


CASE REPORT

Cutis verticis gyrata: Two cases associated with drug-resistant epilepsy

Maria Rattagan¹ | Maria De Francesco^{1,2} | Antonio Kriebaum¹ | Fernando Ferraro³ | Catherine Major⁴ | Deepak Sharma⁴ | Andrew Ojeda⁵ | Oscar Martinez⁵ | Alberto E. Musto⁵ 

¹Department of Neurology, Hospital de Clínicas “José de San Martín”, Buenos Aires, Argentina

²Department of Neurology, Hospital Británico, Buenos Aires, Argentina

³Department of Radiology, Hospital Británico, Buenos Aires, Argentina

⁴Doctor of Medicine Program, Eastern Virginia Medical School, Norfolk, VA, USA

⁵Department of Pathology & Anatomy, Department of Neurology, Eastern Virginia Medical School, Norfolk, VA, USA

Correspondence

Alberto E. Musto, Department of Pathology & Anatomy, Department of Neurology, Eastern Virginia Medical School, 700 W. Olney Road, Lewis Hall, Office 2174, Norfolk, VA 23507.
Email: mustoae@evms.edu

Abstract

Cutis verticis gyrata (CVG) is a neurocutaneous syndrome characterized by the formation of folds in the scalp that resembles the cerebral cortex. We present two cases of CVG and intellectual disability with drug-resistant epilepsy. Recognizing CVG is necessary to provide interdisciplinary support for the treatment of comorbidities associated with this entity.

KEYWORDS

cutis verticis gyrata, drug-resistant epilepsy, epilepsy, intellectual disability, neurocutaneous syndrome

1 | INTRODUCTION

Cutis verticis gyrata is a neurocutaneous syndrome characterized by folds and furrows in the scalp mimicking the cerebral cortex surface. Epilepsy was described in a primary form of presentation with intellectual disability. We present two cases of cutis verticis gyrata with drug-resistant epilepsy, highlighting the interdisciplinary management of comorbidities associated with this entity.

Cutis verticis gyrata (CVG) is an abnormality of the scalp characterized by the formation of symmetric skin folds and furrows that cannot be corrected by pressure or

traction on the scalp and that resemble the surface of the cerebral cortex.

Cutis verticis gyrata was classified as primary (essential and nonessential) or secondary. The essential and nonessential primary terms are used to describe those cases that are not associated with other abnormalities, as long as primary nonessential refers to cases associated with mental retardation, epilepsy, schizophrenia, ophthalmologic abnormalities, or any combination of these. Secondary CVG is the most frequent presentation form and has been associated with conditions such as inflammatory diseases, hamartomatous lesions, tumors, acromegaly, and myxedema.^{1,2}

Brain anomalies detected by CT or MRI are found in about 38% of patients. Cortical or subcortical atrophy in any area of brain is the most common finding. Scalp imaging shows a typical pattern of skin folds on the scalp, resulting in a typical cerebriform pattern. The skull is typically unaffected.³ The term “CVG-ID” was used to describe the association between primary CVG and intellectual disability (ID). In addition to cutaneous abnormalities, epilepsy has been described in CVG-ID.^{4,5} The type of epilepsy could be variable. Generalized tonic-clonic seizures, absences seizures, and Lennox-Gastaut syndrome have been described.⁶

A recent review of CVG-ID of 62 cases³ found that 44% of patients had a history of epilepsy since childhood. However, the association between CVG and epilepsy is not frequently considered. We report two patients, both with CVG-ID and drug-resistant epilepsy.

2 | CASE 1 HISTORY

A 33-year-old left-handed male with an unremarkable family history presented with strabismus and severe psychomotor delay. When he was 4 years old, he developed nocturnal tonic-clonic seizures. He was treated with phenobarbital, carbamazepine, clobazam, and topiramate, without seizure control. An EEG showed generalized epileptiform activity. He had a severe mental retardation with a complete absence of language. After puberty, his parents noticed thickening and

folding of the parietal and occipital regions of the scalp that became more evident over the years (Figure 1, Panel A-B). After treatment with levetiracetam 3000 mg/d and valproate 1500 mg/d, the patient continues to have approximately 1 generalized tonic-clonic seizure per month.

3 | CASE 2 HISTORY

A 36-year-old right-handed male presented with intractable epilepsy and mild intellectual disability. His first seizure was in early childhood. He then continued to have seizures, without response to several antiepileptic drugs such as phenytoin, levetiracetam, carbamazepine, valproate, and lacosamide. An ophthalmological examination showed strabismus. At the age of 14, he was diagnosed with acromegaly and a surgical resection of a pituitary tumor was performed. Years later, furrows separated by folds running anterior to posterior involving the vertex and the occipital were noted (Figure 1, Panel C-D). This patient continues to have frequent seizures despite the administration of valproate 2000 mg/d and lacosamide 400 mg/d. The implant of a vagus nerve stimulator is being considered.

4 | DISCUSSION

Several case reports of CVG-ID have been published in the literature.^{3,7-10} (Appendix) CVG-ID was mainly identified in

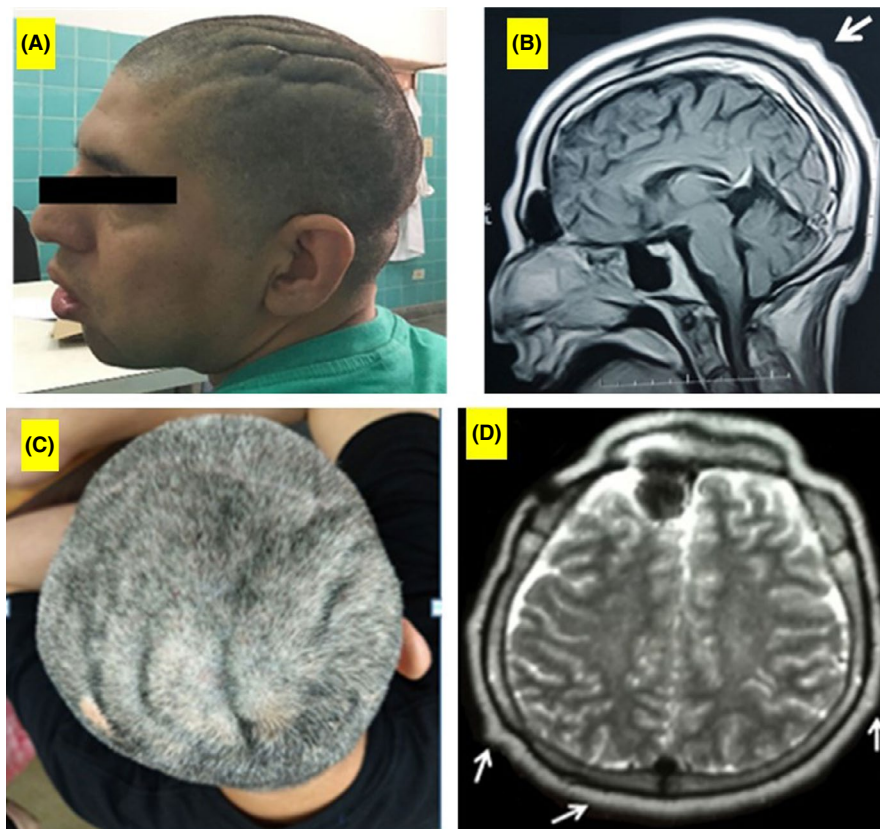
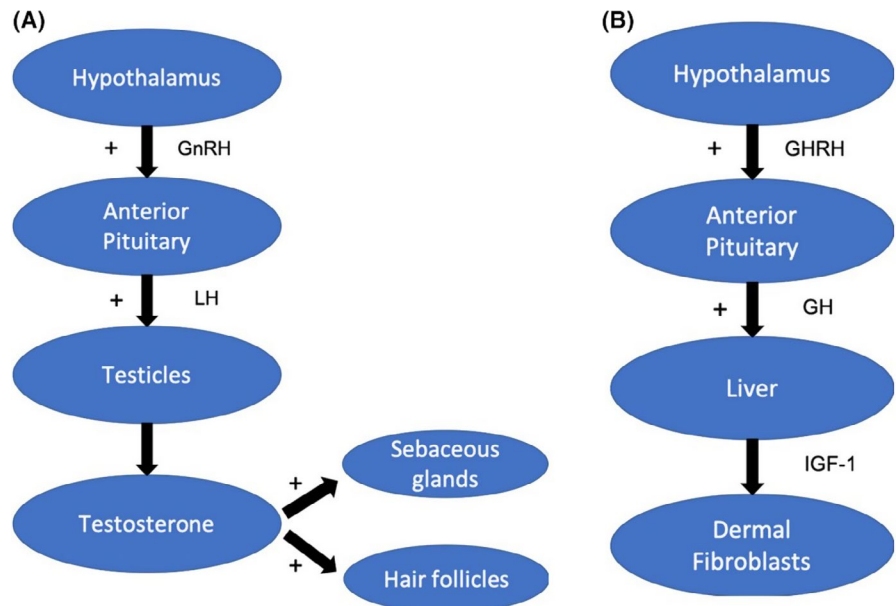


FIGURE 1 A, Cutis verticis gyrata: skin folds and furrows, B, noncontrast brain MR: hypoplasia of the splenium. Diffuse thickening and folds of the superficial layers of the scalp (arrow), C, cutis verticis gyrata: scalp hypertrophy with anteroposterior folds in the parietal region, D, noncontrast brain MR: postoperative changes involving the right frontal region (craniectomy). Diffuse thickening and folds of the superficial layers of the scalp (arrows)

FIGURE 2 A, Testosterone's effect on adnexal structures in the scalp, B, acromegaly induced secondary CVG



subjects living in psychiatric institutions, where it was a prevalence of up to 11.4%.¹¹ CVG was described in some genetic disorders¹²⁻¹⁴; however, the etiology and pathogenesis of CVG-ID is unknown. According to Tucci et al,³ (Appendix) the clinical manifestations of CVG-ID include cutis verticis gyrata that is evident after puberty, severe psychomotor retardation, childhood-onset epilepsy, strabismus, and microcephaly.

We report two patients with CVG and drug-resistant epilepsy. The first had a CVG-ID, and the second patient presented a secondary CVG to an endocrinological disease (acromegaly). Similar to previous reports, both patients were male, epilepsy started in early childhood, skin manifestations were evident after puberty, and they have strabismus, which is the most frequent ocular manifestation in this syndrome. CVG is possibly subdiagnosed. The knowledge of clinical manifestations and a careful physical examination in patients with mental retardation and epilepsy would facilitate the early diagnosis of this syndrome. Although the pathophysiology of nonessential primary CVG-ID is relatively unknown, it is hypothesized that decreased levels of free testosterone possibly due to peripheral use have been implicated in the development of this pathology¹⁵ (Appendix). Additionally, CVG is seen more commonly in males rather than females, further supporting this hypothesis. The normal testosterone axis is depicted below (Figure 2A).

It is hypothesized that free testosterone is lowered in patients with nonessential primary CVG due to peripheral use contributing to the development of the gyrata in the scalp of affected individuals. The histopathology of cutis verticis gyrata further supports this hypothesis as it shows hypertrophy of sebaceous glands and hair follicles within the lesion.¹⁶ This pathogenesis is depicted in Figure 1. Furthermore, two cases have been reported of resolution of CVG upon castration of the affected individual, further implicating the role of testosterone in the pathophysiology of this disease.¹⁷

Secondary cutis verticis gyrata can be seen due to a variety of conditions as described above; in our second case described here, it is secondary to a growth hormone-secreting pituitary adenoma. Although the pituitary adenoma was removed prior to the presentation of CVG, this presentation could be due to residual effects of the tumor or a recurrence of the adenoma.¹⁸

Excess secretion of growth hormone from a pituitary adenoma can have dramatic downstream effects on the production of insulin-like growth factor 1. This can, in turn, lead to the proliferation of dermal fibroblasts and the development of secondary CVG (Figure 2, Panel B).¹⁹ (Appendix) Recognizing this neurocutaneous syndrome is necessary in order to provide the interdisciplinary support that is required for the treatment of comorbidities associated with this entity.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

MLR: performed the clinical history and wrote the manuscript. MLDF; AMK; and FMF: performed the Clinical history. CKM and DKS: involved in pathophysiology of CVG. AAO: involved in formulation of questions. OAM: involved in clinical history, reviewed and wrote the manuscript. AEM: discussed, involved in conception of figures, reviewed, and wrote the manuscript.

ORCID

Alberto E. Musto  <https://orcid.org/0000-0002-0877-8883>

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APPENDIX

Questions:

- What are common genetic syndromes that can be associated with Cutis verticis gyrata?
 - Turner syndrome.
 - Noonan syndrome.
 - Other craniosynostosis syndromes.
 - All of the above.**
- What type of patient shows a higher prevalence of CVG?
 - Children.
 - Adult males.**
 - Patients with intellectual disabilities.
 - Adult females.
- On histology, CVG can be characterized by what factors?
 - Normal epidermis with increased number and size of collagen bundles along with increased matrix in the dermis.**
 - Abnormal epidermis.
 - Subsequent lesions throughout all dermal layers.
 - Decreased number and size of collagen bundles.
- What is the pathognomonic clinical presentation for CVG in male patients?
 - Appears before puberty, between 12 and 15 years old.
 - Appears after puberty, before the age of 30.**
 - Widespread variability in presentation, unable to determine specific timeline of disease.
 - Appears at birth.
- What are some associated comorbidities patients with CVG may present?
 - Benign scalp tumors or other intracerebral tumors.
 - Inflammatory dermatoses, eczema, psoriasis, acne, and pemphigus.
 - Internal malignancies.
 - Endocrine diseases, acromegaly, myxedema, Graves' disease, acanthosis nigricans, insulin resistance syndrome.
 - Amyloidosis.
 - All of the above.**