SONOGRAPHIC DIAGNOSIS OF SCHIZENCEPHALY IN A NEWBORN – CASE REPORT

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Abstract: *Schizencephaly is a rare neuronal migration disorder with diverse etiology and prognosis, occurring most often sporadically. Aim: report of a case of schizencephaly diagnosed using head ultrasound (HUS) in a neonate. Materials and methods: Immediately after birth, unilateral schizencephaly and agenesis of the septum pellucidum were accurately diagnosed in a newborn using US. Results: During the HUS screening performed in newborns presenting various pathology, a complex cerebral malformation – right sided, parietal, type I schizencephaly (closed lips), agenesis of the septum pellucidum, and mild ventriculomegaly – was diagnosed, confirmed subsequently by computer tomography in a newborn. No neurological symptoms were reported during the first 4 months of life. After 4 months, increased cerebral irritability and left sided paralysis were noted. Despite physiotherapy only improvement of the behaviour was observed. Conclusion: Head ultrasonography, performed with modern equipment, allows a diagnosis even more accurate than computer tomography even in cerebral malformations as schizencephaly.*

INTRODUCTION

Schizencephaly is a rare neuronal migration disorder (prevalence of 1/100.000 pregnancies (1)) characterized by the presence of a cerebral cleft filled with cerebrospinal fluid, extending from the pial sheath to the lateral ventricle wall, unilateral or bilateral. The edges of the cleft are limited by grey cerebral substance and can be fused – schizencephaly type I, with fused/closed lips – or opened – schizencephaly type II, with opened lips.

The etiology of the malformation is unclear, complex, most probably multifactorial, vascular, genetic, toxic, metabolic, and infectious factors being involved. Very often, schizencephaly is associated with other cerebral malformations like hydrocephaly/ventriculomegaly, pachygyria, polymicrogyria, lissencephaly, heterotopias, septo-optic dysplasia, septum pellucidum agenesis, optic nerve hypoplasia, callosal agenesis/hypoplasia, arachnoid cysts.

Diagnosis is, essentially, imagistic, magnetic resonance imaging being the elective method due to multiplanar approach of the abnormality and a better discrimination between the white and grey substance. Clinically, schizencephaly is evolving typically, in most of the cases, with seizures, paresis, and developmental deficits, the severity of the anomalies being correlated with the extent of the malformation. Treatment is addressing clinical problems.

PURPOSE

The authors are presenting the case of an infant diagnosed with a complex cerebral malformation accurately using head ultrasonography.

CASE REPORT

This is the report of a newborn diagnosed during the third day of life with a complex cerebral malformation. Head ultrasonography described the malformation more accurately than cranial computer tomography. The course of the child over the first 5 years of life is presented. Authors are also shortly reviewing the data in the literature regarding prevalence, etiology, diagnosis, imaging, clinical picture, treatment, and outcome of schizencephaly.

Male neonate, L.D., birth weight 2730 g, height 50 cm, cranial circumference 30 cm, vaginally delivered, in cranial presentation, Apgar score 9 at 1 minute was evaluated during the first day of life for suspicion of maternal-fetal infection (spontaneous rupture of the amniotic membranes 48 hours before delivery, feeding difficulties, abnormal tone). The neonate was born after a physiologic pregnancy, with incomplete follow up at the family physician. The parents and the 5 brothers and sisters at home were all healthy. Investigations confirmed maternal-fetal infections, most probably with *Escherichia Coli*, isolated in the gastric aspirate, and intravenous treatment with Penicillin G and Netromycin was started. Head ultrasonography, performed as routine screening in neonates with pathology, identified a complex cerebral malformation: right sided, parietal, type I schizencephaly, agenesis of the septum pellucidum, and mild ventriculomegaly of the lateral ventricles (figures no. 1-4). During the third day of life, cranial computer tomography confirmed the diagnosis (figures no. 5,6).

The clinical course of the newborn was favourable under antibiotic treatment, with normalization of the inflammatory tests. Repeated neurological examinations were normal, without critical manifestations, therefore the infant was discharged with recommendation for neurological monitoring.
Growth and neurodevelopment of the infant were normal up to the age of 4 months and a follow-up head ultrasonography showed no progression of the ventriculomegaly. At 4 months, the infant presented significant irritability and onset of a motor deficit on the left side of the body (hemiparesis). Physiotherapy was started and monitoring of the child was continued with a more complex team involving pediatric neurologist, physiotherapist and psychologist. No seizures – clinical or on

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electroencephalography - were noted up to the age of 5 years, behavioural disturbances disappeared but left hemiparesis persisted.

Figure no. 1. Right sided, parietal schizencephaly type I (posterior coronal scan)

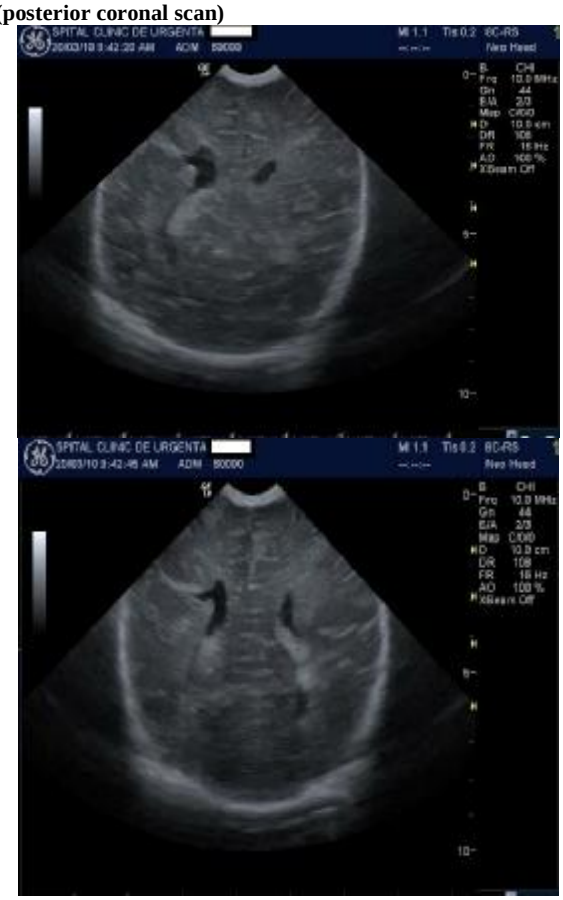


Figure no. 2. Atrial and occipital deformity of the lateral ventricle due to schizencephaly cleft (lateral sagittal scan)

DISCUSSIONS

Schizencephaly is a rare neuronal migration disorder characterized by the presence of a cerebral cleft filled with cerebrospinal fluid, limited by grey matter, crossing the entire cerebral hemisphere from the surface (pia mater) to the ventricular ependyma. The cleft may be seen on one or both sides of the brain. According to the type of cleft, two types of schizencephaly are described: type I – with fused/closed lips, a more subtle, rarer, and more difficult to diagnose abnormality – and type II – with opened lips, more frequent and easier to identify on imaging.(2-4)

Figure no. 3. Schizencephaly cleft seen through the posterior fontanel

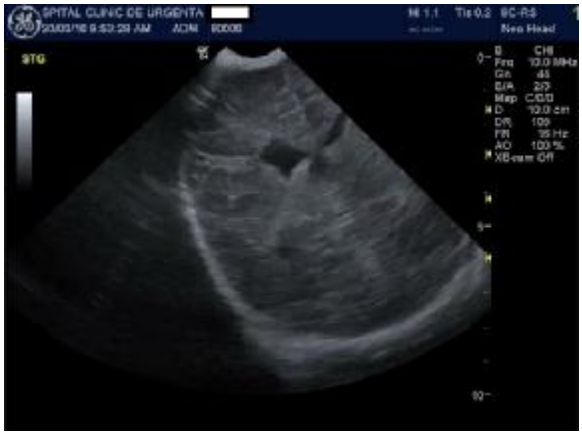


Figure no. 4. Absent septum pellucidum (median coronal scan)

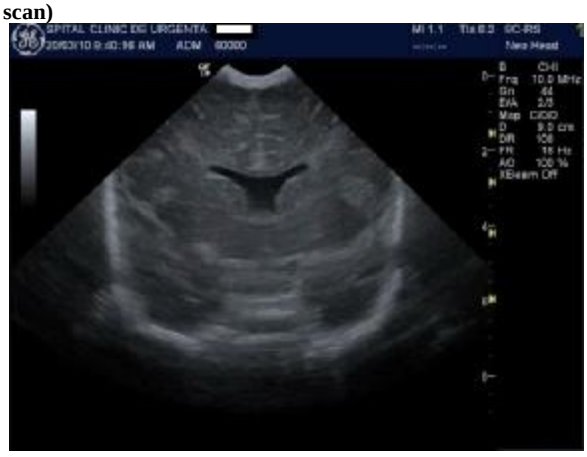


Figure no. 5. Cranial CT – right sided parietal cleft

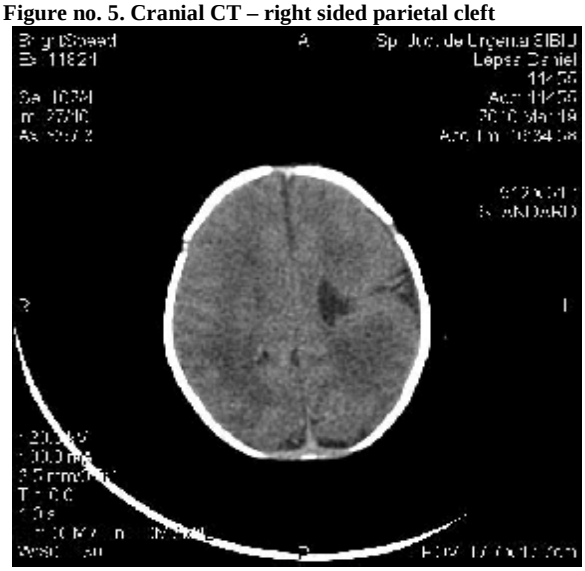
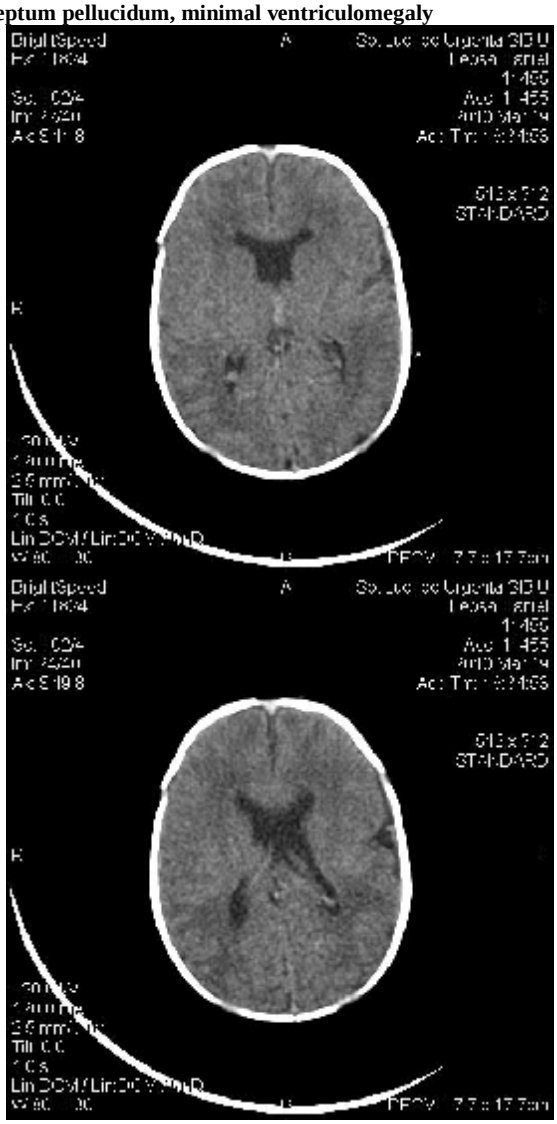


Figure no. 6. Cranial CT – right sided parietal cleft, absent septum pellucidum, minimal ventriculomegaly



The condition was described for the first time in 1887 by Wilmart.(5) In 1946, in two different studies, Yakolev and Wadsworth (6,7) described type I schizencephaly, and type II, respectively. The prevalence of schizencephaly is not well known.(8) In 2005, Curry et al.(9) estimated a prevalence of 1.54/100.000 pregnancies. A more recent study, published in 2012 by Howe et al (10) estimated that schizencephaly occurs with a prevalence of 1.48/100.000 deliveries and showed that prenatal identification of the defect is possible in 47% of the cases. Data in the literature estimate that schizencephaly is representing 3-11% of the congenital defects of the mantle and cerebral cortex.(11)

Most of the cases published in the literature are sporadic but familial cases were also reported (11), suggesting, in these cases, a genetic etiology. The great majority of the authors are accepting the vascular theory suggested by Barkovich and Norman (12) for the etiology of schizencephaly. According to this theory, the cerebral cleft occurs secondary to an infarct in the germinal matrix during the seventh week of pregnancy. Starting the eight week of pregnancy neuronal migration begins (from the germinal matrix), under radial glial cells, in order to form the cerebral cortex. Other authors are extending the cerebral vulnerability period for cerebral clefts from the first to the fifth month of pregnancy.(8,11)

A multifactorial etiology is suspected for schizencephaly with multiple possible factors involved: genetic (in familial cases but also in some sporadic cases; mutations of the homeobox gene EMX2 on the chromosome 10q16.1 were incriminated), toxic, metabolic, vascular (through drugs – warfarin, recreational drugs, exposure to organic solvents -, through abdominal trauma during pregnancy, associated with alloimmune thrombocytopenia, or in various syndromes), and infectious (as, for example, cytomegalovirus infection).(2,3,8,10,11,13)

Usually, the cerebral cleft is almost never the only cerebral anatomic anomaly. Often, beside the hemispheric cleft, a communication between the subarachnoidian space and homolateral lateral ventricle, folding, and abnormalities of the grey substance on the edges of the cleft may be identified.(8,11) Absent septum pellucidum is seen in association with schizencephaly in 80-90% of the cases.(2,3,8) Other cerebral anomalies described in association with schizencephaly are: hydrocephaly, pachygyria, polymicrogyria, lissencephaly, heterotopias, septo-optical dysplasia (de Morsier syndrome), optic nerve hypoplasia, abnormalities of the corpus callosum (hypoplasia, agenesis), arachnoid cysts.(2,3,8,10,11,13)

Diagnosis of schizencephaly, including differential diagnosis, is performed by imaging. Magnetic resonance imaging (MRI) is the most accurate imagistic technique for schizencephaly and associated anomalies since it allows optimal visualization of the cleft, good discrimination of the white and grey cerebral substance and a multiplanar view of the lesion.(1,2,3,8,11) Thus, identification of the grey matter on the edges of the cleft allows differentiation between type II schizencephaly and porencephaly.(8,11) Also, MRI offers details of the subcortical anatomy, heterotopias, and cortical anomalies (pachygyria, polymicrogyria etc.) and allows evaluation of the homolateral sylvian vascularization (often absent), of the small medular pyramids, fornix position (often in a lower position), the aspect of the corpus callosum.(1,2) Use of MRI in neonates is limited by the need for sedation, costs, difficulties of execution, and longer duration of the study.(1)

With ultrasound, in schizencephaly type I the diagnosis is difficult but an echogenic line can be observed (the cortex on the cleft edges) from the parasylvian region to the ventricular ependyma. In type II schizencephaly the sonographic diagnosis is easier: a band or an anechoic cavity (the cleft filled with cerebrospinal fluid) from the cortex surface to the lateral ventricle and at the site of contact with the lateral ventricle the aspect is similar to a diverticulum or ventricular hole. Also, the thalamic and lenticular nuclei are smaller and ventriculomegaly is often associated.(1)

Cranial computer-tomography is not so helpful in type I schizencephaly as it doesn't allow an accurate estimate of the cleft width but may be useful for evidencing other associated cerebral abnormalities (hydrocephaly, heterotopias, polymicrogyria, subdural hygroma, arachnoid cysts).(1,3)

Differential diagnosis of type II schizencephaly implies differentiation from porencephalic cysts, ventriculomegaly, holoprosencephaly, corpus callosum agenesis associated with interhemispheric cyst, hydranencephaly.(3,11,13)

Prenatal diagnosis is possible most often after the 22 week of gestation, in severe cases, and is useful for parental counseling and pregnancy management.(3,10,11,13)

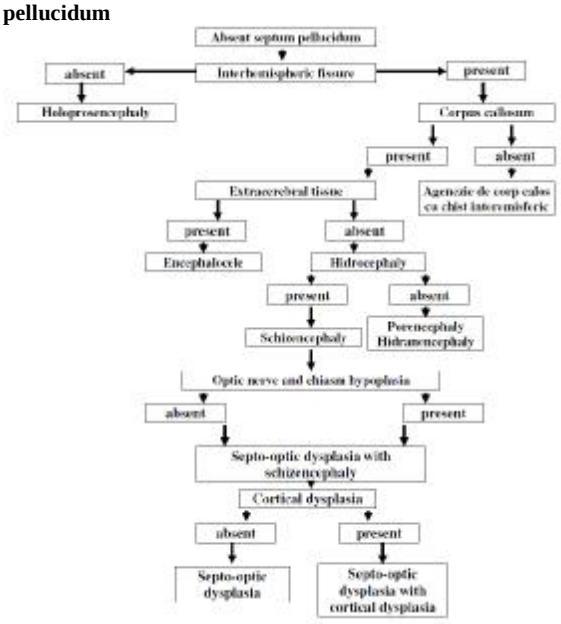
Clinically, schizencephaly evolves, in most of the cases, with the triad: seizures, paresis, and developmental deficits (1,2,8,11,13), the severity of the symptoms being

proportional with the extent of the lesion.(1,3,8,13) Seizures are occurring in 33-57% of the cases (11), mostly in type II, and are, sometimes refractory to treatment. Neurological and behavioural abnormalities are reflecting the site of the lesion.(13) Paresis is unilateral or bilateral and is often associated with cognitive, language and sensorial deficits.(11) Microcephaly (8,11), bipolar disorders (2), psychotic manifestations (14) were also cited. Usually, in type I schizencephaly the neurological deficit is minor, seizures have a late onset and resistant to treatment, school attendance is possible, and survival is prolonged.(12,13) In schizencephaly type II, the neurological deficit is severe, seizures are rare but easy to treat, academic performances are often affected, and survival is limited.(13)

The treatment is addressed to symptoms and comprises anticonvulsants and physiotherapy. In cases associated with hydrocephaly, ventriculo-peritoneal shunting may be necessary.(8)

The prognosis is unfavourable in the type II schizencephaly – early death due to growth failure, chronic infections, and respiratory problems.(12)

Figure no. 7. Diagnosis algorithm in absent septum pellucidum



In the presented case, ultrasonography proved to be more accurate than computer tomography in describing the complete picture of the cerebral malformation. Association with absent septum pellucidum is often cited in the literature and the diagnosis algorithm suggested by Barkovich and Norman (15) was usefully for the classification of schizencephaly (figure no. 7). Since the eye examination was normal, the final diagnosis of the presented case was schizencephaly associated with agenesis of the septum pellucidum.

CONCLUSIONS

Head ultrasound used initially as screening diagnostic tool in a newborn with infectious perinatal pathology allowed early accurate identification of a severe cerebral anomaly – schizencephaly associated with agenesis of the septum pellucidum. Therefore, careful monitoring allowed early intervention for optimization of the long term outcome.

REFERENCES

1. Close KR, Naul LG. Schizencephaly Imaging. 2015; http://emedicine.medscape.com/article/413051-overview; accesed January 2016.
2. Kalia V, Saggar K Vibhuti. Schizencephaly. J. K Science. 2009;11(2):108.
3. Bhatnagar S, Kuber R, Shah D, Kulkarni VM. Unilateral Closed Lip Schizencephaly with Septo-Optic Dysplasia. Ann Med Health Sci Res. 2014;4(2):283-5.
4. Rajderkar D, Phatak SV, Kolwadkar PK. Septo-optic dysplasia with unilateral open lip schizencephaly: A case report. Indian J Radiol Imaging. 2006;16:321-3.
5. Wilmarth WA. Presentation to the Philadelphia Neurological Society. J Nerv Ment Dis. 1887;395-407.
6. Yakolev PI, Wadsworth RC. Schizencephalies: a study of congenital clefts in the cerebral mantle. II. Clefts with hydrocephalus and lips separated. J Neuropathol Exp Neurol. 1944;5:169-206.
7. Yakovlev PI, Wadsworth RC. Schizencephalies: a study of the congenital defects in the cerebral mantle. I. Clefts with fused lips. J Neuropathol Exp Neurol. 1946;5:116-30.
8. Pradhan M, Malla KK, Chowdhury SR, Baral MR. Case of Schizencephaly: a case report. Kathmandu University Medical Journal. 2003;2(3/7):234-7.
9. Curry CJ, Lammer EJ, Nelson V, Shaw GM. Schizencephaly: heterogeneous etiologies in a population of 4 million California births. Am J Med Genet A. 2005;137:181-9.
10. Howe DT, Rankin J, Drape ES. Schizencephaly prevalence, prenatal diagnosis and clues to etiology: a register-based study. Ultrasound Obstet Gynecol. 2012;39:75-82.
11. Pascual-Castroviejoa I, Pascual-Pascuala SI, Velazquez-Fraguaa R, Vianob J, Quinones D. Schizencephaly: A study of 16 patients. Neurologia. 2012;27(8):491-9.
12. Avcu S, Özen Ö, Ünal Ö. Bilateral giant open lip schizencephaly with associated cerebral anomalies: a case report. Cases Journal. 2009;2:7012.
13. Oh KY, Kennedy AM, Frias AE Jr, Byrne JL. Fetal Schizencephaly: Pre- and Postnatal Imaging with a Review of the Clinical Manifestations. RadioGraphics. 2005;25:647-57.
14. Alexander RC, Patkar AA, Lapointe JS, Flynn SW, Honer WG. Schizencephaly associated with psychosis. J of Neurology, Neurosurgery, and Psychiatry. 1997;63:373-5.
15. Barkovich AJ, Norman D. MR imaging of schizencephaly. AJR Am J Roentgenol. 1988;150:1391-6.