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Neonatal Cerebral Stroke: A Two-Center Retrospective Case Series — Clinical Analysis of 10 Cases

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What is known on this subject?

Neonatal cerebral stroke is an uncommon event in the first 28 days of life, most often presenting with focal seizures but sometimes with non-specific neurological signs. Brain magnetic resonance imaging (MRI)—especially diffusion-weighted imaging (DWI)—is the diagnostic gold standard, and outcomes may include long-term sequelae [e.g., cerebral palsy (CP), epilepsy, cognitive/language difficulties], warranting prolonged follow-up; arterial ischemic stroke and cerebral sinovenous thrombosis are commonly treated as distinct subtypes with differing mechanisms and prognosis.

What this study adds?

This case series reports clinical/MRI features and 12-month outcomes of 10 neonates with stroke: 60% normal development, 20% CP, 20% mild motor impairment. It also highlights the role of early MRI with DWI and suggests deep gray matter involvement may be associated with poorer motor outcomes.

ABSTRACT

Objective: Neonatal cerebral stroke (NCS) is a significant cerebrovascular condition that occurs within the first 28 days of life and is associated with long-term neurological sequelae. In this study, we evaluated the demographic characteristics, clinical findings, imaging results, treatment approaches, and neurodevelopmental outcomes at 12 months of age of 10 neonates diagnosed with NCS in two tertiary-level neonatal intensive care units (NICUs).

Material and Methods: The medical records of 10 neonates diagnosed with NCS in the NICUs of two centers between January 2022 and November 2024, each of whom had at least 12 months of follow-up data, were retrospectively reviewed. A diagnosis was established in all cases using brain magnetic resonance imaging (MRI) [diffusion-weighted imaging (DWI), susceptibility-weighted imaging, T1, and T2 sequences]. Neurodevelopmental assessment at 12 months was based on clinical neurological examination and evaluation of developmental milestones. The cases were categorized as either arterial ischemic stroke (AIS) or cerebral sinovenous thrombosis (CSVT).

Results: Of the 10 neonates, six (60%) were male and four (40%) were female. Nine (90%) were born at term, and one (10%) was born late preterm. Seizures were the most common presenting symptom, observed in seven (70%) patients. Imaging findings were consistent with AIS in eight cases and with CSVT in two cases. Among patients with AIS (n=8), the most frequently involved vascular territory was the middle cerebral artery (MCA) (6/8, 75%); unilateral left MCA involvement was observed in three patients (37.5%), right MCA involvement was observed in two patients (25%), and bilateral MCA involvement was observed in one patient (12.5%). At the 12-month clinical assessment, six of ten cases (60%; 95% confidence interval: 26.2-87.8) were classified as having grossly age-appropriate development on neurological examination and developmental milestone assessment. Both cases with involvement of deep gray

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ABSTRACT

matter (basal ganglia/thalamus) developed cerebral palsy; this observation is consistent with the literature but is based on only two cases.

Conclusion: Neonatal stroke should be considered in newborns with asphyxia, seizures, and neurological symptoms. Brain MRI with DWI should be performed to confirm the diagnosis. AIS and CSVT may be considered and classified separately, given their different pathophysiologies and prognoses. All infants diagnosed with neonatal stroke require long-term follow-up, including developmental assessments, and those with adverse outcomes should be referred for rehabilitation.

Keywords: Neonatal cerebral stroke, arterial ischemic stroke, cerebral sinovenous thrombosis, neurodevelopment, case series.

Introduction

Neonatal cerebral stroke (NCS) is defined as focal ischemic necrosis resulting from the occlusion of one or more branches of a cerebral artery or parenchymal injury secondary to thrombosis of the cerebral venous sinuses, occurring within the first 28 days of life (1). Its incidence has been reported to range from approximately 1 in 1,600 to 1 in 4,000 live births, and the diagnostic rate has increased with advances in neuroimaging modalities (2). NCS is a major cause of long-term neurological sequelae, including cerebral palsy (CP), epilepsy, cognitive impairment, and language delays (3).

NCS has a multifactorial etiology. The conditions reported in the literature to be associated with NCS include maternal preeclampsia, chorioamnionitis, thrombophilias, intrapartum asphyxia, congenital heart disease, dehydration, and sepsis (4,5). However, in a substantial proportion of cases, no identifiable predisposing factors have been identified.

The clinical presentation is generally non-specific. The most common presenting symptom is focal motor seizures, which typically occur within the first few days of birth (6). Brain magnetic resonance imaging (MRI), particularly diffusion-weighted imaging (DWI), is the gold standard for diagnosing NCS (7). Treatment is primarily supportive and includes seizure control and management of the underlying etiologies. The prognosis varies markedly depending on the location and size of the lesion and the structures involved (8,9).

NCS is classified into two main subtypes: arterial ischemic stroke (AIS) and cerebral sinovenous thrombosis (CSVT). The pathophysiology, neuroimaging findings, and prognostic profiles of these entities differ; therefore, they should be evaluated separately (10).

In this study, we aimed to share our clinical experience through assessment of the clinical characteristics, imaging findings, treatment approaches, and neurodevelopmental outcomes at 12 months of age of 10 neonates diagnosed with NCS in two tertiary-level neonatal intensive care units (NICUs). Our findings are hypothesis-generating and are intended to provide a foundation for larger-scale prospective studies.

Material and Methods

This descriptive case series was based on a retrospective review of neonates diagnosed with NCS in the NICUs of two tertiary care hospitals between January 2022 and November 2024. Infants were included if they developed neurological symptoms within the first 28 days of life, had brain MRI findings consistent with acute cerebral stroke [defined as DWI hyperintensity with corresponding apparent diffusion coefficient (ADC) hypointensity and/or evidence of venous thrombosis on MR venography (MRV)], and had at least 12 months of follow-up data. Patients with incomplete medical records, a follow-up duration <12 months, or evidence of prenatal stroke detected on antenatal ultrasonography were excluded. Retrospective ethics committee approval was obtained from Alanya Alaaddin Keykubat University, Faculty of Medicine, Clinical Research Ethics Committee (approval number: 26-10, date: 11.12.2024). As this was a retrospective study based on a review of existing medical records, the requirement for informed consent was waived by the Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Data Collection

Demographic data (sex, gestational age, birth weight, and Apgar scores), maternal history (maternal age, gravidity, mode of delivery, and pregnancy complications), and perinatal history (delivery-related complications and need for resuscitation) were obtained retrospectively from hospital records. The time interval between the onset of the first neurological symptom and cranial MRI acquisition was calculated using nursing observation notes, physician order forms, and electronic record time stamps. The presenting symptoms, neurological examination findings, laboratory results (complete blood count, coagulation studies, and infection markers), and electroencephalography (EEG) findings were recorded.

Laboratory investigations recorded in the hospital charts included complete blood count (with platelet count),

C-reactive protein, and basic coagulation parameters [prothrombin time/ international normalized ratio (PT/INR) and activated partial thromboplastin time (aPTT)]. These tests were performed as part of the routine clinical evaluation of all patients upon admission to the NICU.

Extended thrombophilia testing, including fibrinogen, D-dimer, protein C activity, protein S activity, antithrombin III activity, factor V Leiden (G1691A) mutation, prothrombin gene mutation (G20210A), antiphospholipid antibodies [anticardiolipin immunoglobulin (Ig) G/IgM, lupus anticoagulant], homocysteine, and lipoprotein (a), was not systematically performed in all patients. Comprehensive thrombophilia screening was performed only in selected cases: specifically, in two patients classified as having CSVT and in one patient with a documented family history of coagulation disorders.

Neuroimaging and Classification

Neonatal stroke was classified as arterial AIS or CSVT based on neuroimaging features interpreted by attending radiologists in conjunction with the clinical context. Images were interpreted by radiologists at the respective centers as part of routine clinical care; no centralized blinded imaging review was performed.

AIS was diagnosed when cranial MRI demonstrated a focal parenchymal lesion conforming to a recognized arterial vascular territory middle cerebral artery (MCA) or posterior cerebral artery (PCA), with hyperintensity on DWI and corresponding hypointensity on ADC maps, indicative of acute diffusion restriction, in the absence of imaging evidence of CSVT.

Indications for MRV. MRV was not systematically performed on all patients. There was no predefined written institutional protocol governing MRV acquisition. MRV was obtained at the discretion of the attending neonatologist and radiologist when one or more of the following findings raised suspicion for CSVT: (i) parenchymal lesion in a non-arterial distribution (parasagittal, bilateral, or posterior-predominant); (ii) hemorrhagic transformation or intraparenchymal hemorrhage within the infarct zone; (iii) suspected venous sinus abnormality on conventional sequences (e.g., absent flow void on T2-weighted images or hyperintense sinus signal on T1-weighted images suggesting acute thrombus); or (iv) clinical risk factors strongly associated with CSVT, including dehydration, polycythemia, sepsis, catheterization, or documented systemic thrombosis.

CSVT was diagnosed when MRV demonstrated the absence of flow signals in one or more cerebral venous sinuses, which was confirmed on conventional T1- and T2-weighted sequences to exclude flow-related artifacts. Associated parenchymal lesions in CSVT are characterized by a non-arterial distribution (parasagittal, bilateral, or posterior predominance), hemorrhagic transformation, or an atypical location for arterial-territory infarction. In our cohort, MRV confirmed the absence of flow in the affected venous sinuses in both CSVT cases, including one involving the superior sagittal sinus.

Exclusion of CSVT in patients who did not undergo MRV. In the eight cases classified as AIS, the diagnosis was based on the following convergent findings: (a) the parenchymal lesion conformed precisely to a unilateral arterial vascular territory (MCA or PCA); (b) no hemorrhagic transformation or imaging signs of venous congestion were present; (c) conventional MRI sequences demonstrated patent venous sinuses with preserved flow voids on T2-weighted images; and (d) the clinical presentation, including focal seizures with lateralizing features, was consistent with an arterial territory infarction. (Figures 1-3)

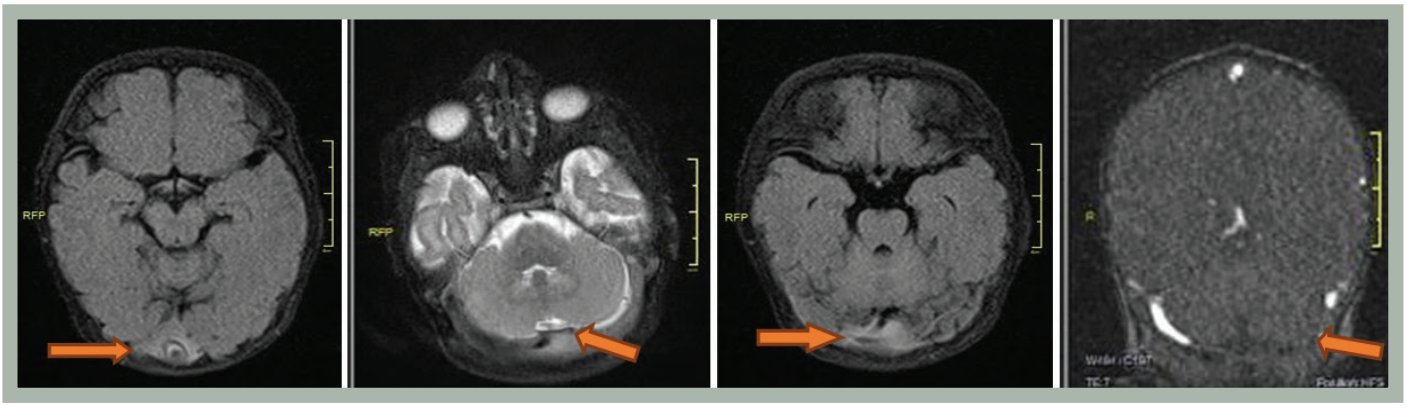

Figure 1. Cranial magnetic resonance imaging. Loss of signal void and non-visualisation of the left sagittal sinus indicate thrombosis of the superior sagittal sinus. A filling defect is seen in the left transverse sinus

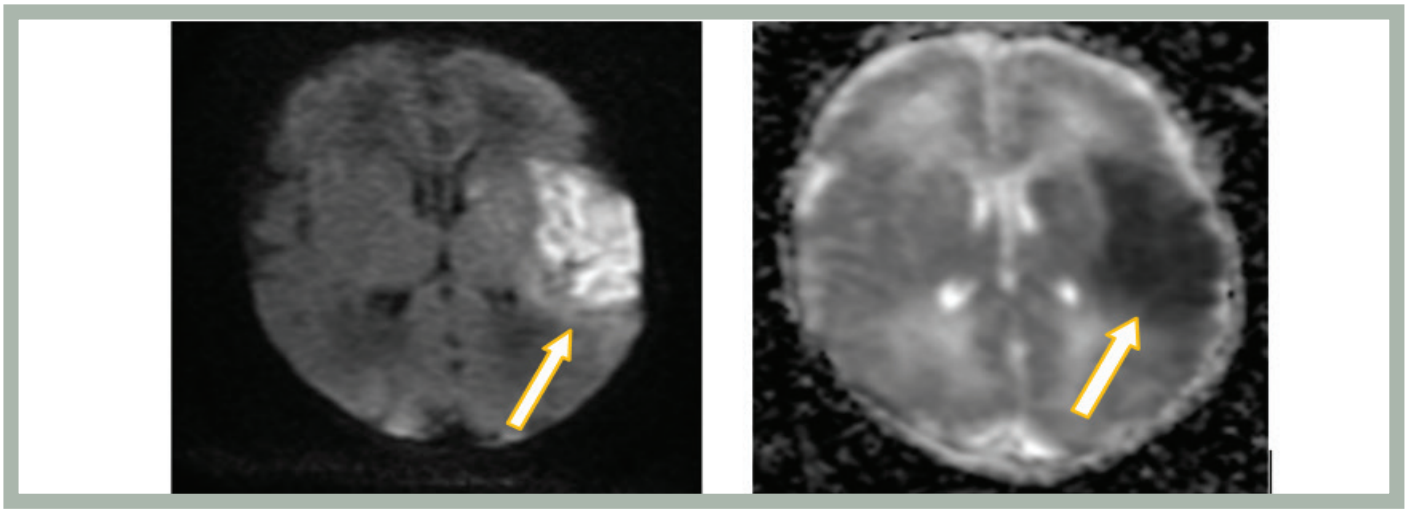

Figure 2. Diffusion-weighted magnetic resonance brain imaging axial section, showing extensive acute infarct areas in the posterior cerebral artery supply regions of the right temporo-occipital region, hyperintense on T2-weighted sequences, and hypointense signal change on T1-weighted sequences

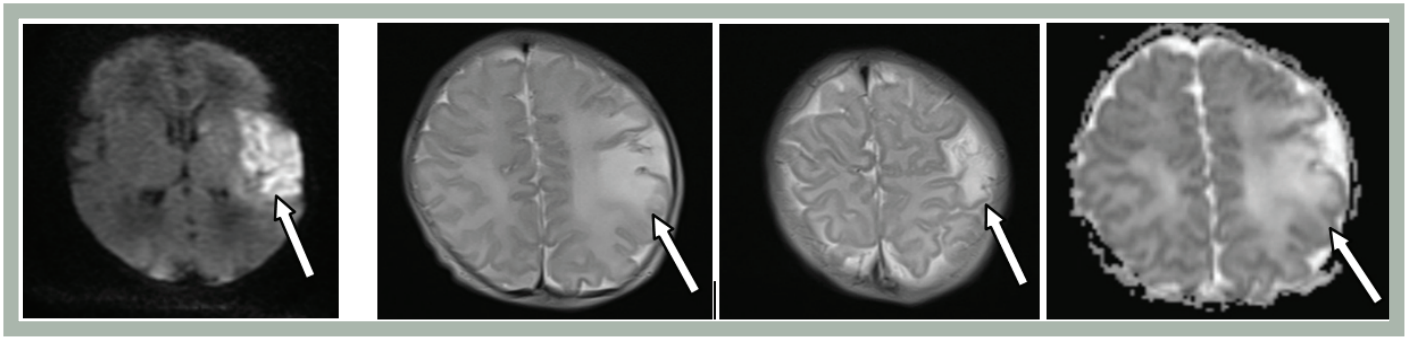

Figure 3. Sagittal T1, transverse T2, T2/FLAIR, T1, susceptibility-weighted imaging, diffusion-weighted images. Brain magnetic resonance imaging showing a thrombus filling the lumen of the right transverse sinus. Haemorrhagic infarct area in the left caudate nucleus, basal ganglia, and left frontoparietotemporal region (left middle cerebral artery territory) with accompanying cortical laminar necrosis

Echocardiography was performed in all cases to assess intracardiac shunts or structural anomalies.

Treatment and Follow-up

All patients received standard NICU supportive care, including fluid and electrolyte management, metabolic support, and respiratory support. In infants with clinical seizures, oral maintenance phenobarbital (5 mg/kg/day in two divided doses) was initiated, and no second-line antiepileptic agents were administered. Anticoagulation for CSVT was individualized based on thrombus characteristics and bleeding risk. After discharge, the patients were clinically followed up for at least 12 months.

Outcome Classification

Neurodevelopmental assessment at 12 months was based on clinical neurological examination and evaluation of age-appropriate motor, cognitive, and language milestones. A standardized multidomain developmental instrument (e.g., Bayley-III) was not systematically administered. Outcomes were classified as follows: (i) normal, neurological examination findings and milestones appropriate for age; (ii) mild sequelae, ≥2 month motor developmental delay, mild tone asymmetry, or language delay not meeting CP criteria; or (iii) severe sequelae, CP (abnormal tone and posture), refractory epilepsy, or severe cognitive impairment.

Statistical Analysis

This study is a descriptive case series, and the sample size (n=10) is insufficient to provide reliable effect estimates. Descriptive statistics are presented as counts and percentages for categorical variables [with 95% exact binomial confidence intervals (CIs)] and as the median [interquartile range (IQR) and range] for continuous variables. No hypothesis-testing comparisons (e.g., chi-square or Fisher's exact tests, p values) were performed; with (n=10), the power to detect even a large

effect (e.g., 70% vs. 30%) is <40% . All findings should therefore be interpreted as hypothesis-generating.

Results

The demographic and perinatal characteristics of the 10 patients are summarized in Table 1. Six infants were male (60%), and four (40%) were female. The median gestational age was 39 weeks (IQR: 38-40; range: 35-41), nine infants (90%) were born at term (≥37 weeks), and one (10%) was a late preterm born at 35 weeks. The median birth weight was 3,250 g (IQR: 3,000-3,500 g; range: 2,900-3,600 g). Six infants (60%) were delivered by cesarean section (four emergency and two elective), and four (40%) were delivered vaginally. The median 5 minute Apgar score was 7 (IQR: 6-9; range: 4-9).

A history of perinatal asphyxia was identified in six cases (60%), preeclampsia in three (30%), fetal distress in four (40%), prolonged labor in one (10%), umbilical cord entanglement in one (10%), and gestational diabetes in one case. One patient (10%) had a family history of coagulation disorders. No identifiable perinatal characteristics were detected in three cases (30%).

Cranial MRI was performed at a median of 36 h after symptom onset (IQR: 24-48 h; range: 12-72 h). All imaging studies were performed within 72 h of the initial neurological presentation.

The most common presenting symptom was seizure, which was observed in seven cases (70%). The seizures were predominantly focal and clonic. Two (20%) presented with lethargy and poor feeding and one (10%) with hypotonia. Among the eight patients who underwent EEG, six (75%) demonstrated focal slowing or epileptiform discharges. Echocardiography was performed in all cases, and patent foramen ovale (PFO) was detected in seven (70%) cases; however, PFO may be a physiological finding in the neonatal period (Table 2).

AIS was identified in eight patients (80%), and CSVT with secondary venous infarction was identified in two patients (20%). In the AIS cases, the most frequently involved vascular territory was the left MCA: unilateral left MCA in three patients (37.5%); unilateral right MCA in two patients (25%); bilateral MCA in one patient (12.5%); left PCA in one patient (12.5%); and right temporo-occipital region (PCA branches) in one patient (12.5%) (Table 3).

In one case of CSVT, superior sagittal sinus thrombosis was identified, and in the other, extensive acute infarction was detected in the PCA perfusion territories within the right temporoparietal region. The parenchymal lesions in these cases were not included in the arterial territory classification

Table 1. **Demographic and perinatal characteristics of the cases (n=10)**

Characteristic	Number (n, %)
Sex	
Male	6 (60%)
Female	4 (40%)
Gestational age	
Median, weeks (IQR: 38-40)	39
Term (≥37 weeks)	9 (90%)
Late preterm (35-36 weeks)	1 (10%)
Birth weight (g)	
Median (IQR: 3.000-3.500)	3,250
Mode of delivery	
Vaginal	4 (40%)
Cesarean section—emergency	4 (40%)
Cesarean section—elective	2 (20%)
5-minute Apgar score	
Median (IQR: 6–9)	7
Perinatal characteristics	
Perinatal asphyxia	6 (60%)
Preeclampsia	3 (30%)
Fetal distress	4 (40%)
Prolonged labor	1 (10%)
Nuchal cord	1 (10%)
Gestational diabetes	1 (10%)
Family history of coagulation disorder	1 (10%)
No identifiable characteristic	3 (30%)

IQR: Interquartile Range

Table 2. **Clinical findings (n=10)**

Finding	n (%)
Presenting symptoms	
Seizures (predominantly focal clonic)	7 (70%)
Lethargy/poor feeding	2 (20%)
Hypotonia	1 (10%)
EEG findings (n=8)	
Abnormal (focal slowing/epileptiform discharges)	6 (75%)
Normal	2 (25%)
Echocardiography finding	
Patent foramen ovale	7 (70%)

EEG: Electroencephalography

Table 3. Imaging findings

Stroke subtype (n=10)	
Arterial ischemic stroke (AIS)	8 (80)
Cerebral sinovenous thrombosis (CSVT)	2 (20)
Arterial vascular territory among AIS cases (n=8)	
Left MCA (unilateral)	3 (37.5)
Right MCA (unilateral)	2 (25)
Bilateral MCA	1 (12.5)
Left PCA	1 (12.5)
Right temporo-occipital (PCA branches)	1 (12.5)
CSVT pattern (n=2)	
Superior sagittal sinus thrombosis	1
Extensive venous infarction	1
Deep gray matter involvement (n=10)	2 (20)

Vascular-territory percentages are calculated within AIS cases (n=8); subtype and deep gray matter percentages are calculated for the whole cohort (n=10). MCA: Middle cerebral artery, PCA: Posterior cerebral artery

system because they reflect the pathophysiology of venous congestion. Deep gray matter involvement (basal ganglia and/or thalamus) was observed in two patients (20%).

All patients received standard supportive NICU management. Oral maintenance phenobarbital (5 mg/kg/day) was initiated in all seven patients. The median length of hospital stay was 14.5 days (IQR, 10-19 days; range, 7-25 days).

At 12 month follow-up, six (60%; 95% CI: 26.2-87.8) infants had grossly age-appropriate development based on clinical neurological examination and milestone assessment, two (20%) had hemiparetic CP, and two (20%) had mild motor impairment. Notably, in this cohort, both patients (2/2) with deep gray matter involvement (basal ganglia and/or thalamus) developed hemiparetic CP; however, this observation was limited by the small number of affected patients.

The basic coagulation parameters (PT/INR and aPTT) were within the age-adjusted normal reference ranges in nine of the ten patients. In the patient with a family history of coagulation disorders, the PT, aPTT, and results of the extended thrombophilia panel were normal. Thrombophilia tests, including measurements of protein C and protein S levels, antithrombin III activity, and D-dimer levels, were performed in two cases of CSVT. Thrombophilia test results were normal. Among newborns with AIS who had no clinical risk factors for thrombophilia, no thrombophilia screening was performed during their stay in the NICU.

Discussion

Neonatal stroke is a major neurological emergency in the neonatal period, with the potential for significant long-term morbidity (5). In this small cohort, both infants with basal ganglia and/or thalamic involvement on MRI developed hemiparetic CP by 12 months, whereas none of the eight infants with lesions confined to cortical or subcortical white matter territories developed CP. Although this observation is consistent with the prognostic significance attributed to deep gray matter involvement in the literature (7), it is based on only two affected cases and, therefore, cannot establish a predictive relationship.

In two cases of CSVT, anticoagulant therapy was tailored based on the extent of the thrombus, risk of bleeding, and current hemostatic parameters rather than a specific diagnosis of thrombophilia. In the first case of CSVT, low-molecular-weight heparin was initiated at a therapeutic dose. In the second CSVT case, supportive therapy without anticoagulation was preferred because of hemorrhagic components of the infarction. None of the underlying coagulation abnormalities in the AIS cases led to the initiation of anticoagulation therapy, as current guidelines do not recommend routine anticoagulation for neonatal AIS in the absence of confirmed prothrombotic disorders or cardioembolic sources (7).

Basal ganglia and thalamic involvement in neonatal AIS are strongly associated with subsequent hemiparetic CP and motor impairment (7). This relationship is primarily attributed to the vulnerability of deep gray matter structures and the adjacent posterior limb of the internal capsule during the perinatal period, when active myelination and corticospinal tract development render these regions particularly susceptible to ischemic injury (5,7). In addition to motor sequelae, thalamic injury may contribute to later cognitive, sensory, and behavioral difficulties that may not be evident in early infancy (3,11,12). Accordingly, while our limited data do not allow independent prognostic conclusions, the existing literature supports the view that deep gray matter involvement on acute MRI should alert clinicians to a potentially higher risk of motor sequelae and may inform early referral for rehabilitation and structured neurodevelopmental follow-up (7).

In our cohort, AIS predominated CSVT, consistent with previous neonatal stroke series (2,8). Despite the limited number of CSVT cases, the two subtypes showed clinically meaningful differences in pathophysiology, presentation,

imaging, management, and short-term outcomes. AIS is characterized by focal arterial territory lesions and early seizures or focal neurological signs, whereas CSVT presents with more non-specific symptoms and non-arterial, sometimes hemorrhagic, imaging patterns requiring MRV for definitive diagnosis (10). Management also differed, with AIS treated mainly supportively and CSVT evaluated for anticoagulation on an individualized basis (7). Although both CSVT cases had normal 12 month outcomes, this finding should be interpreted cautiously, given the small sample size and the possibility of later cognitive or seizure-related sequelae reported in the literature. Overall, these observations support the view that AIS and CSVT should be classified and analyzed separately in neonatal stroke research and clinical practice (10).

The male predominance (60%) in our cohort is consistent with the literature, which reports that male sex is a risk factor for neonatal stroke (5). There are significantly higher rates of perinatal AIS in males, attributed to the adverse effects of androgen hormones on neuroprotective mechanisms and sex-specific differences in coagulation (6). Most of our cases (90%) were term infants, consistent with the predominance of term neonates with AIS reported in the literature. No identifiable perinatal risk factors were found in three (30%) of our cases. This is consistent with the literature, in which no predisposing factor can be identified in up to 45.5% of neonatal AIS cases (8). Among the identifiable risk factors, perinatal asphyxia (60%) and preeclampsia (30%) were the most common in our cohort. In comparison, Grunt et al. (8) reported perinatal asphyxia in 27.2% of cases and preeclampsia in 9.1% of cases. The higher rates observed likely reflect the demographic and obstetric characteristics of our study population, including limited access to fetal monitoring and a high proportion of emergency cesarean deliveries.

PFO was detected on echocardiography in seven (70%) patients. PFO is a physiological remnant of fetal circulation that remains patent in approximately 50-60% of neonates during the first days of life, with gradual functional closure occurring in the majority by 3-12 months of age (9). The slightly higher prevalence in our cohort (70%) likely reflects the timing of echocardiographic examination (performed within the first week of life in all cases) and the limited sample size rather than representing a pathological excess. The paradoxical embolism hypothesis posits that thrombi originating from the placental, umbilical venous, or systemic venous circulation may traverse a PFO during transient right-to-left shunting (e.g., during crying, straining, or transitional hemodynamic changes) and embolize into the cerebral arterial circulation (7). Although this mechanism is biologically plausible, our data do not permit attributing a causal role to PFO. The observed PFO rate of 70% does not clearly exceed the expected physiological prevalence among neonates, especially since echocardiography was performed within the first week of life. In addition, no matched control group was available for comparison; contrast-enhanced echocardiography with a bubble study was not performed to document right-to-left shunting; and the small sample size precluded a meaningful assessment of statistical associations. Accordingly, the PFO findings in this cohort are reported descriptively and should not be interpreted as evidence of a causal relationship with neonatal stroke.

In our cohort, seizures were the most prevalent presenting symptom, occurring in 70% of cases, consistent with previous reports of focal motor seizures in 70-90% of neonates with stroke within the first 12-72 hours of life (12). The predominance of focal clonic seizures and their contralateral localization relative to the side of the lesion are distinctive features that should prompt clinicians to consider focal brain injury. Two cases (20%) presented with non-specific neurological signs (lethargy, hypotonia, and poor feeding) without overt seizures, highlighting the heterogeneous presentation of neonatal stroke (13).

At the 12 month clinical assessment, six of ten cases (60%; 95% CI: 26.2-87.8) were classified as having grossly age-appropriate development based on clinical neurological examination and milestone evaluation. However, this figure should be interpreted with considerable caution: the wide CI reflects substantial imprecision due to the small sample size; the absence of standardized multidomain testing (e.g., Bayley-III) means that subtle cognitive, language, and behavioral deficits may have remained undetected at the time.

Anticoagulation for cerebral venous thrombosis was individualized based on thrombus characteristics and bleeding risk. This approach aligns with the current guidelines, which recommend a case-by-case evaluation (14). Left MCA territory predominance (37.5% of AIS cases) is consistent with the well-established predilection for left hemisphere involvement in neonatal stroke, which is attributed to the direct origin of the left carotid artery from the aortic arch, facilitating embolic traffic to the left cerebral circulation (14,15). DWI demonstrated characteristic hyperintensity with ADC hypointensity (diffusion restriction) in all ischemic cases, confirming its critical role in early diagnosis (16). At 12 months, six of ten cases (60%; 95% CI: 26.2-87.8) demonstrated age-appropriate development. The four patients with adverse outcomes (40%) had infarcts involving deep gray matter structures and/or bilateral MCA territories, consistent with

the literature reporting that involvement of the basal ganglia, posterior limb of the internal capsule, and multiple vascular territories is associated with poor motor prognosis (17,18). Follow-up imaging (performed in five cases) demonstrated the expected evolution of infarcts into encephalomalacia or gliosis, providing structural correlations with clinical outcomes. Follow-up EEG was valuable in guiding the discontinuation of antiseizure medications. Direct comparison with prior studies is facilitated by our use of standardized outcome definitions (adverse neurodevelopment outcome including CP, motor delay, hemiparesis, or epilepsy), which align with criteria used in major cohort studies (7,17,19).

Thrombophilia testing was not systematically performed in all patients. Extended evaluation [protein C, protein S, antithrombin III, factor V Leiden, prothrombin G20210A, antiphospholipid antibodies, homocysteine, and lipoprotein(a)] was performed only in selected cases, based on clinical judgment. This represents a significant limitation because undetected hereditary or acquired thrombophilia may have contributed to the pathogenesis of stroke in cases classified as having "no identifiable risk factor" (9,11). Furthermore, the physiological immaturity of the neonatal hemostatic system complicates the interpretation of protein C, protein S, and antithrombin levels in this age group, as normative values are substantially lower than in older children and adults (14). A systematic, protocolized thrombophilia evaluation with age-adjusted reference ranges—ideally repeated at 3-6 months of age when hemostatic maturation has occurred—is recommended for future prospective studies (7).

MRV was not systematically performed in all patients. In eight cases classified as AIS, CSVT was excluded based on arterial territory conformity of the parenchymal lesion and on preserved flow voids on conventional T2-weighted sequences, rather than on dedicated venous imaging. This approach, while consistent with clinical practice patterns reported in the literature, carries the inherent risk that subtle, partial, or non-occlusive venous thrombosis may have been overlooked (16). Consequently, misclassification of CSVT as AIS cannot be entirely excluded, particularly in cases with posterior or parasagittal lesion distributions. Prospective studies should incorporate universal MRV to improve diagnostic accuracy.

Cognitive, language, visuoperceptual, and behavioral domains, well-recognized areas of impairment affecting 30%–60% of survivors after neonatal stroke, have not been systematically evaluated using standardized test instruments (12,13). In addition, a 12 month follow-up period is insufficient to capture the cognitive and behavioral sequelae that typically become apparent after 18-24 months or at school age (14). Without a control group, these features cannot be considered "risk factors"; rather, they are presented only as clinical characteristics observed in the present study. Case-control studies are required to determine whether these findings exceed the population baseline rates (16).

Study Limitations

This study had several limitations. First, the small sample size provided insufficient statistical power to generate reliable effect estimates for the outcomes. Accordingly, all findings should be regarded as hypothesis-generating and require confirmation in larger cohorts. Another limitation is the retrospective design, which precluded standardized data collection, blinding, and prospective follow-up. Another important limitation is the narrow scope of the neurodevelopmental assessment. No standardized multidomain developmental test (e.g., Bayley-III) was administered. Instead, evaluations relied on clinical neurological examinations and developmental milestones, which may have been insufficient to detect impairments in cognitive, language, and behavioral domains and may have artificially inflated the rate of favorable outcomes. In addition, the 12 month follow-up period does not encompass the 18-24 month window or the school-age period, during which cognitive and behavioral sequelae typically become apparent.

Conclusion

Neonatal stroke should be considered in any newborn presenting with asphyxia, seizures, or unexplained neurological symptoms. In accordance with current diagnostic standards, brain MRI with DWI should be used to confirm the diagnosis of NCS. Given their distinct pathophysiology and prognostic trajectories, AIS and CSVT should be classified separately. All infants diagnosed with neonatal stroke require structured, long-term follow-up through school-age using standardized developmental assessments, and those with adverse outcomes should be referred for timely multidisciplinary rehabilitation, including physiotherapy, occupational therapy, and speech-language therapy.

Ethics

Ethics Committee Approval: Retrospective ethics committee approval was obtained from Alanya Alaaddin Keykubat University, Faculty of Medicine, Clinical Research Ethics Committee (approval number: 26-10, date: 11.12.2024).

Informed Consent: As this was a retrospective study based on a review of existing medical records, the requirement

for informed consent was waived by the Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.L.S., Y.K., A.A., Concept: B.L.S., Y.K., A.A., Design: B.L.S., Y.K., A.A., Data Collection or Processing: B.L.S., Y.K., A.A., Analysis or Interpretation: B.L.S., Y.K., A.A., Literature Search: B.L.S., Y.K., A.A., Writing: B.L.S., Y.K., A.A.

Conflict of Interest: The authors, Birgül Livaoğlu Say and Arzu Akdağ, are members of the journal's review board. The editorial and peer-review process was conducted independently of these authors. No conflict of interest was declared by the other author.

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