Clinical Findings in 16 Patients With Tomographic Diagnosis of Schizencephaly*

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Abstract

Objective: To establish a correlation between clinical features in a group of children with tomographic diagnosis of schizencephaly and clefts extent and localization. Materials and Methods: Retrospective study of 16 patients, nine female and seven male, with tomographic diagnosis of schizencephaly investigated for clinical findings, psychomotor development, motor/cognitive deficits and epilepsy. Results: Prematurity of male clefts was frequent (10:16 patients). As regards clinical findings, 15 patients presented with developmental delay and motor deficit, six patients with cognitive deficit and ten with epilepsy. Three patients, we observed discordant clinical findings and cleft sizes, although the clefts were small, the clinical features severity was high because of other cerebral anomalies. Conclusion: The clinical features of schizencephaly are related to the size of the clefts, regardless laterality, presenting higher severity when associated with other cerebral anomalies.

Keywords: Schizencephaly; Computed tomography; Clinical findings.

INTRODUCTION

Schizencephaly(1) is an extremely rare congenital disorder characterized by a full-thickness cleft within the cerebral hemispheres, delimited by an abnormal cortex extending from the ventricular surface to the arachnoid space.(3,4) Frequent, schizencephaly involves the perisylvian regions(2,3) and large portions of the cerebral hemispheres may be absent and replaced by fluid.(2)

Presentations are highly variable, depending on the clefts extent and localization, but patients present from a normal intelligence to convulsions and severe neurological involvement.(2,3,5,6) The differential diagnosis should take into consideration holoprosencephaly(7), porencephaly(7,9), hydranencephaly(7,9,10) and subarachnoid cysts(9,10).

Dubey et al.(7) have reported the cardinal characteristics of schizencephaly: a hemispheric cleft delimited by an usually bilateral ependymal-pia sheath in the perisylvian region; a cleft lined by gray-matter linking the subarachnoid space with the ependyma of the lateral ventricle, and the association with multiple intracranial anomalies such as polymicrogyria, heterotopias, absence of pellucid septum, optic nerve hyperplasia and corpus callosum agenesis.
The majority of cases described are of a sporadic nature, although there are reports on familial cases\(^3\,^6\). Some authors\(^3\,^3\,^6\) have described homeotic gene EMX2 (Empty Spiracles, Drosophila, 2, Homolog of) mutations in patients with schizencephaly.

Many features of schizencephaly still remain obscure, such as etiology, developmental mechanisms and stages involved in the disorder pathogenesis. Data reported in specialized scientific publications indicate towards a heterogeneously anomalous pathogenesis and etiology, describing genetic and environmental causes, abnormal cerebral morphogenesis resulting from disruptive factors, and cell proliferation and/or neuronal migration defects, neuronal migration and/or cortical organization defects and cortical areas specification defects.

Amongst the diagnostic imaging methods, computed tomography (CT) may detect the characteristic findings, although magnetic resonance imaging (MRI) is the gold standard method for a more detailed anatomical evaluation\(^9\). However, MRI disadvantages are its high cost and inaccessibility for the general population\(^18\).

The objective of the present study was to establish a correlation between clinical features in a group of children with tomographic diagnosis of schizencephaly and clefts extent and localization.

**MATERIALS AND METHODS**

Retrospective study of dossiers of patients with tomographic diagnosis of schizencephaly from the archives of Neurology and Medical Genetics Services at Instituto Fernandes Figueira/Fiocruz (IFF-Fiocruz) and Hospital Municipal Jesus (SUS/RJ), Rio de Janeiro, RJ, Brazil, in the period between 2000 and 2003. Of an initial group of 28 patients, 12 were excluded due impossibility of contact or refusal from the part of the patients’ family to include them in the study. Of the remaining 16 patients, nine were female and seven were male. Terms of Free and Informed Consent were signed by all the persons responsible for the patients and the research was approved by IFF/Fiocruz National Committee of Ethics in Research (process no. 208/2002) and Comissão Nacional de Ética em Pesquisa (Conep) (process no. 4912/2002).

The following clinical parameters were analyzed: neuropsychomotor development, motor deficit, cognitive deficit (in school-aged children) and the presence of epilepsy (type of convulsive crisis, refractoriness to antiepileptic drugs).

Cranial CT studies of each patient were independently analyzed by two examiners and only those presenting diagnostic agreement were included in the present study. The Barkovich & Kjos\(^5\) criterion was adopted for classification of schizencephalic clefts, considering the cleft type (open-lip or closed-lip) and size (small, medium or large).

**RESULTS**

The data on the clinical-tomographic correlation are summarized in Table 1. Twenty-seven clefts were observed in the 16 patients. As regards the sizes of the clefts, 14:27 were small (Figure 1), 11:27 were large (Figure 1) and 2:27 were medium (Figure 2). As regards localization, parietal clefts predominated (16:27), followed by frontoparietotemporal clefts (5:27). As regards laterality, bilateral clefts predominated (Figures 1, 2 and 3) in 10:16 patients, 5:10 patients presenting open-lip clefts and 5:10 with open and closed (or fused)-lip clefts (Figure 3). Of six patients with unilateral clefts (Figure 4), five presented open-lip clefts.

Periventricular calcifications (Figure 4) were observed in 3:16 patients, all of them presenting negative serology for congenital TORCH infection.

Thirteen of 16 patients presented other central nervous system anomalies associated with schizencephaly, the pellucid septum absence (Figure 1) and cortical dysplasias (Figure 5) being the most frequent findings respectively in 10:13 patients and in 4:13 patients.

Neuropsychomotor development delay was present in 15 patients and six school-aged patients also presented cognitive defi-

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<tr>
<td>1</td>
<td>Open-lip, medium, unilateral</td>
<td>NPMD delay, spastic tetraparesia, axial hypotonia, Babinski’s reflex, epilepsy</td>
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<td>2</td>
<td>Open-lip, large, unilateral</td>
<td>NPMD delay, right hemibody spasticity</td>
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<td>Open-lip, large and small, bilateral</td>
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<td>Open-lip, large, unilateral</td>
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<td>6</td>
<td>Open-lip, one large and two small, bilateral</td>
<td>NPMD delay, spastic tetraparesia, difficult-to-control epilepsy</td>
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<td>7</td>
<td>Open-lip, large and closed-lip, bilateral</td>
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<td>Open-lip, large, unilateral</td>
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<td>Open-lip, small, unilateral</td>
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<td>Open-lip, large and closed-lip, bilateral</td>
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<td>13</td>
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<td>Normal, epilepsy</td>
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<td>14</td>
<td>Open-lip, small and closed-lip, bilateral</td>
<td>NPMD delay, cognitive deficit, spastic tetraparesia, difficult-to-control epilepsy</td>
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<td>15</td>
<td>Open-lip, large, bilateral</td>
<td>NPMD delay, spastic tetraparesia, difficult-to-control epilepsy</td>
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<tr>
<td>16</td>
<td>Open-lip and closed-lip, small, bilateral</td>
<td>NPMD delay, spastic tetraparesia</td>
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NPMD, neuropsychomotor development.
Clinical findings in 16 patients with tomographic diagnosis of schizencephaly

cit. Neurological examination detected anomalies in 15:16 patients, the most frequent finding being pyramidal release signs (spastic tetraparesia) in 11:15 patients. Amongst the 16 patients, ten presented epilepsy, with the first crisis onset in the first year of life of 4:10 patients. The most frequent type of seizure was the generalized tonic-clonic one, reported in 5:10 patients. Epilepsy was difficult to control in 6:10 patients.

DISCUSSION

The clinical feature severity was related to the affected cortical area, both in patients with bilateral and unilateral clefts, according data reported in the specialized scientific literature\(^\text{2,3,5,6}\). Although clefts in three of our patients were small, the clinical feature was severe as a result of the presence of other cerebral anomalies associated with schizencephaly. Therefore, our data suggest that the clinical feature is also related to the presence of other central nervous system anomalies, corroborating the findings of Granata et al\(^\text{13}\).

The clinical feature was in agreement with data reported by other authors\(^\text{6,9,14,15}\), with the majority of patients presenting motor deficit and neuropsychomotor development delay\(^\text{8,9}\).

Also, we have observed that epilepsy was more frequent and severe in patients with a more significant loss of cortical area, an aspect that has not been described in the studies of Barkovich & Kjos\(^\text{5}\), Granata et al\(^\text{14}\) and Denis et al\(^\text{15}\).

In a comparative analysis of the tomographic data, there was an agreement with data reported by other authors as regards laterality\(^\text{5}\), cleft type\(^\text{5,9}\) and localization and size\(^\text{5,14,15}\). Amongst associated anomalies, pellucid septum absence was our most frequent finding, similarly to the findings reported by other authors\(^\text{9,10,13}\).

Although the presence of cleft(s) is significant for determination of the neurological picture, in some cases there was disagreement between the cleft extent and
clinical findings, as result of the presence of other cerebral anomalies associated with schizencephaly.

REFERENCES