The role of venous sinus outflow obstruction in pediatric idiopathic intracranial hypertension

Clinical article

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Objective. The authors examined the role of venous sinus obstruction in the etiology of idiopathic intracranial hypertension (IIH) by reviewing more than 200 MR venograms performed in suspected cases of IIH.

Methods. Individual MR venograms performed in cases of suspected IIH at the Children’s Hospital at Westmead in Sydney, Australia, were reviewed. The authors excluded cases in which an intervention was performed before the scan or a structural cause for venous obstruction was identified. Cases with confirmed hydrocephalus were also excluded.

For each of the 145 remaining scans, the authors completed a detailed review on a slice-by-slice basis of the 2D source images used to compile the rendered 3D MR venogram. The anatomical configuration of the dural venous sinuses and any areas of decreased flow in circulation were then noted. Where possible, they correlated their radiological findings with evidence of raised intracranial pressure based on LP opening pressures. They also reviewed a control group of 50 MR venograms.

Results. Seventy-six (52%) of 145 scans showed evidence of venous obstruction in the dominant-side circulation. Substantial nonphysiological collateral circulation was seen in 68% of cases with dominant-sided obstruction, suggesting a process of recanalization. In contrast, in the absence of dominant-sided obstruction, collateral circulation was uncommon.

In 27 cases, CSF opening pressure measurements were available. In 20 cases the opening pressures were in excess of 20 cm H₂O. Of those, 17 demonstrated evidence of dominant-sided venous outflow obstruction. Among those cases, the median opening pressure was 34 cm H₂O.

Dominant-sided venous outflow obstruction was seen in only 2 of 50 MR venograms in the control group. Furthermore, evidence of collateral circulation was also uncommon in the control group. There was a highly statistically significant difference between rates of dominant-sided venous obstruction in the suspected IIH and control groups (p ≤ 0.001).

Conclusions. A majority of patients presenting for investigation of suspected IIH demonstrated evidence of dominant-sided venous obstruction on MR venogram. In addition there was a high correlation between elevated CSF opening pressures and dominant-sided venous sinus obstruction. This correlation was further supported by evidence of collateral recanalization in patients with elevated CSF pressures and dominant-sided venous obstruction. A control group of 50 MR venograms indicated that dominant-sided venous outflow obstruction is an unlikely incidental finding, and a highly statistically significant difference was found between rates of obstruction in the suspected IIH and control groups.

Key Words • idiopathic intracranial hypertension • venous sinus obstruction • magnetic resonance venogram • cerebrospinal fluid opening pressure

Idiopathic intracranial hypertension is a well-described condition of unknown etiology. The disease presents with raised intracranial pressure, which can cause headache, nausea, pulsatile tinnitus, transient visual disturbance, and in severe cases, permanent visual loss.

Abbreviations used in this paper: ICD = International Classification of Diseases; IIH = idiopathic intracranial hypertension; LP = lumbar puncture.
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tions is 1 in 100,000.14 Idiopathic intracranial hypertension typically presents in overweight women of childbearing age and is associated with a history of recent weight gain. Within the pediatric population, while it may occur in any child older than 1 year, there is a clear predominance of the condition in adolescents.13 Although the association with female sex seen in the adult population is also present in pediatric cases of IIH, a statistical association with overweight and obesity has not been established in the pediatric population.4,8

Venous sinus outflow obstruction is a recognized cause of IIH through impaired CSF absorption. Its prominence in the pathophysiology of IIH has been highlighted in several prospective adult studies.3,10 Reports of successful treatment of IIH through venous sinus stent placement, including 2 pediatric cases, have demonstrated the importance of recognizing venous sinus outflow obstruction in IIH.9,13

We aimed to investigate the role of venous sinus pathology in pediatric cases of IIH. We retrospectively reviewed MR time-of-flight venograms conducted in cases in which the differential diagnosis included IIH, and we examined these studies for evidence of venous outflow obstruction.

Methods

We accessed a database of MR venograms performed at the Children’s Hospital at Westmead between May 1998 and February 2011. We received approval from the Human Research Ethics Committee of the Children’s Hospital at Westmead. We selected MR venograms that were performed in the context of investigations for suspected IIH, as defined by the ICD coding associated with each patient record. This yielded more than 500 potential MR venograms for review. In order to include a broad spectrum of potential cases of IIH, no review of the clinical record was made prior to radiological assessment, and a confirmed diagnosis of IIH was not required for consideration in this review. Rather, for a case to be included in our review, the database used to identify the MR venograms need only note via ICD code that a diagnosis of IIH was considered.

We excluded any cases involving an obvious structural abnormality or anatomical cause for outflow obstruction. Thus, cases involving documented arteriovenous malformations or a history of meningitis, trauma, achondroplasia, or congenital or neoplastic conditions were excluded. We also excluded cases in which previous surgery, including CSF shunt placement, had been performed. As a result, the total number of MR venograms selected for detailed assessment was reduced to 202, each unique to an individual patient.

For each patient, we calculated the Evans ratio and head circumference. The Evans ratio was calculated as the ratio of the maximum width of the frontal horns to the maximum width of the inner table of the cranium,2 with a ratio greater than 0.3 indicating hydrocephalus.1 Venograms with confirmed hydrocephalus by Evans ratio calculation were excluded on the basis of the modified Dandy criteria, reducing the number of studies for detailed review to 145.

For each MR venogram we performed a detailed review on a slice-by-slice basis of the 2D source images used to compile the rendered 3D MR venogram. We assessed the caliber and signal intensity of the sagittal, straight, transverse, and sigmoid sinuses, along with the jugular bulbs. We noted either right- or left-sided dominance based on the communication of venous flow from the sagittal to the transverse sinuses. We also examined the patency of the deep venous sinuses as well as the presence or absence of occipital sinuses and other substantial collateral drainage.

The absence of a flow void was considered primary evidence of venous sinus thrombus, while the presence of altered signal intensity indicated slow or turbulent flow in the sinus.12

We then reviewed the associated clinical record for all 145 patients to assess whether an LP had been performed at or around the time of the original MR venogram. Where data were available, we made note of the CSF composition and recorded the documented LP opening pressures. In 27 cases, contemporaneous CSF opening pressures had been recorded in the notes.

To calibrate the significance of our radiological findings, we also reviewed 50 MR venograms performed in age-matched controls in cases in which IIH was not a suspected diagnosis. Again, these studies were selected by reference to the associated ICD code. An identical slice-by-slice review of the 2D source images was performed, and notation was made of any outflow obstruction or abnormal venous anatomy.

Results

Suspected IIH Group

Among the 145 cases of suspected IIH selected for detailed review, the median patient age at the time of imaging was 12.4 years (range 0.6–17.1 years). This median age concurs with the understanding that pediatric IIH predominantly occurs in adolescent children.8

Anatomical analysis confirmed the findings of prior studies in this area.12 The sagittal sinus drained predominantly to the right transverse sinus in 89 (61%) of 145 cases and to the left transverse sinus in 50 cases (34%), and in 6 cases (4%) there was relatively equal flow to the right and left transverse sinuses.

The straight sinus drained to the right transverse sinus in 73 (50%) of 145 cases, to the left in 61 (42%), and equally to each side in 10 (7%).

When dominant-sided outflow obstruction was demonstrated, we found a common pattern of left-sided pathology, typically with multiple points of absent flow. The most common configuration involved obstruction in the distal portion of the left transverse sinus, although other segments of the venous sinus were also commonly involved. Where dominant-sided obstruction was seen we found a pattern of frequent collateral circulation. In the absence of dominant-sided outflow obstruction, however, collateral circulation was uncommon.

Overall, 76 (52%) of 145 MR venograms demonstrated venous outflow obstruction in the dominant-side circulation. In 31 (41%) of 76 cases there was a single site obstruction. In 14 cases (19%), obstructed venous drainage involved the contralateral side.

Venous outflow obstruction typically presents in overweight women of childbearing age and is associated with a history of recent weight gain. Within the pediatric population, while it may occur in any child older than 1 year, there is a clear predominance of the condition in adolescents.13 Although the association with female sex seen in the adult population is also present in pediatric cases of IIH, a statistical association with overweight and obesity has not been established in the pediatric population.4,8

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Overall, 76 (52%) of 145 MR venograms demonstrated venous outflow obstruction in the dominant-side circulation. In 31 (41%) of 76 cases there was a single site obstruction. In 14 cases (19%), obstructed venous drainage involved the contralateral side.
of obstruction, while in 45 (59%) of 76 cases there were multiple sites of obstruction. Among the 76 cases with obstruction in the dominant-side circulation, we identified 150 discrete obstructions to venous outflow. Of those obstructions 87 (58%) of 150 occurred on the left, although the difference between left- and right-sided distribution was not statistically significant ($p = 0.176$).

Diminished venous outflow was most commonly identified in the transverse sinuses. Of the 150 discrete obstructions, 74 (49%) occurred at some point along the transverse sinuses. Conversely, 46 (31%) obstructions were seen in the sigmoid sinuses, and 30 (20%) involved the jugular bulbs. The distal left transverse sinus was the single most common point of venous obstruction, with 18 (12%) of 150 discrete points of diminished outflow.

We identified a large number of venograms in which the presence of significant collateral circulation suggested recanalization secondary to outflow pathology. Of 76 cases with evidence of venous outflow obstruction in the dominant-side circulation, 52 (68%) demonstrated the presence of nonphysiological collateral circulation. In contrast, we did not see elevated rates of collateral circulation in venograms without evidence of dominant-sided venous sinus outflow obstruction. Only an additional 3 venogram studies without dominant-sided outflow obstruction demonstrated evidence of nonphysiological collateral circulation.

Figure 1 demonstrates a time-of-flight MR venogram of a dominant left transverse sinus with an occlusion at the junction between the distal transverse and sigmoid sinuses. A concomitant atresic right transverse sinus and substantial collateral circulation are also evident. Conversely, Fig. 2 demonstrates a time-of-flight MR venogram of a dominant right transverse sinus with stenoses at its proximal and distal ends. Again, a concomitant atresic left transverse sinus and substantial collateral circulation are demonstrated.

Radiological findings were then correlated with data from contemporaneous LP. Data from these LPs are presented in Table 1. In total, 34 cases had associated LP data. In 27 of these cases, CSF opening pressure measurements were available.

In 20 cases the opening pressure was in excess of 20 cm H$_2$O. Of those, 17 demonstrated evidence of dominant-sided venous outflow obstruction. The median opening pressure in that group was 34 cm H$_2$O, and the highest recorded pressure was 65 cm H$_2$O. Of the 17 cases with elevated opening pressure on LP and dominant-sided venous obstruction, 15 demonstrated evidence of nonphysiological collateral circulation. In 3 cases, elevated LP opening pressures were recorded in the absence of dominant-sided venous outflow obstruction.

Among the 17 cases with dominant-sided venous obstruction and raised opening pressure on LP, the side of dominance was evenly split between left and right (8 each), with one study demonstrating equal flow into the left and right transverse sinuses.

In contrast, in the 7 cases in which the opening pressure was less than 20 cm H$_2$O, all MR venograms demonstrated right-side dominant circulation. As raised CSF pressures are required to meet the terms of the modified Dandy criteria, these studies were excluded from further analysis. Among the 34 LPs reviewed for this study, elevated CSF protein was seen in only one instance. That
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TABLE 1: Summary of available LP data*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>total no. of contemporaneous LPs</td>
<td>34/145 (23)</td>
</tr>
<tr>
<td>no. of LPs w/ opening pressure recorded</td>
<td>27/34 (79)</td>
</tr>
<tr>
<td>no. of LPs w/ opening pressure &gt;20 cm H_2O</td>
<td>20/27 (74)</td>
</tr>
<tr>
<td>no. of LPs w/ opening pressure &gt;20 cm H_2O &amp; dominant-sided venous sinus obstruction</td>
<td>17/20 (85)</td>
</tr>
<tr>
<td>median opening pressure</td>
<td>34 cm H_2O</td>
</tr>
<tr>
<td>average opening pressure</td>
<td>31 cm H_2O</td>
</tr>
<tr>
<td>max opening pressure</td>
<td>65 cm H_2O</td>
</tr>
</tbody>
</table>

* Values in parentheses represent percentages.

case did not involve elevated CSF opening pressure and was similarly excluded from further analysis on the basis of the modified Dandy criteria.

Control Group

Among the 50 cases used for the age-matched control group, the median patient age at the time of imaging was 13.2 years (range 6.9–17.2 years).

The sagittal sinus drained to the right transverse sinus in 35 (70%) of 50 cases and to the left transverse sinus in 10 (20%), and in 5 cases (10%) there was relatively equal flow to the right and left transverse sinuses. The straight sinus drained to the right transverse sinus in 25 (50%) cases, to the left in 22 (44%), and equally to each side in 3 (6%).

Dominant-sided outflow obstruction was demonstrated in 2 (4%) of 50 cases; in one case the left transverse sinus was considered dominant, and in the other case outflow from the superior sagittal sinus was considered equal, with codominant transverse sinuses. Both cases involved obstruction in the distal portion of the left transverse sinus.

In contrast to the 145 scans performed in suspected cases of IIH, the sigmoid sinus and jugular bulbs were largely spared from pathology in the control group. Diminished venous outflow in the sigmoid sinuses was seen in 3 (6%) of the 50 cases, with 1 case involving the right sigmoid sinus and 2 cases involving the left sigmoid sinus. In 2 cases (4%) diminished outflow was seen in the jugular bulbs, divided evenly between the right and left side. No sigmoid or jugular occlusions occurred on the dominant side of the circulation.

Collateral circulation was seen in 7 cases (14%), with an even distribution between right, left, and bilateral evidence of collateral circulation.

Data comparing the rates of obstruction in the suspected IIH and control groups are presented in Table 2. A highly statistically significant difference was seen between rates of dominant-sided venous outflow obstruction in the suspected IIH and control groups (p ≤ 0.001).

Discussion

The etiology of IIH in adult and pediatric patients remains an area of ongoing investigation. Cranial venous sinus obstruction is a recognized cause of raised CSF pressure in some cases of IIH.10 While controversy still surrounds whether venous sinus stenosis is a primary or secondary phenomenon, there is no doubt that cranial venous outflow obstruction can cause raised CSF pressure and symptoms consistent with IIH. This is particularly true in children in whom venous outflow obstruction due to thrombosis associated with mastoiditis can cause a clinical picture similar to that of IIH.7

Although the prevalence of venous sinus stenosis has

TABLE 2: Evidence of venous sinus obstruction*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Suspected Cases of IIH</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>total no. of venograms for review</td>
<td>145</td>
<td>50</td>
</tr>
<tr>
<td>age (yrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>range</td>
<td>0.6–17.1</td>
<td>6.9–17.2</td>
</tr>
<tr>
<td>median</td>
<td>12.4</td>
<td>13.2</td>
</tr>
<tr>
<td>no. of cases w/ obstruction in dominant-sided circulation</td>
<td>76 (52)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>no. of cases w/ 1 obstruction</td>
<td>31 (41)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>no. of cases w/ multiple obstructions</td>
<td>45 (59)</td>
<td>0</td>
</tr>
<tr>
<td>total no. of obstructions</td>
<td>150</td>
<td>2</td>
</tr>
<tr>
<td>no. of lt-sided obstructions</td>
<td>87/150 (58)</td>
<td>2/2 (100)</td>
</tr>
<tr>
<td>no. of rt-sided obstructions</td>
<td>63/150 (42)</td>
<td>0</td>
</tr>
<tr>
<td>no. of obstructions in TVS</td>
<td>74/150 (49)</td>
<td>2/2 (100)</td>
</tr>
<tr>
<td>no. of obstructions in sigmoid sinus</td>
<td>46/150 (31)</td>
<td>0</td>
</tr>
<tr>
<td>no. of obstructions in jugular bulb</td>
<td>30/150 (20)</td>
<td>0</td>
</tr>
<tr>
<td>no. of cases w/ evidence of collateral circulation among all cases</td>
<td>55/145 (38)</td>
<td>7/50 (14)</td>
</tr>
<tr>
<td>among cases w/ dominant-sided obstruction</td>
<td>52/76 (68)</td>
<td>1/2 (50)</td>
</tr>
</tbody>
</table>

* Values in parentheses represent percentages. The most common site of obstruction was the distal left transverse venous sinus (18 [12%] of 150 cases). Abbreviation: TVS = transverse venous sinus.
been documented in adult cases of IIH, its role of venous outflow obstruction in pediatric IIH has not been investigated. Hence, we undertook this retrospective study to examine whether venous sinus stenosis may also be a factor in pediatric IIH. This is important, as pediatric cases have a different profile in relation to body habitus and obesity compared with adult cases and therefore may have a different etiology. In addition, there are 2 documented cases of pediatric IIH in which venous sinus stenosis was identified and successfully treated by venous sinus stent placement.10

In this study of pediatric patients we have demonstrated that just over 50% of MR venograms showed dominant-sided venous outflow obstruction. More importantly, of those with confirmed IIH by elevated CSF opening pressure, 85% had venous outflow obstruction involving the dominant-side venous sinus. In comparison, those with CSF pressure of less than 20 cm H2O, only 33% had venous sinus obstruction.

In addition, there was a strong correlation between venous obstruction and the presence of nonphysiological collateral circulation in venograms with dominant-sided obstruction. The close correlation between high LP opening pressures and significant collateral circulation suggests that a process of recanalization takes place in settings of elevated CSF pressures, secondary to dural venous outflow obstruction.

Our radiological findings are supported by the results from a control group of 50 MR venograms. These studies were performed in diverse cases in which IIH was not a suspected diagnosis. We found that evidence of dominant-sided venous outflow obstruction was rare in these cases, with potentially relevant pathology seen in only 2 of 50 studies. This result was highly statistically significant. Moreover, collateral circulation was similarly an uncommon finding in cases with normal venous outflow, lending weight to our theory that recanalization takes place in settings of venous obstruction and resulting high CSF pressures.

In adult IIH, venous sinus obstruction tends to be concentrated in the distal end of the transverse sinus. In this study, however, venous sinus obstruction was distributed more widely, with stenosis apparent in the sigmoid sinus and jugular bulb in half of the cases. The reasons for this are unclear but most likely reflect the more heterogeneous nature of pediatric IIH.

There are several limitations to the current study. It is retrospective in nature, and the MR venograms examined were performed using evolving techniques and equipment, with both 1.5- and 3-T magnets. Certain subjects were anesthetized at the time of imaging, which altered cerebral perfusion and dilation. In addition, the MR venograms assessed in this study were selected on the basis of ICD coding rather than clinical diagnoses. We believe this approach allowed us to capture otherwise missed incidences of radiological abnormalities in the context of potential diagnoses of IIH. Finally, there is a relative paucity of CSF pressure data, although the LP findings do support the conclusion that venous sinus pathology is prominent in pediatric IIH. While the paucity of LP data is regrettable, it seems to reflect an increasing hesitancy on the part of clinicians to perform this procedure in pediatric settings. This spares patients from a somewhat traumatic and invasive procedure, but it comes at the cost of potentially diagnostic data.

Conclusions

We found that a majority of patients presenting for investigation of suspected IIH demonstrated evidence of dominant-sided venous obstruction on MR venogram. In addition, we found a high correlation between elevated CSF opening pressures and dominant-sided venous sinus obstruction. This correlation was further supported by the evidence of collateral recanalization in patients with elevated CSF pressures and dominant-sided venous obstruction. We also found that the distribution in terms of the site of the venous outflow obstruction appears to be wider in pediatric cases as compared with adults. Our results were supported by a control group of 50 MR venograms performed in settings other than suspected IIH. Evidence of dominant-sided venous outflow obstruction as an incidental finding was very uncommon. A highly statistically significant difference was found between rates of obstruction in the suspected IIH and control groups.

Accordingly, we conclude that venous sinus outflow obstruction has a role in the pathophysiology of pediatric IIH and may have an etiological role in some cases. Further studies of pediatric IIH are still required to better elucidate the role of venous outflow obstruction in pathophysiology and etiology of this condition.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: Dwyer, Prelog. Analysis and interpretation of data: Dwyer, Owler. Drafting the article: Dwyer. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Dwyer. Study supervision: Owler.

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