Neonatal Developmental Venous Anomalies: Clinicoradiologic Characterization and Follow-Up


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ABSTRACT

BACKGROUND AND PURPOSE: Although developmental venous anomalies have been frequently studied in adults and occasionally in children, data regarding these entities are scarce in neonates. We aimed to characterize clinical and neuroimaging features of neonatal developmental venous anomalies and to evaluate any association between MR imaging abnormalities in their drainage territory and corresponding angioarchitectural features.

MATERIALS AND METHODS: We reviewed parenchymal abnormalities and angioarchitectural features of 41 neonates with developmental venous anomalies (20 males; mean corrected age, 39.9 weeks) selected through a radiology report text search from 2135 neonates who underwent brain MR imaging between 2008 and 2019. Fetal and longitudinal MR images were also reviewed. Neurologic outcomes were collected. Statistics were performed using χ², Fisher exact, Mann-Whitney U, or t tests corrected for multiple comparisons.

RESULTS: Developmental venous anomalies were detected in 1.9% of neonatal scans. These were complicated by parenchymal/ventricular abnormalities in 15/41 cases (36.6%), improving at last follow-up in 8/10 (80%), with normal neurologic outcome in 9/14 cases. Developmental venous anomalies were usually considered benign anatomic variants. However, they represent areas of venous fragility that can become symptomatic through diverse pathomechanisms. Indeed, DVAs associated brain abnormalities are frequently depicted, including...

Developmental venous anomalies (DVAs) are the most frequently diagnosed intracranial vascular malformations, often encountered as incidental neuroimaging findings. On MR imaging, DVAs are recognized on postcontrast T1WI as radially oriented veins with a “caput medusae” pattern converging into 1 (or rarely more) dilated venous collector. These features may also be detected on precontrast MR images, especially if T2*weighted sequences such as high-resolution SWI are included in the protocol. In addition, DVAs may be occasionally recognized in utero using fetal MR imaging.

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All procedures performed in the studies involving human participants were in accordance with the ethical standards of 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was waived by the institutional research committee.

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but-not limited-to sporadic cerebral cavernous malformations (CCMs). Moreover, a higher prevalence of DVAs has been described in patients with different pathologies and/or genetic conditions.

Although DVAs are widely described and characterized in adults, they remain under-reported in the pediatric population. Indeed, there are noticeably fewer studies focusing exclusively on DVAs in this age group, especially in the neonatal period. In particular, the largest case series of neonatal DVAs described so far included 14 neonates, mostly detected using ultrasound during routine scanning for other reasons, with limited information on the prevalence and perinatal characteristics of these vascular abnormalities, including complications and longitudinal evolution. Moreover, additional data on neonatal and fetal DVAs would be of great interest because there is an ongoing debate regarding their congenital or postnatal etiology.

In this study, we aimed to describe the pre- and postnatal appearance of DVAs and associated brain abnormalities in a relatively large single-center group of neonates, providing information on their imaging and clinical follow-up. In addition, we tested a possible association between parenchymal and ventricular abnormalities in the drainage territory of neonatal DVAs and their angioarchitectural features.

**MATERIALS AND METHODS**

**Population**

After institutional review board approval, 1 pediatric neuroradiologist (M.S.) searched in the radiology information system of a tertiary pediatric institution (IRCCS Istituto Giannina Gaslini, Genoa, Italy) for reports of brain MR imaging studies performed in subjects up to 28 days of corrected age containing the term “developmental venous anomaly,” during a 12-year period (January 2008 to December 2019). During this period, 2135 neonates underwent brain MR imaging. All procedures performed in the studies involving human participants were in accordance with the ethical standards of 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was waived by the institutional research committee.

**MR Imaging Technique and Image Analysis**

Neonates were scanned on 1.5T or 3T MR imaging units with different imaging protocols, all including at least T1WI, T2WI, DWI, and T2*WI (either gradient recalled-echo or SWI) sequences. Gadolinium-based contrast agents were injected only if clinically indicated. Neonates were fed before the MR imaging examination to achieve spontaneous sleep, with mild oral midazolam sedation (0.1 mg/kg) in case of head movements, and were breathing spontaneously during the examination.

Brain MR imaging studies were reviewed by 2 pediatric neuroradiologists (M.S. and A.F.G. with 10 and 5 years of experience, respectively), who confirmed the diagnosis and evaluated the prevalence and perinatal characteristics of these vascular abnormalities, including complications and longitudinal evolution. Moreover, additional data on neonatal and fetal DVAs would be of great interest because there is an ongoing debate regarding their congenital or postnatal etiology.

In this study, we aimed to describe the pre- and postnatal appearance of DVAs and associated brain abnormalities in a relatively large single-center group of neonates, providing information on their imaging and clinical follow-up. In addition, we tested a possible association between parenchymal and ventricular abnormalities in the drainage territory of neonatal DVAs and their angioarchitectural features.

**RESULTS**

**Neonatal Imaging Features**

Forty-one neonates with DVAs were retrieved by a report search and confirmed by image review (20 males; mean corrected age at first MR imaging, 39.9 weeks; range, 33–44 weeks), corresponding to a real-world MR imaging DVA detection of 1.9% (41/2135) in a tertiary pediatric center. Neonates were preterm in 46.3% of cases (n = 19). Brain MR imaging was obtained on a 3T scanner in 22 cases (53.7%). SWI and postcontrast T1WI were acquired in 38 (92.7%) and 7 cases (17.1%), respectively.

**Clinical Data**

Data on sex, pregnancy history, gestational age at birth, cause of prematurity, type of delivery, Apgar scores, corrected age at first MR imaging, and imaging indications were obtained from the electronic clinical records. For neonates with c-DVAs, additional data including treatment, age at last clinical assessment, and neurologic outcome (graded as normal, mild, moderate, or severe impairment) were also registered.

**Statistical Analysis**

Quantitative data were presented as median and interquartile range, and categoric data, as frequencies and percentages. Fisher exact, χ², and independent samples Student t tests were used to compare clinical characteristics between patient groups with c-DVAs and u-DVAs. Fisher exact, χ², and Mann-Whitney U tests were used to compare angioarchitectural characteristics and associated parenchymal/ventricular abnormalities between individual complicated and uncomplicated DVAs. All results were corrected for multiple-comparison testing using the Bonferroni correction method. Statistical significance was reached if the P value was <0.05/k, where k indicates the number of tests, resulting in thresholds for statistical significance of P < .0045 and .0083 for patient and DVA levels of comparison, respectively. Statistical analyses were performed using SPSS Statistics software, Version 24.0 (IBM).
Fifteen patients (36.6%) had at least 1 DVA (range, 1–6) associated with parenchymal abnormalities and/or CSF obstruction (c-DVA group) (Table 1 and Figs 1–3). Two of these neonates were affected by cerebrofacial venous metamer syndrome (CVMS). The On-line Table summarizes clinicoradiologic associations. In particular, at-term birth (P = .02), higher gestational age (P = .05), and imaging indications other than “preterm screening” (P = .005) were significantly more frequent in the c-DVA group but did not reach statistical significance after adjusting for multiple comparisons. Moreover, multiple DVAs as well as additional craniofacial vascular lesions were also more common in patients with c-DVAs (P = .002 and P = .02, respectively), but only multiplicity remained significant after multiple-comparison correction.

Neonatal seizures likely attributable to a symptomatic DVA were detected in 2/15 patients with c-DVAs. One additional patient with a c-DVA developed probable DVA-related seizures at 11 months. A direct causal relationship between the DVA and neonatal seizures was not identified in 2 patients with u-DVA presenting with this symptom.

Overall, 58 DVAs were identified, comprising multiple DVAs in 9 cases. DVA location and angioarchitecture features are presented in Table 1. Multiple collectors and larger collector calibers were significantly more frequent in complicated DVAs (P = .008 and P < .001, respectively), even after adjusting for multiple comparisons.

DSA was performed in 4 patients with c-DVAs. No signs of arteriovenous shunting through the DVA with or without an associated classic nidus were identified, while a subject with CVMS had an intraorbital AVF.

**Fetal MR Imaging and Postnatal cUS**

Fetal MR imaging was performed in 11 patients (26.8%), of whom 6 belonged to the c-DVA group (21 examinations in total, 1–4 studies per patient, acquired between 20 and 38 gestational weeks). Retrospective analysis of single-shot FSE, b = 0, and/or T2*WI identified a DVA and/or an abnormally enlarged draining pathway in 3 fetuses (27.3%). In another case, a DVA-associated cerebellar hemorrhage was detected but precluded the identification of the subjacent DVA. Of the remaining 7 fetuses in whom the DVA was not visible, 3 presented with craniofacial vascular lesions.

Postnatal cUS was available in 36 neonates: In 3 cases, the DVA was suspected before the MR imaging examination due to the presence of a parenchymal linear hyperechogenic focus.

**Management and Clinicoradiologic Outcome of Neonates with c-DVAs**

Of 15 neonates with c-DVAs, 13 were conservatively managed, with a wait-and-see approach in 10 cases, anticoagulation treatment in 2, and antiepileptic drugs in 1. Endoscopic third ventriculostomy was performed in 1 neonate with DVA-related obstructive

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**Table 1: Location and angioarchitecture characteristics of developmental venous anomalies**

<table>
<thead>
<tr>
<th>Location (%)</th>
<th>Total (n = 58)</th>
<th>Complicated DVA (n = 21) (36.2%)</th>
<th>Uncomplicated DVA (n = 37) (63.1%)</th>
<th>P Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal</td>
<td>24 (41.4)</td>
<td>9 (42.9)</td>
<td>15 (40.5)</td>
<td>.44</td>
</tr>
<tr>
<td>Parieto-occipital</td>
<td>16 (27.7)</td>
<td>6 (28.6)</td>
<td>10 (27)</td>
<td></td>
</tr>
<tr>
<td>Temporal</td>
<td>8 (13.8)</td>
<td>3 (14.3)</td>
<td>5 (13.5)</td>
<td></td>
</tr>
<tr>
<td>Basal ganglia/thalami</td>
<td>5 (8.6)</td>
<td>0 (0)</td>
<td>5 (13.5)</td>
<td></td>
</tr>
<tr>
<td>Brain stem</td>
<td>2 (3.4)</td>
<td>1 (4.8)</td>
<td>1 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Cerebellum</td>
<td>3 (5.2)</td>
<td>2 (9.5)</td>
<td>1 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Infratentorial (%)</td>
<td>5 (8.6)</td>
<td>3 (14.3)</td>
<td>2 (5.4)</td>
<td>.34</td>
</tr>
<tr>
<td>Right side (%)</td>
<td>33 (56.9)</td>
<td>13 (61.9)</td>
<td>20 (54.1)</td>
<td>.59</td>
</tr>
<tr>
<td>Multiple collectors (%)</td>
<td>9 (15.5)</td>
<td>7 (33.3)</td>
<td>2 (5.4)</td>
<td>.008&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Main collector caliber (median) (IQR) (mm)</td>
<td>1.6 (1.18–2.10)</td>
<td>2.1 (1.95–2.30)</td>
<td>1.2 (0–1.6)</td>
<td>.70</td>
</tr>
<tr>
<td>Drainage (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep</td>
<td>31 (53.4)</td>
<td>11 (52.4)</td>
<td>20 (54.1)</td>
<td></td>
</tr>
<tr>
<td>Superficial</td>
<td>19 (32.8)</td>
<td>6 (28.6)</td>
<td>13 (35.1)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>8 (13.8)</td>
<td>4 (19)</td>
<td>4 (10.8)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> P values for group comparisons were determined by χ<sup>2</sup> or Fisher exact tests for categoric variables or by Mann-Whitney U tests for continuous variables, as appropriate.

<sup>b</sup> Value statistically significant (statistical significance was set at P < .0083 after Bonferroni correction for multiple comparisons).

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**FIG 1.** Neonatal developmental venous anomaly complicated by focal areas of venous ischemia. A, Axial SWI shows a left parietal developmental venous anomaly with superficial drainage. B, Axial T2WI reveals small linear hypointense lesions in the surrounding WM (arrow), with corresponding hyperintensity on b = 1000 image (C, arrow) and low ADC values on the ADC map (D, arrow).
hydrocephalus. Multiple interventional procedures were performed in the child with CVMS and an AVF.

Table 2 reports the clinicoradiologic outcome of subjects with c-DVAs. Longitudinal MR imaging was available in 10/15 patients (median follow-up, 39.1 months; range, 2–97 months; age at last follow-up, 2.5 months–8.2 years). Eight patients (80%) showed imaging signs of improvement, while stability (n = 1) or mixed evolution (n = 1) was detected in the remaining cases.

Follow-up neurologic evaluation was available in 14 neonates with c-DVAs (median follow-up, 27.5 months; range, 11–97 months), and findings were judged normal in 9 cases (64.2%), while minor or moderate psychomotor impairment was detected in 4 (28.5%) and 1 (7.1%) patient, respectively.

A brief description of a few illustrative cases of neonatal c-DVA is presented in the On-line Appendix.

DISCUSSION

In this study, we identified 41 neonates with DVAs, for a total of 58 DVAs, from a population of 2135 neonates undergoing brain MR imaging for diverse clinical reasons and with different imaging techniques, corresponding to a real-world detection in a tertiary pediatric center of 1.9%. These findings are similar to a recent retrospective study by Brinjikji et al, describing a prevalence of relationship between age and DVAs. Of note, we retrospectively identified DVAs and/or related enlarged drainage pathways in 27.2% of cases with available fetal MR imaging, confirming a congenital origin of these vascular abnormalities in those patients. Conversely, we did not identify new DVAs in follow-up studies, but we considered this a limited population; thus, we cannot exclude some DVAs actually developing de novo postnatally.

In our cohort, greater than one-third of neonates presented with at least 1 type of vascular complication directly linked to DVAs. Similarly, Horsch et al found a high percentage (42.9%) of abnormalities surrounding neonatal DVAs, while variable frequencies have been described in studies including adults and/or older children. Of note, initial differences regarding the corrected age at first MR imaging, prematurity, and imaging indications between neonates with cDVAs and u-DVAs likely represent a detection bias related to the neuroimaging screening program of preterm neonates with birth weights of <1500 g performed in our institution or even by chance, because these values did not reach statistical significance after multiple-comparison correction.

In detail, associated WM signal abnormalities were present in 17.1% of our neonates and were even more frequent in the series published by Horsch et al (21.4%). Previous studies have suggested that DVA-related WM changes present a bimodal distribution, peaking in younger children and older adults. However,
the underlying mechanisms of these signal changes remain poorly understood. In younger children, delayed myelination in the draining territory of the DVA has been proposed as a potential explanation. Alternatively, these signal alterations may represent venous congestion edema in the DVA territory due to an imbalance of the in- and outflow of blood in the DVA system, raising the pressure in the DVA. Of note, the latter mechanisms can also explain the relatively high frequency of associated hemorrhages and/or ischemic changes identified in our sample (19.5% and 9.8% of cases, respectively). In the general population, the risk of DVA-related hemorrhage is considered to be low (<1%/year) and is usually attributed to adjacent CCM bleeding. However, we detected CCMs in only a small percentage of cases (4.9%), in keeping with the theory that nonfamilial CCMs are acquired lesions related to DVAs through the process of hemorrhagic angiogenic proliferation.

Taken together, our findings suggest that in the neonatal period, there is a higher risk of flow-related complications in DVAs, potentially leading to venous hypertension and associated venous congestion, hemorrhage, and/or infarction. Putative neonatal risk factors of hemodynamic decompensation include mechanical distortion during vaginal birth and immaturity of the venous, immune, and hemostatic systems as well as hypercoagulability, which may be potentiated by maternal factors or inflammation. Finally, angioarchitectural factors yet unexplored in the neonatal setting, including angulation and stenosis of draining veins or tortuosity of medullary veins, could contribute to the development of ischemic or hemorrhagic complications.

Most interesting, the presence of multiple DVAs (ie, multiplicity) was significantly more common in neonates with c-DVAs, even after multiple-comparisons correction, suggesting that more severe and widespread venous pathology may correspond to a more fragile venous outflow system and/or a higher propensity for thrombotic DVA events. Of note, 2 of these neonates presented with clinical-neuroradiologic features consistent with CVMS, a rare craniofacial vascular malformation disorder characterized by a wide spectrum of slow-flow vascular lesions distributed along ≥1 of the 3 craniofacial metameres, further supporting this theory. Remarkably, 1 neonate also presented with a superior orbital fissure AVF, suggesting that this complex disorder may actually be a continuum potentially affecting >1 vessel type.

Our study also revealed focal polymicrogyria in the draining region of a DVA in 2 neonates (4.9%). DVAs or other venous drainage abnormalities or both have already been described adjacent to dysplastic cortical areas using conventional and ultra-high-field MR imaging. Because polymicrogyria is frequently associated with in utero disruptive events, coexistence of these 2 lesions suggests a causative effect of the DVA in the formation of this cortical malformation or, more probably, a shared pathomechanism related to early failure, abnormal development, or intrauterine occlusion of normal cerebral vessels. Finally, in 1 neonate, we observed obstructive hydrocephalus related to another type of DVA complication, ie, mechanical compression of the cerebral aqueduct. As in our patient, CSF diversion techniques usually lead to a good outcome in these rare cases.

Table 2: Neuroimaging abnormalities associated with developmental venous anomalies

<table>
<thead>
<tr>
<th>MRI Abnormalities</th>
<th>Neonatal Period* (n = 15)</th>
<th>Last Follow-Up* (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WM T2 signal abnormalities</td>
<td>7</td>
<td>Reduced 2/5</td>
</tr>
<tr>
<td>Restricted diffusion foci</td>
<td>4</td>
<td>Complete regression, 2/5</td>
</tr>
<tr>
<td>Hemorrhagic foci</td>
<td>8</td>
<td>Gliosis with or without hemosiderin deposits, 3/3</td>
</tr>
<tr>
<td>Multiple CCM</td>
<td>2</td>
<td>Stable, 1/2</td>
</tr>
<tr>
<td>PMG</td>
<td>2</td>
<td>Stable, 2/2</td>
</tr>
<tr>
<td>Calcifications</td>
<td>2</td>
<td>Stable, 2/2</td>
</tr>
<tr>
<td>Triventricular hydrocephalus</td>
<td>1</td>
<td>Resolution, 1/1</td>
</tr>
<tr>
<td>Draining venous varix thrombosis</td>
<td>1</td>
<td>Recanalization, 1/1</td>
</tr>
</tbody>
</table>

Note: PMG indicates polymicrogyria.
*Some patients presented with ≥1 DVA-related complication.
1 Includes 1 neonate with cerebrofacial venous metameric syndrome.
2 Postendoscopic third ventriculostomy.
As previously described, in our neonatal cohort, DVAs were more commonly located supratentorially and in the frontal lobe (41.4%). \(^{10,32}\) Other common locations included the parieto-occipital (27.7%) and temporal (13.8%) lobes, while the basal ganglia and thalamus were involved in only 8.6% of cases. Of note, different from a previous neonatal case series, in our series, we identified infratentorial DVAs in 8.4% of cases, thus confirming a potential selection bias related to the use of cUS to depict posterior fossa DVAs.\(^{22}\)

Regarding angioarchitecture features, we noticed a higher prevalence of multiple DVA collectors, which, together with larger caliber collectors, were significantly associated with DVA-related parenchymal abnormalities. These features may be related to the DVA size and, ultimately, to the volume of parenchyma under hemodynamic stress, ie, with reduced venous drainage capacity. Larger collectors may also be theoretically more prone to abnormal venous flow, with increased stasis and thrombosis. However, other studies performed in adults did not show statistically significant differences between parenchymal abnormalities and collecting vein diameters;\(^{11}\) therefore, the relationship between these neuroimaging features requires more detailed study. Similarly, in the present study, posterior fossa location was not a risk factor for complicated DVAs. Methodologic issues in terms of populations of interest and types of complication may justify this variability,\(^{16,23,32}\) and further studies are needed to also address this topic.

Serial imaging of a subgroup of neonates with c-DVAs revealed that DVAs and adjacent MR imaging abnormalities frequently present a dynamic evolution during the early years of life. These findings are in line with previous studies and probably reflect progressive brain and vascular maturation during early infancy.\(^{22,40}\) Indeed, neuroimaging follow-up demonstrated overall improvement in most cases of c-DVAs. More specifically, WM abnormalities were reduced in size or even completely resolved. Furthermore, ischemic and hemorrhagic foci also tended to subside without signs of intracranial re-hemorrhage. Of note, clinical outcomes of patients with c-DVAs was concordant with their favorable MR imaging evolution, with normal neurologic examination findings in most cases. Good clinical and neurologic outcomes were also reported by Horsch et al\(^{22}\) and are probably related to intrinsic brain plasticity as well as normalization of potential risk factors present in the neonatal phase.

**Limitations**

This study has some limitations. First, case selection was based on a retrospective single-center search of radiology reports. Therefore, although DVAs are routinely described in our institution by all staff members, the true DVA prevalence might be underestimated. Similarly, a relevant number of neonates was scanned on a 1.5T system, and gadolinium-based contrast media were only occasionally used, potentially leading to lower DVA detection.\(^{34}\) However, SWI was performed in almost all neonates (92.7%) and has a high diagnostic sensitivity for DVAs in children, especially when sedation is achieved without propofol and sevoflurane.\(^{8}\) Second, this study was performed in a tertiary pediatric institution, leading to potential selection bias toward inclusion of more severe DVA cases and limiting generalizability toward a different setting. Moreover, DVA collectors were measured on axial T2*WI, and this sequence can be influenced by the level of blood oxygenation and the magnetic field strength. However, none of the neonates were examined under general anesthesia, and complicated DVAs were actually less frequent in the group of subjects scanned using a 3T magnet. Therefore, if there were any bias related to the examination technique in terms of DVA collector size and MR imaging complications, it would actually exert its influence toward the null hypothesis. Finally, longitudinal data were missing in some patients, and clinical evaluation at follow-up was obtained from clinical records, though formal neurologic evaluation was performed in all assessed cases.

**CONCLUSIONS**

Real-world DVA detection in this population of neonates with clinically-indicated brain MR imaging reached 1.9%, which is lower than percentages of studies including older children and adults and might be an underestimate of the true prevalence. Of all neonates with detected DVAs, around one-third presented with DVA-related complications. The latter group had a significant tendency toward multiplicity and additional vascular malformations but usually had favorable neuroimaging findings and neurologic evolution at follow-up. DVAs could be retrospectively diagnosed in utero in one-quarter of neonates with fetal MR imaging, confirming, at least in these cases, a congenital origin.

**REFERENCES**


*Money paid to the institution.

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