REVIEW

Lenticulostriate vasculopathy in routine brain ultrasonography in infants: next step?

Suada Heljic[1], Sabina Terzic[2], Hajrija Maksic[2]

[1]Faculty of Health Sciences, International University Goražde, [2]Pediatric Clinic, Clinical University Centre Sarajevo; Bosnia and Herzegovina

ABSTRACT

Lenticulostriate vasculopathy (LSV) is a relatively common finding in routine cranial ultrasound examination that has been associated with many infectious and non-infectious conditions. The aim of this review was to provide a better understanding of LSV ultrasound finding, as well as the need for further laboratory and imaging examinations in infants. The most of the published studies represented small series, with few prospective long-term studies involving the control groups. Authors have mostly found an association between LSV, especially higher-grade (although there is no universally accepted classification) with congenital cytomegalovirus (CMV) infection, classifying those children as at risk for sensorineural hearing loss. In contrast, some authors pointed out that LSV could be found relatively often, and believe that isolated LSV, especially lower-grade, is not predictive for an unfavourable outcome and a long-term prognosis. Therefore, although 35 years have passed since the first publication of LSV, there is still no consensus among experts on the clinical significance of isolated LSV, but caution is certainly needed given the fact that most infants with congenital CMV are asymptomatic.

Key words: brain ultrasonography, cytomegalovirus, lenticulostriate vasculopathy, newborn lenticulostriate vasculopathy

Corresponding author:
Suada Heljić
Faculty of Health Sciences,
International University Goražde
Seada Sofovića Sofe 27, 73000 Goražde,
Bosnia and Herzegovina
Phone: +38738 941 842;
Fax: +38738 941 843;
E-mail: suadaheljic@hotmail.com
ORCID ID: https://orcid.org/0000-0003-3929-2541

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INTRODUCTION

Lenticulostriate vasculopathy (LSV) is a term that refers to bright or hyperechoic blood vessels in the region of the thalamus and basal ganglia, visible on cranial ultrasound examination of a newborn. LSV was first observed and described by Grant at al. in 1985 on the second-born twin with body weight (BW) of 1240 g, with cytomegalovirus (CMV) infection (1). The frequency of LSV varies from 0.5-2% in live births, or 0.3-32% depending on the population that is the subject of research in some studies (2-5).

Some studies done after the first report showed an association with congenital infections, such as cytomegalovirus, toxoplasmosis, rubella, herpes, as well as with some other conditions including chromosomal abnormalities, a wide range of perinatal conditions (perinatal asphyxia, maternal-foetal alcohol syndrome feto-fetal transfusions) (6-10). However, a large number of studies have been related to case reports or small retrospective studies (11-16), suggesting a significant gap in assessing significance of LSV on routine neonatal brain ultrasound.

The aim of this paper was to assess significance of LSV finding in routine ultrasound examination, i.e. the need for possible additional diagnostics.

LENTICULOSTRIATE VASCULOPATHY AND CONGENITAL INFECTIONS

It is especially important to determine the association between LSV and congenital cytomegalovirus (cCMV) infection because the vast majority of children with cCMV are asymptomatic (17,18), meaning they appear healthy, with no clinical sign of disease, and are therefore not evaluated by either laboratory or imaging methods.

Dozens of papers were found related to the association of LSV and CMV, which differ in methodological approach and research results (19-24).

In one of the early reports none of 38 children with LSV had a urine culture positive test for CMV (2). In Wang et al. early study (23), 586 children with signs of encephalopathy were examined (including seizures, psychomotor retardation, congenital malformations, dysmorphism, and prematurity) and LSV was found in 34 (5.8%) children in various conditions (prenatal, acquired), but also nonspecific ones (such as hypoglycaemia or uncomplicated prematurity); in 10 of 34 cases the cause was not found, so the authors concluded that LSV was a nonspecific marker of previous insults on developing brain, with foetal brain hemodynamics playing a significant role in pathogenesis.

Later studies, especially ones after the introduction of the classification that graded LSV (although there is no classification that is uniquely adopted) showed a stronger correlation between LSV and CMV (17-22, 24-28). However, the results of individual studies differ significantly from each other. In a study by Amir et al. (24) LSV was detected on initial ultrasonography in 54.3% of children with congenital CMV infection suggesting that LSV was a possible high-risk marker for sensorineural hearing loss. The same conclusion is drawn from a study by Bilavsky et al. (25) in 141 children who had only LSV on initial brain ultrasound and who were followed for one year: significant hearing impairment was found in the group that did not have hearing impairment at birth and was not treated with acyclovir (85%), compared to the group with LSV who were asymptomatic and treated with gan/valgancyclovir. The authors concluded that LSV could be a sign of CNS involvement and future hearing impairment, and that it would be prudent to treat these children (25). Similarly, in a small series of asymptomatic children with congenital cCMV it was found that a total of 45% of children had an abnormal imaging or laboratory findings (LSV, intraventricular haemorrhage - IVH, calcifications, sensorineural hearing loss), which in some cases requires prompt antiviral treatment (26). In a recent study (27) on 858 children, CMV PCR was positive in 69% severe and 23% mild LSV cases with a strong association between LSV and other brain abnormalities. A study (28) analysing data of 161 newborns with cCMV and LSV alone or with other brain abnormalities, found 39.7% of newborns with cCMV compared to 18% in controls; however, the finding of LSV alone or together with other findings in a group of newborns with cCMV did not represent a risk factor for neurological hearing loss, so the authors concluded that although common, the finding was not predictive of an adverse outcome and that ultrasound finding itself was unreliable in the selection of candidates for antiviral therapy (28). In a recent update on cCMV infection by Barton

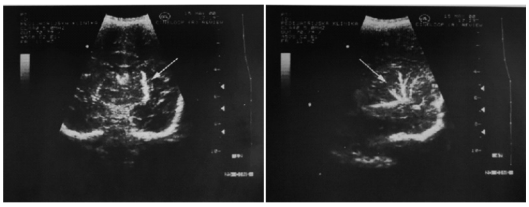

Figure 1. High grade lenticulostriate vasculopathy on coronal (left) and parasagital plane (right) (Clinical University Centre, Sarajevo, Bosnia and Herzegovina, 2000)

et al. head imaging abnormalities are classified as ventricular/periventricular, structural-cerebral migration disorders and vascular LSV. Vascular disorders are indicated as a common finding of questionable clinical significance (29).

According to all these studies, there is no consensus on whether isolated LSV is sufficient to include a child in the group of risk or high-risk children for cCMV and neurological hearing loss. Some authors believe (28,30) that low-grade LSV can be considered as a normal variant, while some others (17, 26) believe that all children with LSV should be evaluated for possible intracranial infections. Further large prospective observational studies are needed to assess the incidence of LSV and association with infectious and noninfectious conditions in neonates (6,31).

NON-INFECTIOUS CONDITIONS ASSOCIATED WITH LENTICULOSTRIATE VASCULOPATHY

Various LSV-related conditions have been described in the literature, including trisomy 13 syndrome, Down syndrome, hypoxia-ischemia, hyperbilirubinemia, heart diseases, foetal alcohol syndrome, congenital malformations, respiratory distress syndromes, neonatal lupus erythematosus, feto-fetal tranfusion, sialidosis, hydrops fetalis and diabetic fetopathy. However, these associations were found mainly in individual cases or small batches of patients (6).

In a study by Coley et al. (32) on a series of 2400 sonograms, 63 cases of LSV were found, of which hypoxic-ischemic conditions were found in 33 cases (including heart defects, respiratory distress syndrome and perinatal asphyxia), and progressive changes were found in 12 patients with heart and lung disease, so the authors concluded that hypoxic-ischemic conditions and postnatal hypoxia/ischemia are important etiological factors. In a prospective randomized study by Mittendorf et al. (33) in 149 pregnant women, the use of tocolytics ≥50 g MgSO4 during preterm birth was found to be significantly associated with the occurrence of LSV, but additional studies were needed in a larger number of patients to confirm this observation.

LENTICULOSTRIATE VASCULOPATHY AND NEURODEVELOPMENT

Children with isolated LSV generally have a normal neurodevelopmental pattern and a favourable long-term prognosis (34,35).

In a study by El Ayoubi et al. among 53 children with LSV followed for 2-9 years, 66% had normal neurodevelopment at the end of follow-up, 15% had minor abnormalities, 7.5% moderate, and 11.3% major deficits; of the 34 children with isolated LSV, 79% had normal development, compared with 42% who had also an associated condition. Most children with LSV and developmental delay had some associated disease, such as CMV infection, major malformations, foetal alcohol syndrome, neonatal hypoxia, and systemic neonatal sepsis (35). According to Shin et al. study there is a significant association of LSV with neurodevelopmental delay if it is a higher-grade LSV (including 3 or more branches) with an absence of colour doppler flow (36).

In the studies focused on long-term sequelae (23,34) that included 34 children with LSV aged 7-9 years, 28 children had one or more disorders, including tics, hyperactivity, obsessive compulsive disorders, or neurological deficits; the children was categorized into 3 subgroups: LSV with perinatal etiology, with acquired disorders and with unknown etiology (idiopathic). The rate of disorders (54%) was highest in the third (idiopathic) group. However, this was also a small series of children and should be confirmed in large-scale studies.

Fabre et al. study (30) suggests that since there are no uniform diagnostic criteria for LSV on cerebral ultrasound examination, application of apparent diffusion coefficient values to magnetic resonance imaging of the basal ganglia may contribute to the prediction of long-term outcome.

In conclusion**,** it has been proven that LSV is a relatively common finding on brain sonograms during routine ultrasound examination of newborns. Although studies suggest that the finding of LSV classified as low-grade LSV does

not represent a significant risk factor, caution is needed regarding possible CMV infection and neurological hearing impairment in asymptomatic children. Also, further, larger, prospective research is needed to assess the long-term impact of LSV on children's neurological development.

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