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Multidisciplinary Approach in a Patient with Encephalocele and Agenesis of the Corpus Callosum due to Pai Syndrome: A Case Study

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Abstract

Introduction: *Pai Syndrome is a rare condition characterized by midline craniofacial anomalies. The occurrence of encephalocele has been described but is not shared. The signs of the triad include cleft lip, skin polyps on the face, and lipoma in the central nervous system. The aim here is to present a case of a patient diagnosed with Pai Syndrome in association with encephalocele.*

Case Presentation: *A patient aged three years and five months old had a frontal encephalocele treated by surgery in October 2020at another health service. After genetic evaluation, the diagnostic hypothesis of Pai Syndrome was obtained. This syndrome includes agenesis of the corpus callosum, hypertelorism, and, in this case, frontal encephalocele. Before the surgery, the patient was assessed through clinical observation, and neuropsychomotor development, and behaviors within the normal range for her age group were observed. Postoperatively, the patient exhibited a favorable recovery but progressed with speech delay and is currently undergoing multidisciplinary treatment. These midline anomalies are directly related to embryological processes that induce frontonasal dysplasia, and the association between encephalocele and hypertelorism is possible, as in this case report. Affected patients may also present symptoms later in life, such as delayed neuropsychomotor development.*

Conclusion:*According to the literature, delayed neuropsychomotor development symptoms can appear late. Despite good motor development and an excellent post- operative evolution, the patient evolved with delayed speech development. Thisreinforces the importance of multidisciplinary monitoring of patients with Pai Syndrome to minimize possible damage to quality of life.*

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Introduction

In 1897, Pai et al. noticed a complete cleft lip, skin polyps, and lipomas in a patient's central nervous system (CNS); when they described the combination of these three clinical findings, they characterized Pai Syndrome as a form of frontonasal dysplasia. This syndrome is estimated to be 1 in every 20,000 to 40,000 live births [1,2].

Concerning the syndrome's etiology, Olivero et al. elucidated the possibility of autosomal dominant and recessive inheritance linked to the X chromosome. However, the authors generally point out that there is no precise information on the etiology or prevalence of gender in this condition [3,4].

Several studies agree that there is vast phenotypic variability in Pai Syndrome [3,5-7].However, it is associated with various facial anomalies involving the anterior skull based the meninges due to malformation of the embryonic mesenchyme [3].

For this reason, it is common to find case reports describing the appearance of encephalocele and agenesis or hypoplasia of the corpus callosum [3,4,5,8].

Due to this variability, there is no consensus on the diagnostic criteria, but it is usually diagnosed at birth through neuroimaging tests, which are necessary to screen for anomalies associated with the corpus callosum [1,3-7,9,10].

The basis of the treatment is surgical, with an aesthetic nature, in the removal of skin polyps, and functional when there is a cleft lip [3,4].

As a result, there are still gaps in the clinical picture of Pai syndrome. These gaps extend to the cognitive and neuropsychomotor development of patients due to the small number of cases with published long-term follow-up, making it impossible to observe developmental delays that may be associated with the clinical picture, as pointed out by different authors [3,4,9,10].

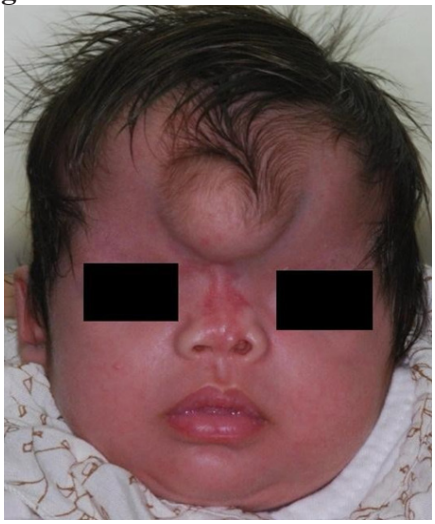
Considering the problem described above, we understand the importance of the present study, which aims to describe the development of a patient with Pai Syndrome, associated with neurological characteristics, encephalocele, and agenesis of the corpus callosum, through the perspective of neuropsychology, little referred to in the literature on the subject.

Case Report

"A 03-year-old and five-month-old female was born by Caesarean section at 39 weeks gestation, weighing 2,393g and 44cm, with immediate crying. The mother said she had prenatal care and had used antidepressants in early pregnancy, as well as having developed gestational diabetes. An amniocentesis was carried out in the fifth month of pregnancy, which showed no alterations.

At birth, cranioencephalic alterations were observed, and in the first month and14 days of the patient's life, a genetic evaluation was carried out, which found frontal encephalocele, hypertelorism, agenesis of the corpus callosum, epicanthus and telecanthus, submucosal fissure, rare Tessier fissure 0-14, hemangioma in the frontonasal region (Figure 1). On this occasion, it was not possible to carry out a direct assessment of neuropsychomotor development (NPMD). However, through a semi-structured interview with the person responsible, no complaints were observed regarding the individual’s development.

Figure 1: The Patient with 3 Months old.



After this assessment, the diagnostic hypothesis of Pai Syndrome was obtained, manifested with agenesis of the corpus callosum (Figure 2), hypertelorism, and frontal encephalocele (Figure 3).

Figure 2: MRI in Axial Section, where Agenesis of the Corpus Callosum can be Observed.

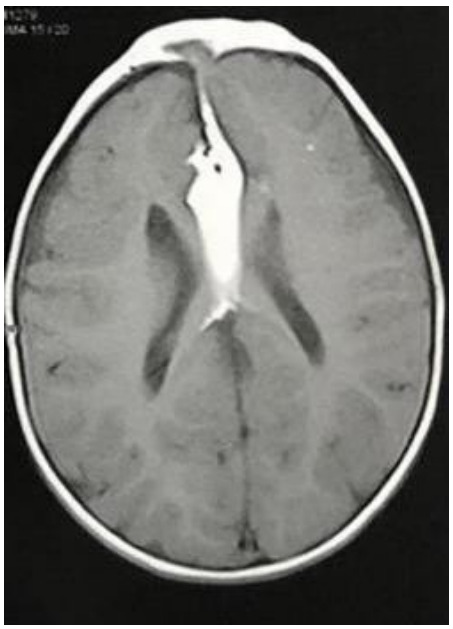
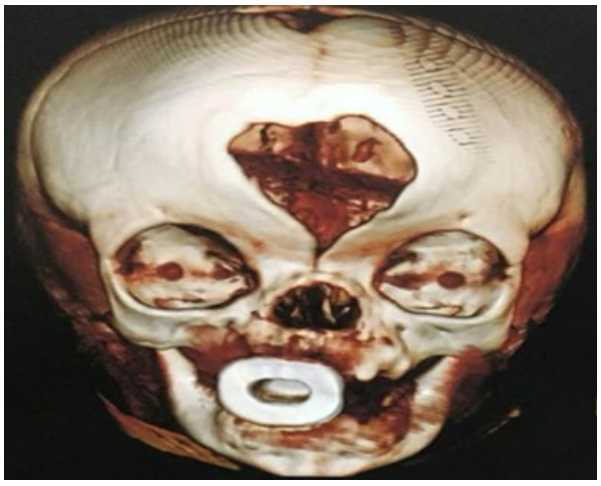


Figure 3: Skull Tomography of the Patient Indicating Hypertelorism and Frontal Encephalocele.



In October 2020, at the age of 11 months, she underwent a surgical procedure to treat frontal encephalocele and is currently awaiting frontal remodeling. At three years and five months, she was assessed by the Psychology Department of the Craniofacial Anomalies Rehabilitati on Hospital, where they carried out a post-Surgi neuropsychological assessment using the Dimensional Inventory for the Assessment of Child Development (IDADI).

This instrument assesses child development through parental reports from zero to72 months of age, covering the Cognitive, Motricity (broad and exemplary),Communication and Language (receptive and expressive), Socio-emotional, and Adaptive Behavior domains. The score follows the pattern of 2 points for ""Yes,"" 1 point for ""Sometimes,"" and 0 points for ""Not yet"" for the skills described in the inventory. Finally, each sub-item is classified quantitatively and qualitatively according to the criteria in the instrument's manual [11].

It was possible to conduct a clinical observation with the interview, which revealed an individual with agitated and irritable behavior. Through the IDADI, the individual scored well below expectations in the Cognitive, Socio-emotional, Receptive Communication and Language, Expressive Communication and Language, Broad Motricity, and Adaptive Behavior domains. Moreover, the result was within expectations in the Fine Motricity domain. These results suggest that the individual evolved with a global delay in NPMD after encephalocele correction surgery.

The person responsible reports that the individual has been attending nursery school for one year and is undergoing rehabilitation with speech and occupational therapy professionals. It is worth mentioning that the individual is still being monitored by the Craniofacial Team, composed of craniofacial surgery, neurosurgery, psychology, orthodontics, speech therapy, genetics, and social work. "

Discussion

Pai Syndrome has a significant variability of phenotypes, and although it has been described for some time, it is not common to find reports with longitudinal information on the individuals diagnosed [3,5-7].

One rationale would be the potential underreporting of cases due to their association with various facial anomalies that also originate in the embryonic mesenchyme and because they do not necessarily exhibit the three main characteristics postulated by Pai et al [1,3,5].

Among the other alterations associated with the syndrome, some authors commonly describe the presence of encephalocele and agenesis or hypoplasia of the corpus callosum, as described in this case [3-5,8].

Considering the case described, it was possible to observe significant craniofacial alterations at birth. Nevertheless, genetic evaluation is essential to a more thorough examination and to investigate potential alterations in the CNS.

Although there were no complaints at birth about the NPMD and the individual had been exposed to continuous monitoring, surgical treatment in an appropriate period, and intervention by a multi-professional team, after surgery to correct the encephalocele, at 11 months, she evolved with global delay.

In the studies by Morice et al.no changes in NPMD were observed in the sample evaluated. Despite this, the authors point out that the NPMD is not widely explored in Pai syndrome and that many other associated conditions can cause neuropsychological delays and deficits[3]. This can be seen in the case of the individual diagnosed with Autism Spectrum Disorder(ASD) after an assessment in his hometown. These characteristics are compatible with the finding of corpus callosum agenesis. According to Lábadi and Beke due to changes in interhemispheric connections patients with corpus callosum agenesis have difficulties perceiving paralinguistic aspects and metaphors, which are essential for interpreting receptive language, aspects present in social cognition, and the same characteristics can be observed in patients with ASD [12,13].

Conclusion

Given the clinical findings described above, it is deduced that Pai Syndrome warrants additional examination owing to its considerable variability, highlighting the need for refined diagnostic approaches. Consequently, the documentation of clinical cases with longitudinal assessment, as exemplified in this study, plays a crucial role in characterizing the syndrome, given its multisystemic prognosis. Furthermore, it underscores the significance of multidisciplinary collaboration and care in ensuring a high quality of life for affected individuals.

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