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Case Report

Acalvaria in a patient with neurofibromatosis type-1: Case report

Daniel Antunes Pereira[1]

Shara Aline Bueno Dantas[2]

Marco Antônio Orsini Neves[3]

Gilberto Canedo M. Jr[4]

Roberta Araújo de Arruda Camara[5]

Antonio Marcos da Silva Catharino[6]

[1]Medical student at Iguaçu University. Iguaçu University - UNIG / RJ, Nova Iguaçu - RJ, Brazil.

[2]Medical student at Iguaçu University. Iguaçu University - UNIG / RJ, Nova Iguaçu - RJ, Brazil

[3]Physician, Neurologist, Adjunct Professor of Medicine at Universidade Iguaçu, Iguaçu University - UNIG / Nova Iguaçu, RJ,Brazil

[4]Professor of Neurology - Universidade Iguaçu- UNIG-RJ, Nova Iguaçu - RJ; Physician of the Neurology Service of Nova Iguaçu General Hospital, Nova Iguaçu, RJ, Brazil

[5]Professor at Iguaçu University – UNIG – Radiologist at Hospital Geral de Nova Iguaçu, Nova Iguaçu, RJ, Brazil.

[6]Department of Neurology of Hospital Geral de Nova Iguaçu, PhD student in Neurology at the Federal University of the State of Rio de Janeiro - UNIRIO, Adjunct Professor of Medicine at Iguaçu University - UNIG / Nova Iguaçu, RJ, Brazil.

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ABSTRACT

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a heterogeneous disorder of autosomal dominant inheritance. It is characterized by neurofibromas, skin and skeletal changes, and multiple organs and systems involvement. Acalvaria is a rare condition of congenital malformation, usually defined by the absence of the flat bones of the skull, adjunct musculature and dura mater. It is a fatal condition and accompanied by other abnormalities in most cases. The most widely accepted theory suggests that acalvaria is a post-neurulation defect in which there would be a change in mesenchymal tissue migrations but normal ectoderm development.

CASE REPORT

How to Cite

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We present the case of a patient with NF1 with a report of a convulsive crisis, who, on examination, showed depression in the posterior portion of the skull, facial asymmetry, diffuse fibromatous lesions, Café au lait macules (CALMs), bilateral horizontal nystagmus and left upper limb hyperreflexia. A cystic mass was identified in the posterior region and agenesis of the occipital bone through imaging, characterising acalvaria.

CONCLUSION

Most calvaria defects are often associated with a mass lesion, typically a plexiform neurofibroma, However, the correlation between abnormalities of the lambdoid suture or occipital bone with NF1 is rare. In contrast, total loss of the NF1 gene is likely to be correlated with focal congenital events, as seen in this patient. This case report reinforces the embryonic theory of acalvaria and correlates the possibility of mutations in the NF1 gene.

Keywords: Acalvaria; acrania; Neurofibromatosis type 1; occipital dysplasia

INTRODUCTION

Neurofibromatosis type 1, also called von Recklinghausen's disease, is the most common disease of three heterogeneous disorders, composed of schwannomatosis and neurofibromatosis type 2 (NF2). This group of syndromes has an autosomal dominant tumor predisposition and a preference for nervous system involvement. [1,2]

While NF1 is an autosomal-dominant inherited cancer syndrome, is fully penetrant without asympto-matic carriers or skipped generations, it occurs about half of the time in people who have no known family history. The NF1 is characterized by neurofibromas, skin and skeletal changes, and multiple organs and systems involvement. [3,4] Individuals with this disease have a higher incidence of skeletal abnormalities, and calvarial defects are uncommon and are thought to occur primarily near the lambdoid suture. [5,6] The prevalence of this disease worldwide is 1 case per 3,000 inhabitants and can vary between countries and regions. [4]

On chromosome 17q11.2, the NF1 gene is found. Its gene product, neurofibromin, is a tumor suppressor that inhibits cell proliferation pathways. These pathways are targets of current research and treatment. [7]

Café au lait macules are flat, hyperpigmented skin lesions that appear in childhood and are one of the diagnostic features of NF1 and Lisch nodules which are hyperpigmented hamartomas of the iris found in 95-100% of adults with this disorder. [1] Furthermore, Scoliosis, osteopenia or osteoporosis, sphenoid dysplasia and tibial dysplasia are common NF1-related orthopedic problems in early childhood. [2,8]

This case report relates agenesis of the occipital bone, compatible with acalvaria, in a patient with NF1. Acalvaria or acrania is a rare condition of congenital malformation, usually defined by the absence of the flat bones of the skull, adjunct musculature and dura mater. It is a fatal condition

Corresponding Author's: Antônio Marcos da Silva Catharino, Rua Gavião

and accompanied by other abnormalities in most cases. [9,10]

As for etiology and pathogenesis, the most widely accepted theory suggests that acalvaria is a post-neurulation defect in which there would be a change in mesenchymal tissue migrations but normal ectoderm development. [11]

CASE REPORT

A 30-year-old man with NF1 seeks neurological care due to a seizure report. Physical examination revealed depression in the posterior portion of the skull (figure 1), facial asymmetry, diffuse fibromatous lesions, café au lait spots, bilateral horizontal nystagmus, and hyperreflexia in the left upper limb. Cranial magnetic resonance imaging identified a large cystic formation in the posterior cranial fossa with signs of bone remodelling (figure 2). A skull radiograph demonstrated agenesis of the occipital bone compatible with acalvaria (figure 3). Treatment with oxcarbazepine was started with reasonable seizure control.

DISCUSSION

According to the case, the patient had a seizure, possibly due to a sizeable cystic formation in the posterior fossa. However, according to the literature, bone remodelling may or may not be linked to cystic lesions. [5] Vertebral morphostructural changes are also described in NF1 patients [8] Dysplasias of the skull occur, but they are almost always limited to the sphenoid region. Occipital dysplasias are highly uncommon, with only a few cases documented in the literature. [12, 13]

Correlation between abnormalities of the lambdoid suture or occipital bone with NF1 is rare. However, the cohort study by Arrington et al. [5] noted that most calvaria defects are often associated with a mass lesion, typically a plexiform neurofibroma.

Another relevant aspect regarding the pathogenesis of acalvaria and this disease is that heterozygous mutations in the NF1 tumor suppressor gene at 17q11.2[12,13] generate neurofibromas and several important interactions. In contrast, the total loss of the NF1 gene is probably correlated with congenital focal events, as seen in this patient. [12]

CONCLUSION

Head malformations correlated with NF1 are rare. Acalvaria in patients with such a disease is even rarer. This case report supports the theory that acalvaria is a post-neurulation defect in which there would be an alteration in the migrations of mesenchymal tissue. There may be a relationship with the loss or mutation of the NF1 gene.

FIGURE LEGENDS

Figure 1: depression in the posterior portion of the skull (arrow).

Figure 2: T2 Sagital magnetic resonance imaging identified a large cystic formation in the posterior cranial fossa with signs of bone remodeling (arrow).

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Figure 3: Skull radiograph (A – Sagital, B Coronal) showing midline parieto-occipital bone defect (arrows) compatible with acalvaria.

FIGURES

Figure 1: Depression in the posterior portion of the skull (arrow).

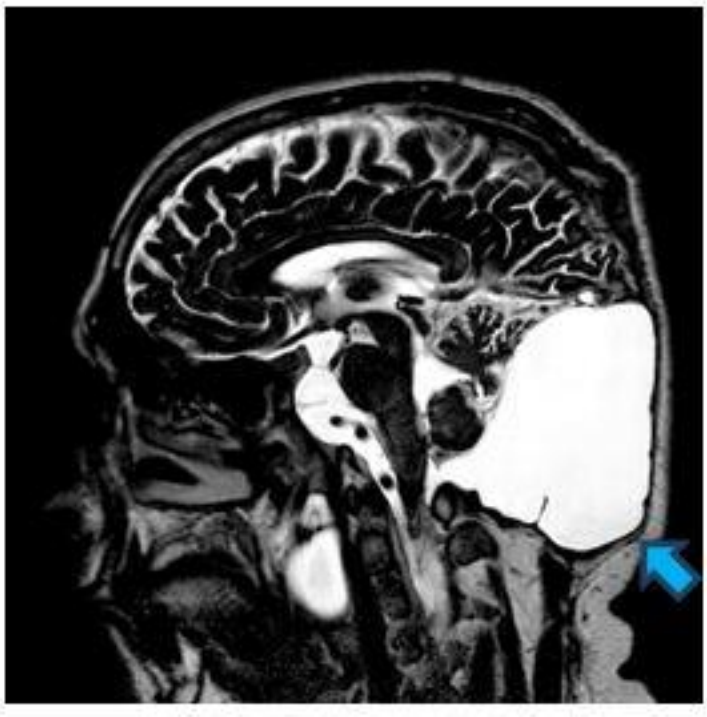

Figure 2: T2 Sagital magnetic resonance imaging identified a large cystic formation in the posterior cranial fossa with signs of bone remodeling (arrow)

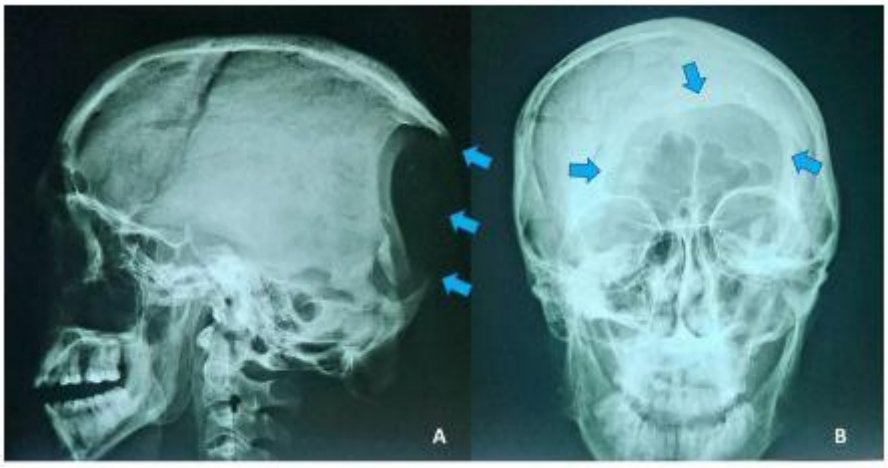

Figure 3: Skull radiograph (A – Sagital, B Coronal) showing midline parieto-occipital bone defect (arrows) compatible with acalvaria.

AUTHOR'S CONTRIBUTIONS

Daniel Antunes Pereira

Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data,

Revising the work critically for important intellectual content, Final approval of the version to be published,

Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Shara Aline Bueno Dantas

Analysis of data,

Revising the work critically for important intellectual content,

Final approval of the version to be published,

Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Marco Orsini

Acquisition of data, Analysis of data,

Drafting the work, revising the work critically for important intellectual content,

Final approval of the version to be published,

Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Gilberto Canedo M. Jr

Acquisition of data, Analysis of data,

Revising the work critically for important intellectual content, Final approval of the version to be published,

Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or

Corresponding Author's: Antônio Marcos da Silva Catharino, Rua Gavião

integrity of any part of the work are appropriately investigated and resolved.

Roberta Araújo de Arruda Camara
Analysis of data,
Drafting the work, Revising the work critically for important intellectual content,
Final approval of the version to be published,
Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Antônio Marcos da Silva Catharino
Analysis of data,
Revising the work critically for important intellectual content,
Final approval of the version to be published,
Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST

There is No conflict of interest.

Corresponding Author's: Antônio Marcos da Silva Catharino, Rua Gavião