Enigma of raised intracranial pressure in patients with complex craniosynostosis: the role of abnormal intracranial venous drainage


Department of Neuroradiology and Craniofacial Surgery, Great Ormond Street Hospital for Children, London, United Kingdom; and Unite De Neuroradiologic Vasculaire, Diagnostique et Therapeutique, Hopital Bicetre, Kremlin Bicetre, France

Object. In this study the authors investigated whether patterns of intracranial venous drainage in children with complex craniosynostosis associated with raised intracranial pressure (ICP) were abnormal and, thus, could support the theory that venous hypertension is a major contributor to raised ICP that can lead to impaired visual function or even blindness in these patients.

Methods. The authors analyzed the anatomy of intracranial venous drainage as demonstrated in the results of 24 angiography studies obtained in 23 patients, all of whom had either a craniosynostosis-related syndrome (18 patients) or a nonsyndromic multisutural synostosis (five patients). Twenty-one patients had experienced raised ICP (in 19 patients diagnosis was based on invasive ICP monitoring and in two patients on clinical grounds alone) 1 to 6 weeks before undergoing angiography. Of the two remaining patients (both with Apert syndrome) whose ICP monitoring was normal immediately before angiography, each had undergone two previous cranial vault expansion procedures.

On results of 18 angiography studies a 51 to 99% stenosis or no flow at all could be observed in the sigmoid–jugular sinus complex either bilaterally (11 patients) or unilaterally (seven patients). In 11 of these patients a florid collateral circulation through the stylomastoid emissary venous plexus was also seen. Two angiography studies were performed in one patient with Crouzon syndrome. A comparison of the two studies demonstrated a progression of the abnormal venous anatomy in that case. The authors found no obvious correlation between each patient’s baseline ICP and the degree of abnormality of their venous anatomy, as judged on the basis of a venous-phase angiography severity score.

Conclusions. Based on their findings, the authors assert that in children with complex forms of craniosynostosis in whom other factors, such as hydrocephalus, are absent, abnormalities of venous drainage that particularly affect the sigmoid–jugular sinus complex produce a state of venous hypertension that, in turn, is responsible for the majority of cases of raised ICP. The incidence of these changes is unknown, but an analysis of the ages of the children in this study indicated that the period of particular vulnerability to the effects of venous hypertension lasts until the affected child is approximately 6 years old. After that age the collateral venous drainage through the stylomastoid plexus will likely become sufficient to allow ICP to normalize.

KEY WORDS • craniosynostosis • intracranial pressure • hypertension

Raised ICP may complicate all forms of craniosynostosis. It rarely occurs when only one suture is involved, becomes more prevalent as more sutures become involved, and is most common in syndromic cases—particularly in patients with Crouzon or Pfeiffer syndrome. Several factors are known to contribute to raised ICP in patients with craniosynostosis, including craniocerebral disproportion, hydrocephalus, the secondary effects of respiratory obstruction, and venous hypertension. Although in rare but well-recognized instances it can cause papilledema leading to optic atrophy, reduced visual acuity, and even blindness, the significance of increased ICP in most children with syndromic craniosynostosis remains unknown. Nevertheless, in cases in which ICP monitoring may record plateau pressures as high as 40 to 50 mm Hg, it is clearly an important factor to consider when making decisions concerning treatment.

The practical importance of anomalous intracranial venous drainage became clear to us in a dramatic fashion in an 8-year-old girl who had cloverleaf skull deformity and Pfeiffer syndrome. Having made a bicoronal incision in this patient, at the start of an operation designed to expand her skull posteriorly (to allow subsequent reduction of temporal bossing to be achieved without raising ICP), we...
encountered an enormous transosseous venous channel emerging in the midline of the parietooccipital region. Bleeding from this channel was easily controlled using bone wax, but within a short time the child’s ICP rose sharply to levels that necessitated termination of the operation. All attempts at reducing this patient’s ICP were unsuccessful and she died shortly thereafter. At autopsy it became apparent that most of the normal pathways for intracranial venous drainage were severely narrowed and that the transosseous venous channel we had occluded during the operation had been the major pathway for venous drainage in this patient. (A detailed account of this patient can be found in a previously published article.22)

Following that case, we performed MR angiography in several patients with syndromic craniosynostosis to assess their patterns of intracranial venous drainage. However, we decided that this method provided detail insufficient for us to complete our analysis and we switched to DS angiography instead.

The purpose of the present study was to analyze intracranial venous drainage in patients with complex craniosynostosis that is complicated by raised ICP. In the majority of cases, the presence of raised ICP had been confirmed by ICP monitoring, and DS angiography was performed to determine whether anomalies of intracranial venous drainage could be a contributing factor.

**Clinical Material and Methods**

**Patient Population**

The patient population consisted of 23 children—13 boys and 10 girls—ranging in age at the time of angiography from 3 months to 8 years and 10 months (Table 1). Patient ages were not evenly distributed throughout this range; however, 18 of the 24 angiography studies were obtained in children aged 36 months or younger.

**Monitoring of ICP**

All patients in this study were referred to the Supraregional Craniofacial Unit at Great Ormond Street Hospital for Children in London. All but two patients had undergone ICP monitoring, which was performed using the Camino system (Camino NeuroCare, Inc., San Diego, CA). Indications for ICP monitoring were as follows: 1) clinical symptoms of raised ICP (headaches, papilledema, or others); 2) no palpable open fontanelle through which ICP could be assessed; and 3) syndromic craniosynostosis or,
Venous anatomy in craniosynostosis and raised ICP

in nonsyndromic cases, the involvement of more than one skull-vault suture.

Children with single-suture synostosis do not routinely undergo ICP monitoring in our unit unless they have been referred with a clinical problem that could be attributed to raised ICP (such as a developmental delay or a learning difficulty) and there are accompanying clinical or radiological indicators of raised ICP, such as papilledema or a beaten-copper appearance on skull radiographs.

Intracranial pressure monitoring was conducted over a 24-hour period to include recordings obtained while the patient slept.

**Angiography Sessions**

Patients were selected to undergo cerebral angiography for the following reasons: 1) ICP monitoring or clinical examination had revealed raised ICP; and/or 2) the patient was being considered for skull-vault surgery (usually performed to relieve raised ICP), which could become compromised by venous hypertension and the presence of anomalous transosseous venous channels (as occurred in the case we described earlier). All angiography sessions in this series were performed within 1 to 6 weeks after ICP monitoring.

Selective four-vessel DS angiography was performed while the patient was in a state of general anesthesia. The sessions were conducted predominantly by one operator (W.J.T.). Detailed images of the anatomy during the venous phase were obtained in lateral and frontal views, and an assessment was made of both the intracranial and extracranial veins and the venous sinuses. Appearances of veins that were specifically recorded included the following: 1) the presence or absence of cavernous sinus capture and any transosseous venous drainage; 2) the degree of any angiographically demonstrated stenosis of the transverse sinuses, sigmoid sinuses, jugular bulbs and segments (defined as the intrasosseous portion of the jugular vein), and the sagittal sinus; 3) filling of the marginal and occipital sinuses; and 4) the presence and degree of any apparent collateral drainage through the stylomastoid emissary veins.

**Severity Scoring**

To identify possible correlations between angiographically demonstrated abnormalities that were observed and other factors such as the patient’s baseline ICP and disease diagnosis, a severity score was calculated on the basis of each angiogram. Because the majority of observed abnormalities affected the sigmoid–jugular sinus complex and the presence of what was interpreted as a collateral venous circulation through the stylomastoid plexus of veins, the severity score was derived from data recorded in Table 2. For the sinuses, no stenosis was assigned a score of 0, stenosis of 1 to 50% of normal diameter (S+) a score of 1, stenosis of 51 to 99% of normal diameter (S++) a score of 2, and no visualization a score of 3. For the stylomastoid collateral veins, prominent collateral veins (+) were assigned a score of 1 and florid collateral vein circulation (+++) was assigned a score of 2. The score from each side was added together to reach the final score for each patient.

**Results**

Of the 23 children in the study 18 had phenotypical features of a particular eponymous syndrome (four Crouzon, four Pfeiffer, seven Apert, two Saethre–Chotzen, and one Antley–Bixler). The remaining five children suffered from multisutural synostoses that were not associated with a named syndrome.

The mean age (in months) at angiography of the children in each diagnostic category was as follows: Crouzon syndrome 18.4, Pfeiffer syndrome 13, Apert syndrome 49.6, Saethre–Chotzen syndrome 29, Antley–Bixler syndrome 11, and multisutural synostosis 34. One child (Case 5) underwent two angiographic examinations—at 6 months and 16 months of age (see later description).

In this series angiography sessions were performed between January 1995 and February 1999, with the majority performed from 1995 through 1997. These sessions represent all angiography studies performed in patients in the craniofacial unit during this period. During this period a total of 76 patients with diagnoses of complex craniosynostosis (syndromic or multisutural) were first referred to our craniofacial unit. The total number of children with craniofacial disorders undergoing ICP monitoring during this period was 116.

No patients had active hydrocephalus (defined as progressive ventricular dilation for the purpose of this study), and airway obstruction, when present, had already been treated using measures such as relief of choanal stenosis or atresia, nasal airway prongs, continuous positive airway pressure, or, rarely, tracheostomy. This is not to claim, however, that all patients were free from some degree of airway obstruction—particularly those manifested during sleep.

Phenotypical diagnoses in the children, their ages at the time of the angiography study, and the results of their ICP monitoring (including both baseline pressures and the height of any plateaus maintained for more than 20 minutes and repeated at least twice during the monitoring period) are given in Table 1. Also included in this table are details of any surgical procedure previously performed in each child that might have had an effect on their ICP. Five patients had undergone one such operation and three had undergone two.

Two children with Apert syndrome (Cases 7 and 17) had normal ICPs before they underwent angiography, although they had each undergone two surgical procedures (at 7 and 52 months of age and 3 and 9 months, respectively) that may have reduced their ICPs. In Case 7 the previous operations were preceded by ICP monitoring, which had confirmed the diagnosis of raised ICP. In Case 17 the patient had not previously been examined in a specialist craniofacial unit and there was no record of any preoperative ICP monitoring. In these two cases angiograms and ICP recordings had been obtained because skull x-ray films had indicated the presence of large vascular channels in the bones of the skull vault and it was thought that these channels might compromise the reconstructive surgeries that had been planned.

Detailed venous-phase angiography results are listed in Table 2 and illustrated in Figs. 1–5; however, they may be summarized as follows. If, for the purposes of these examinations, the sigmoid sinus, the jugular segment (the intra-
osseous portion of the jugular sinus), and the jugular bulb on each side are considered as one unit, we either observed a significant degree of stenosis (51–99% reduction in normal diameter) or were unable to record flow at all on 18 of the 24 angiography studies that we reviewed (lack of unilateral flow on seven angiograms and lack of bilateral flow on 11 angiograms). A lesser degree of narrowing (1–50% reduction in normal diameter) was noted in an additional four studies.

Of the 18 angiography studies in which there was a serious lack of flow, there was evidence of florid collateral vein circulation (Table 2 and Fig. 5) in the region of the stylo mastoid emissary veins on one or both sides in 11 children (Table 2). Among these 17 patients (18 angiography studies) there appeared to be no greater propensity toward angiographic evidence of absence of bilateral cavernous sinus capture (nine instances). Angiographic evidence of filling of the marginal and occipital sinuses was an unusual finding; it was found in only three children. Nevertheless, some degree of transosseous venous drainage was seen in the majority of patients (18 of 24 angiography studies).

The mean age at angiography of those children whom the diagnosis of raised ICP had been made on clinical ICP recordings (excluding those two patients in whom the diagnosis of raised ICP had been made on clinical grounds alone); however, our analysis of the results revealed no significant linear relationship—either straight ($r^2 = 0.0068$) or curved ($r^2 = 0.167$)—between them (Fig. 6).

We plotted these scores against each patient’s base line ICP recordings (excluding those two patients in whom the diagnosis of raised ICP had been made on clinical grounds alone); however, our analysis of the results revealed no significant linear relationship—either straight ($r^2 = 0.0068$) or curved ($r^2 = 0.167$)—between them (Fig. 6).

The two children who had Apert syndrome and normal ICP (Cases 7 and 17) were among the three oldest patients in the study. The third child was 106 months of age at the time of angiography and had bicornal synostosis that was associated with other dysmorphic features as well as.

---

**Table 2**

Details of intracranial venous drainage in children with raised ICP and craniosynostosis*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Rt</th>
<th>Lt</th>
<th>Rt</th>
<th>Lt</th>
<th>Rt</th>
<th>Lt</th>
<th>Rt</th>
<th>Lt</th>
<th>Rt</th>
<th>Lt</th>
<th>Rt</th>
<th>Lt</th>
<th>Rt</th>
<th>Lt</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>yes</td>
<td>yes</td>
<td>NS</td>
<td>NS</td>
<td>S+</td>
<td>NS</td>
<td>NV</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>yes</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>S++</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>3</td>
<td>yes</td>
<td>no</td>
<td>NV</td>
<td>NS</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>4</td>
<td>no</td>
<td>no</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>5</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NV</td>
<td>NS</td>
<td>S+</td>
<td>NS</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>no</td>
<td>no</td>
<td>NV</td>
<td>NV</td>
<td>S++</td>
<td>S++</td>
<td>S+</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>7</td>
<td>no</td>
<td>yes</td>
<td>NV</td>
<td>NS</td>
<td>NV</td>
<td>S+</td>
<td>NV</td>
<td>S+</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>8</td>
<td>no</td>
<td>no</td>
<td>S+</td>
<td>S+</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>9</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>S++</td>
<td>S++</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>10</td>
<td>no</td>
<td>yes</td>
<td>NS</td>
<td>NS</td>
<td>S+</td>
<td>S++</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>11</td>
<td>yes</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>S+</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>no</td>
<td>no</td>
<td>S++</td>
<td>S++</td>
<td>S++</td>
<td>S++</td>
<td>S+</td>
<td>S+</td>
<td>S++</td>
<td>S++</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>13</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>S+</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>14</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>15</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>S+</td>
<td>NS</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>16</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>S++</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>17</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>18</td>
<td>no</td>
<td>no</td>
<td>S++</td>
<td>S++</td>
<td>S++</td>
<td>S++</td>
<td>S+</td>
<td>S+</td>
<td>S++</td>
<td>S++</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>19</td>
<td>no</td>
<td>yes</td>
<td>NS</td>
<td>NS</td>
<td>S++</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>20</td>
<td>yes</td>
<td>yes</td>
<td>NS</td>
<td>NS</td>
<td>S+</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>21</td>
<td>yes</td>
<td>no</td>
<td>NV</td>
<td>S+</td>
<td>S++</td>
<td>S++</td>
<td>S+</td>
<td>S+</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>22</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NV</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>23</td>
<td>no</td>
<td>no</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

* NS = no stenosis, normal appearance; NV = not visualized; S+ = stenosis of 1 to 50% of normal diameter; S++ = stenosis of 51 to 99% of normal diameter; – = normal; + = prominent collateral veins; ++ = florid collateral vein circulation.
small stature, for which no syndromic diagnosis had yet been made. That patient later experienced a recurrence of raised ICP, despite having undergone a vault expansion procedure, which followed the ICP monitoring reported here. Her ICP was successfully treated by personnel in the Department of Paediatric Neurology, who viewed the episode as a case of benign (idiopathic) intracranial hypertension. In this patient the angiographic severity score was low and since her treatment for benign intracranial hypertension, her ICP has remained normal.

**Discussion**

Identification of the causes of raised ICP and its treatment form an important part of the treatment of children with craniosynostosis, particularly those with syndromic forms. There are several factors that can contribute to a possible rise in ICP in these patients, including craniocerebral disproportion, hydrocephalus, and respiratory obstruction. Craniocerebral disproportion was traditionally thought to be the most common cause of raised ICP in patients with craniosynostosis; however, in several reports, authors have highlighted the lack of a predictable correlation between intracranial volume and ICP.

The elimination of these various causes, however, leaves us with no satisfactory explanation for raised ICP in the majority of affected children and, thus, no obvious cause-related (as opposed to empirically defined) form of treatment, assuming that treatment is necessary.

It is our contention that, particularly in children with the syndromic forms of craniosynostosis, when other factors such as hydrocephalus have been eliminated, the most common cause of raised ICP is venous hypertension, resulting from the various patterns of anomalous venous drainage that the angiography studies in this series have revealed.

Any conclusions about the functional significance of variations of vascular anatomy based on angiography findings alone must be treated with caution, because angiograms only reveal details commensurate with the amount of contrast agent in the vessel being investigated at each point in time during the examination. Note also that no control examinations were performed in this series such as those in studies of children with complex cranio-synostosis in whom ICP monitoring revealed no evidence of a rise in pressure or in whom raised ICP had not been suspected clinically.

Although it is commonly observed on angiography studies that there is a dominant pattern of transverse sinus blood flow for drainage of the superior sagittal sinus, we only observed unilateral nonfilling of a transverse sinus in four cases and nonvisualization of both transverse sinuses in another. Although it might be imprudent, therefore, to label asymmetries of the transverse sinuses on their own as abnormal, we believe that the presence of severe stenosis or actual nonvisualization of the sigmoid sinus–jugal bulb and segment complex, either unilaterally or bilaterally, on 18 of the 24 angiography studies should be taken as evidence of abnormal intracranial venous drainage, particularly if there is also evidence of a collateral venous circulation. In examining these 18 angiography studies we observed florid stymastoid collateral veins in 11 of them, as well as on four of six angiography studies obtained in patients in whom there was a mild or no abnormality affecting the sigmoid–jugular sinus complex (all of these patients, except the one in Case 7, had raised ICP at the time of angiography). An examination of angiograms obtained in the six patients in whom there was a mild or no abnormality, demonstrated a florid stymastoid venous plexus bilaterally in three patients. In the remaining three patients, one (Case 23) demonstrated florid collateral vein circulation on the right side (where a pulsatile venous swelling complete with a palpable thrill could be felt behind and below her right mastoid process) and prominent collateral veins on the left side. Another patient exhibited prominent collateral veins bilaterally and the last demonstrated prominent collateral veins only unilaterally, indicating some degree of functional interference with the normal pattern of intracranial venous drainage, even in those cases in which the sigmoid–jugular sinus complex appeared less affected. A similar finding in another case of craniosynostosis complicated by raised ICP and venous sinus stenosis has also been described by Kurosu, et al.
the right transverse sinus, sigmoid sinus, and jugular bulb. 

Cavernous sinus capture is a normal phenomenon that develops in the 1st year of life and represents an additional route for cerebral venous drainage. The absence of cavernous sinus capture on an angiogram could, therefore, be suspected of exacerbating any venous hypertension associated with venous outlet occlusion at the skull base. In our series we recorded its absence bilaterally in 14 patients, of whom nine had severe unilateral or bilateral sigmoid sinus–jugular bulb and segment stenosis or nonvisualization. We also failed to find any obvious connection between the presence or absence of the marginal and occipital sinuses and the presence of raised ICP. These sinuses are present in neonates and their persistence in patients with venous outlet obstruction, particularly in older patients, could represent a possible pathway for the reduction of intracranial venous hypertension.

Transosseous venous channels in the occipital bone are normal and may cause troublesome bleeding during posterior fossa surgery (for treatment of tumors, for example), particularly in the presence of raised ICP. In the majority of the angiography studies we examined, we observed some degree of transosseous venous drainage, although in all of them the superior sagittal sinus itself was patent and had a normal diameter. Of the six other studies, not only was no transosseous drainage observed but there was also no obvious abnormality affecting the sigmoid–jugular sinus complex. On none of the angiograms we examined, did we observe any channels large enough to match that of the child who died of acute venous hypertension, which had complicated the occlusion of her large transosseous venous channel during surgery.

We do, however, submit that the presence (unilaterally or bilaterally) of either a 51 to 99% stenosis or nonvisualization of the sigmoid sinus–jugular bulb and segment complex in 18 of our 24 angiography studies, particularly when this is associated with a florid stylomastoid emissary vein collateral circulation, provides strong evidence for the presence of venous hypertension caused by the various patterns of anomalous venous drainage, which we have demonstrated to be the major contributor to raised ICP recorded in these children. We also submit that the recurrence of raised ICP in association with an increasing degree of venous outlet obstruction observed in the patient in Case 5, who underwent two angiography sessions, provides further evidence for this hypothesis.

In a recent study in which MR venography was used, the authors, acknowledging that MR venography is used to determine flow rather than vessel diameter, reported a similar incidence of both venous obstruction and a prominent venous (postcondylar) collateral circulation in 17 children with complex craniosynostosis: 12 of 17 and 11 of 17 patients, respectively. Although ICP was not measured, in 10 children shunts had been inserted for hydrocephalus and in nine of 12 patients with venous outflow obstruction there was herniation of the cerebellar tonsils, indications that their ICP might well have been raised at some stage.

There is a well-recognized incidence of herniation of the cerebellar tonsils in children with craniofacial syndromes; this has been attributed to the small size of the posterior fossa in these patients as well as to raised ICP. However, it can also be provoked by venous hypertention within the posterior fossa and can be relieved when the venous hypertension has been relieved. Unfortunately, in our study an insufficient number of children had undergone MR studies to allow us to comment further on its significance here.

Venous hypertension has also been invoked as a contributor to hydrocephalus, which itself may be responsible for raising ICP in cases of craniosynostosis. This hypothesis would explain those cases in which, following a vault expansion procedure, ventriculomegaly progresses to a level necessitating the insertion of a CSF shunt or a ventriculostomy. Presumably this occurs because the original state of venous hypertension remains high after the operation, whereas the restricting effects of the skull vault have been removed.

Venous hypertension (large emissary veins and intracranial venous hypertension) and acanthosis nigricans have been reported in three patients with Crouzon syndrome harboring the Ala391Glu mutation in exon 10 of fibroblast growth factor receptor 3. An insufficient number of our patients underwent analysis of their genetic structure for those results to be discussed in detail here; however, note that no child had acanthosis nigricans.

Venous hypertension, at least as indicated by alterations in the dynamics of flow (as assessed by transcranial color-coded duplex ultrasonography) in the superior sagittal sinus, has also been identified in cases of craniosynostosis.
Venous anatomy in craniosynostosis and raised ICP

Fig. 5. Case 5.  Left: Initial angiogram revealing nonopacification of the left sigmoid sinus and severe stenosis (S++) of the left jugular bulb and segment. Right: Angiogram obtained during the second angiography session demonstrating progression on the right side to mild narrowing (S+) of the jugular bulb and a florid stylomastoid venous plexus, and progression on the left side to non-opacification of the jugular segment.

We could palpate a large and tense varix behind the right ear. Our findings, therefore, should be interpreted as demonstrating the abnormalities of intracranial venous drainage, which we contend are responsible for raised ICP in the majority of children with complex craniosynostosis in whom no other cause can be found, rather than describing the frequency with which they occur in these children (with or without raised ICP).

We attempted to determine whether there was a relationship between the degree of abnormality of intracranial venous drainage (as defined by our severity score) and the degree to which each child’s ICP was raised. Despite the measures we had taken to overcome upper-airway obstruction, some element of obstruction often persisted. We therefore used the baseline ICP for comparison purposes, theorizing that the effects of any residual airway obstruction would be most obvious during plateaus of raised ICP rather than on the baseline pressure—a relatively constantly acting force such as venous hypertension being more likely to elevate all components of the ICP. Our attempt, however, failed to identify a significant correlation and we do not have sufficient contemporary respiratory data for these patients with which to make a more direct comparison. In this context it is interesting that in one of two patients who had normal ICP (Case 7) preceding her angiography session (albeit not previously—she was one of two children in whom two operations had been required in the past for a confirmed rise in ICP) the angiography severity score was one of the highest in the series—evidence that the correlation between the degree of vascular abnormality and ICP is not a simple one. Another patient with normal ICP before angiography (Case 17) also had Apert syndrome and had undergone two vault-expanding operations during infancy. In contrast with the patient in Case 7, the angiography severity score in the patient in Case 17 was one of the lowest in the series; however, she had not previously been examined in a specialist craniofacial unit and, unfortunately we have no information about her ICP before those operations were performed.
What then is the connection, if any, between the severity of the abnormalities of venous drainage we have demonstrated and the phenotypical diagnosis? Our numbers are too small to draw statistically reliable conclusions; however, note that the children with Crouzon or Pfeiffer syndrome, whose genotypes may overlap,13 had higher severity scores (11.06 and 11, respectively) than those with Apert (severity score 7.9) or Saethre–Chotzen (severity score 6) syndrome, neither of which are as frequently associated with clinically significant raised ICP as Crouzon and Pfeiffer syndromes.22 Our patients who were nonsyndromic and had multiple suture synostosis, however, also had scores in the higher range (severity score 11.2). In this context note that the mean age at angiography for children with Crouzon or Pfeiffer syndromes (18.4 and 13 months, respectively) was also younger than that for the seven children with Apert syndrome (49.6 months—although this drops to 30.8 months if the two children with normal ICP before angiography are excluded), indicating that children with syndromes associated with more severe abnormalities of venous drainage are also more likely to present earlier with symptoms and signs of raised ICP. The mean age of those 11 children with the most severe venous abnormalities (20.4 months) was also younger than those in whom there was no evidence of stenosis at all (54 months). Eight of 23 children had undergone at least one previous operation with the potential to lower raised ICP when they were 13 months of age or younger. Siddiqi and colleagues15 reported an incidence of six of 107 children with syndromic craniosynostosis seen over a 6-year period who required a second vault expansion procedure for raised ICP. The age range in these children was 3 to 32 months for their first operation (five of the six children were ≤ 10 months) and 24 to 61 months for their second (five children were > 32 months). In their paper the authors implied that those first operations had been performed as part of a general management policy (“to treat the underlying craniofacial dysostosis”) rather than selectively in patients with raised ICP. They did not record the ages at which the 101 patients who did not later experience raised ICP first underwent surgery nor did they detail the follow-up findings that led to the detection of raised ICP in the six patients (three of whom were treated at institutions other than the authors’). However, it would not be unreasonable, on the basis of the age range of their patients and ours (with the exception of the one in Case 13, all of our cases of raised ICP were recorded in children aged < 53 months, 18 of whom were aged < 36 months) to assert that raised ICP as a complication of complex craniosynostosis usually manifests itself before the age of 3 years and is unusual in children over 6 years of age—the latter being the age limit first reported by Renier and colleagues in 1982.21 If venous hypertension is indeed the cause of the rise in ICP, then it is likely to be the cumulative opening of collateral venous channels (such as those of the stylomastoid plexus) that is responsible for this natural history.

Conclusions

Raised ICP complicating complex forms of craniosynostosis is—in the absence of progressive ventriculomegaly (which may itself be exacerbated by venous hypertension), craniofacial disproportion, and upper airway obstruction—likely to be due to venous hypertension associated with a variety of patterns of anomalous venous drainage. These involve stenosis or complete monopacification of, in particular, the sigmoid–jugular sinus complex on one or both sides, often in association with what appear to be collateral venous channels through the stylomastoid plexus of veins. The degree to which the ICP is raised and the severity of the abnormality of venous drainage that we propose is responsible for it is not a linear one, indicating that the relationship between the two is complex. It would appear likely, however, that the problem of raised ICP complicating cases of complex craniosynostosis is one that tends to manifest itself before the age of 3 years and is unusual after the age of 6 years.

Acknowledgments

We express our thanks to Dr. Gerardine Quehehebeur and Mr. Guirish Solanki for their assistance during the preparation of this paper.

References


Manuscript received May 23, 2000. Accepted in final form October 23, 2000.

This work was performed by personnel at the Great Ormond Street Hospital for Children NHS Trust who received a proportion of its funding from the NHS executive. The views expressed are those of the authors and not necessarily those of the NHS executive.

Address reprint requests to: Richard Hayward, F.R.C.S., Department of Neuroradiology and Craniofacial Surgery, Great Ormond Street Hospital for Children, Great Ormond Street, London WC1N 3JH, United Kingdom. email: richard.hayward@gosh-tr.nthames.nhs.uk.