal fluid once the Luschka apertures and the Magendie foramen become patent. The fact that under normal conditions the fluid content of the cisterna magna is completely anechoic, with the exception of the thin strands of tissue thought to represent remnants of the Blake’s pouch11, may support this hypothesis.

Another interesting consideration regards the timing of the opening of the Luschka apertures: according to some authors12–15, this event occurs around 14–17 weeks.
However, according to Brocklehurst they become patent at around 26 weeks, precisely coinciding with the time of disappearance of the BPC in the six cases of our series in which this event occurred (Table 1). If the theory that the Luschka foramina do not open before 26 weeks is correct, then it may be speculated that an explanation for the disappearance of the BPC other than its late fenestration might be deflation, as a result of the opening of the Luschka apertures which would release the formerly elevated intraventricular pressure, with consequent disappearance of the ballooning. However, in this case, the Magendie foramen might remain closed in cases in which the BPC disappears by 26 weeks.

Regarding our analysis of the natural history of BPC, from our limited data it seems that in roughly half (6/10) of the cases the cyst eventually fenestrated (or disappeared), and that this event occurred at 24–26 weeks of gestation (Table 1). The long-term outcome of cases in which BPC does not perforate by the time of birth will probably depend on the patency and size of the Luschka apertures. Tortori-Donati et al.1 claim that in individuals with BPC there is always tetraventricular hydrocephaly due to absence of the Magendie foramen. However, it may be speculated that in some cases the presence of the Luschka apertures ensures a precarious equilibrium which may become symptomatic only later in life, leading to hydrocephaly, or may remain asymptomatic.

Another important issue to discuss is the relatively high association rate with major anomalies. In our series, 11/19 cases were isolated and, of the eight associated with other major anomalies, five included a heart defect (Table 1). In addition, 10% (2/19) of all cases and 14% (2/14) of those with a known karyotype had Down syndrome. The series is of course too limited as to allow us to draw any conclusions about whether the recognition of a BPC should prompt fetal echocardiography or karyotyping. However, in our study the usual bias of fetal series – the fact that cases associated with major abnormalities are preferentially referred for expert opinion – does not hold. In fact, more than 50% of the cases were isolated and had been referred only because the transcerebellar view, which is part of the second-trimester anomaly scan checklist, was abnormal, showing the classic keyhole sign (Figure 2c).

Our final comment regards the neurological outcome. BPC derives from the PMA and, as such, does not contain neurons. This is why neurodevelopmental outcome is generally normal in neonates and infants with BPC. Our data provide further support for this concept: the outcome was normal in all nine cases with isolated BPC that survived the early neonatal period. Although, admittedly, normal neurological outcome was ascertained only by contacting the family pediatrician who followed them, nonetheless a major neurodevelopmental delay would certainly have been detected.

An important limitation of this study is that it is very difficult to confirm the presence of BPC at necropsy. In most cases undergoing TOP, it could only be confirmed without doubt that the anatomy of the cerebellar vermis was normal, because dissection of the posterior fossa caused the BPC to empty and the vermis to return to its normal position. In these circumstances, postmortem MRI may help.

In conclusion, we have described the pathogenesis of the BPC, collating evidence from different embryological1,12–16 and pediatric neuroradiological13–7 studies. In addition, we have proposed criteria with which to diagnose a BPC in the fetus, also showing that the cyst may undergo delayed fenestration at 24–26 weeks of gestation. Finally, we have reported on the apparently increased risk of associated anomalies, including congenital heart disease and trisomy 21. Further fetal series are needed to confirm the concepts expressed in this study. However, it should be considered that this, to the best of our knowledge, represents the first analysis of fetal BPC, from diagnosis to natural history, associations and outcome.

REFERENCES


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Ultrasound Obstet Gynecol 2012; 39: 000–000.


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Queries to Author:

AQ1 Please check that all affiliations are correct and complete.

AQ2 Note I have edited your rewording somewhat.

AQ3 Table 1 footnote: ‘gestational age’ changed to ‘gestational age at diagnosis’. I also added ‘?’ to every row in the second column and defined it here as ‘suspected’ – is this ok? Alternatively, we could remove all the question marks and add something to indicate suspicion to the column header.

AQ4 I’ve added ‘fourth ventricle’ and kept ‘4th ventricle’ as these can bring up different results in MEDLINE

AQ5 My query about ‘the last five years’ referred to the 19 cases seen at your institution, not the literature search, sorry. I’ve kept the query:
Query: Should the last 5 years be mentioned here or is this a result, not a retrieval criterion? Note it’s not mentioned in the results either.

AQ6 I’ve added ‘lifted and’ here in response to your reply – is that ok?

AQ7 Fig 1 – I’m not sure the wording of the opening sentence is ideal – let’s see what Sarah suggests at proof stage.

AQ8 Sorry please could you double check – in the Abstract you said it should be seven of eight because of the excluded DS baby, while here you said we should change 7/8 to 8/9 and follow-up time from 15 to 16. Which is correct? Here it sounds like the ‘exception of the DS baby’ means that this is the ninth case that was not normal. Your comment regarding the abstract made it sound more like you excluded the DS baby from the denominator.

AQ9 I’ve reworded slightly to ‘(they may open as late as 26 weeks16)’ – is this ok? However, I’m not sure about the use of ‘probably [still absent] – you cite only one paper that says 26 weeks – the others seem to suggest this occurs much earlier, around 14–17 weeks. Note Fig 4 is 22 weeks

AQ10 Do we need to mention the 28-week NND being excluded or will this be obvious to readers?

AQ11 SARAH – ‘steady state’ changed to ‘equilibrium’ here – agree??

AQ12 How about ‘apparently increased’?

AQ13 Please could you supply all author names for ref 14?
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