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CASE REPORT

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Headache as the presenting manifestation of Gorlin-Goltz syndrome with diastematomyelia: A case report

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Abstract

Gorlin-Goltz syndrome (GGS) is an autosomal dominant multisystemic disease with high penetrance. Headache heralding GGS has been previously reported but without discussing potential sources. We report a patient with headache and a novel association (diastematomyelia), which helped with the diagnosis. A 46-year-old woman presented with persistent holocranial headache. On examination, countless hyperpigmented basal cell nevi over the face, pits over the palmar/plantar surface, and palmar and plantar keratosis were observed. A magnetic resonance imaging (MRI) of the spinal cord revealed diastematomyelia. Diagnosis of GGS was finally made. Headache and diastematomyelia should be included in the clinical picture of GGS.

KEYWORDS
diastematomyelia, Gorlin-Goltz syndrome, headache, malformation, presenting manifestation

1 | INTRODUCTION

Gorlin-Goltz syndrome (GGS) or basal cell nevus syndrome (BCNS) is a rare (1/57,000–1/256,000) autosomal dominant multisystemic disease with a high grade of penetrance.[1,2] Several anomalies in the sonic hedgehog signaling (chromosome 9q22.3q31) result in tumor cell proliferation,[1,2] being basal cell carcinoma the most common association.

Headache as GGS' presenting feature has been previously reported without discussing potential sources.[3] Diastematomyelia is a type of spinal dysraphism that occurs when there is a longitudinal split in the spinal cord.[4] Its association with GGS has never been reported previously.

We report a patient with headache and novel association (diastematomyelia), which helped to make a GGS diagnosis.

Ritwik Ghosh and Moisés León-Ruiz are both considered first authors of the article.

2 | CASE REPORT

A 46-year-old previously healthy female from rural West Bengal, India, presented with moderate-intensity persistent holocranial tightening (non-pulsating) headache, exacerbated by pressure applied to the top part of the cranium. The headache was present for the last month, responded temporarily to non-steroidal anti-inflammatory drugs, and was neither aggravated by routine physical activity such as walking or climbing stairs nor accompanied by nausea, vomiting, photophobia, or phonophobia, and no signs of increased intracranial pressure.

The neurological and neuro-ophthalmological examinations were unremarkable. Physical examination revealed macrocephaly, countless hyperpigmented basal cell nevi over the face, and countless pits over the palmar/plantar surface and palmar and plantar keratosis. Complete blood cell count, liver, thyroid, and kidney function tests, and serum electrolytes (including calcium/phosphorous metabolism) were normal. CT scan of the brain revealed a thick skull (increased calvarial thickening) and lamellar calcification of the falx cerebri, tentorium cerebelli, and bilateral basal ganglia (Figure 1A–D). MRI of the brain reaffirmed CT findings. MRI of the spinal cord revealed diastematomyelia (Figure 1E).

Electroencephalography, echocardiography, electrocardiography, and ultrasonography of the abdomen and pelvis were normal. Genetic testing could not be carried out due to financial and infrastructural constraints. BCNS Colloquium Group diagnostic criteria (Table 1) for GGS were fulfilled.[1,2]

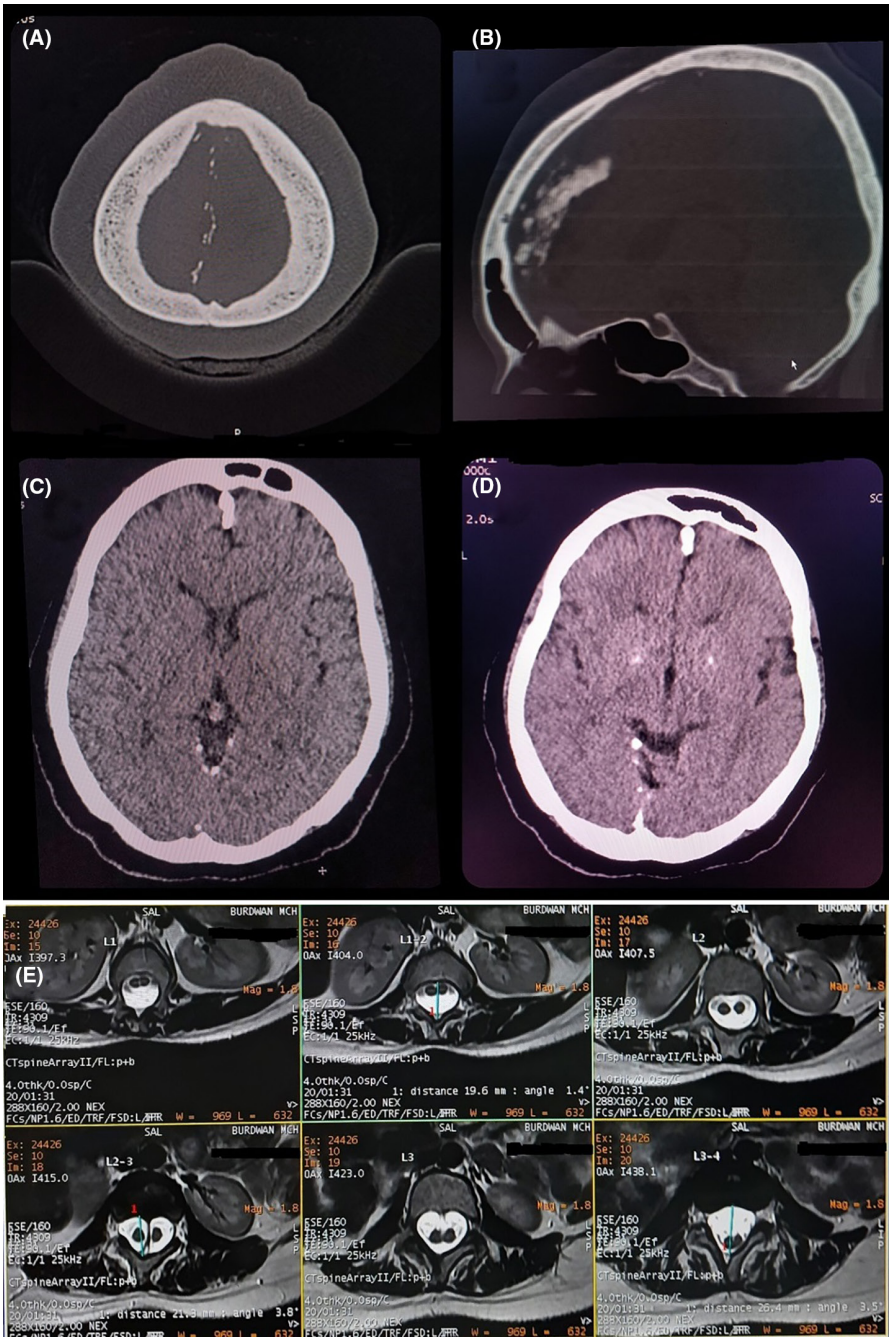

FIGURE 1 (A–D) Non-contrast CT scan of the brain shows increased calvarial thickening and extensive calcification along falx cerebri, tentorium cerebelli, and mild calcification over bilateral basal ganglia (A and B are axial and sagittal bone windows, respectively; C and D are axial parenchymal windows). Alongside, there is partially bridged sella turcica, as shown in image B. (E) MRI of the lumbosacral spine (axial T2-weighted image) showing diastematomyelia at L1 to L3-L4 level.

TABLE 1 Diagnostic criteria and clinical manifestations of basal cell nevus syndrome.[1,2]

Major criteria
(1) Basal cell carcinomas before age 20 or multiple for solar exposure and phototype
(2) Odontogenic keratocysts before age 20 years
(3) Palmar or plantar pitting
(4) Lamellar calcification of the falx cerebri
(5) Medulloblastoma (desmoplastic variant)
(6) First-degree relative with basal cell carcinomas
Minor criteria
(1) Rib anomalies
(2) Other specific skeletal malformations and radiological changes (i.e., vertebral anomalies, kyphoscoliosis, short fourth metacarpals, and/or postaxial polydactyly)
(3) Macrocephaly
(4) Cleft/lip palate
(5) Ovarian/cardiac fibromas
(6) Ocular abnormalities (i.e. strabismus, hypertelorism congenital cataracts, glaucoma, and coloboma)
(7) Lymphomesenteric cysts

Note: The diagnosis can be established based on: (1) one major criterion and genetic confirmation, (2) two major criteria, or (3) one major criterion and two minor criteria.

3 | DISCUSSION

Potential causes of headache in GGS are (1) intracranial space-occupying lesions (i.e., meningioma, medulloblastoma, hydrocephalus, choroid plexus tumor, among others); (2) referred pain from odontogenic diseases; (3) thick skull and/or foraminal compression; and (4) psychogenic.[3,5–7]

Regarding headache, in our case, the most probable diagnosis according to ICHD-3 classification was headache attributed to a disorder of cranial bone (11.1),[8] since it was exacerbated by pressure applied to the top part of the cranium and localized to the site of the cranial bone lesions (thickening of the calvaria). Because this patient's headache source was not better accounted for by another ICHD-3 diagnosis, including migraine (it did not have a unilateral location, was not throbbing, aggravated by or causing avoidance of routine physical activity, with no nausea, vomiting, photophobia, and/or phonophobia), tension-type headache (it was exacerbated by pressure applied to the cranial bone), and other primary and secondary headaches.[8]

Unlike the other previously reported similar case,[3] ours was more clearly aggravated by pressure applied to the top part of the skull because of a transient local increased intracranial pressure, triggered by pressing in that region in which coexist thick skull and dural involvement related to falx cerebri calcification. Hence, the origin was probably due to cranial bone disorder.

Split cord malformations account for 5% of all congenital spinal cord defects.[4,9] They are classified into type I: duplicated dural sac, with common midline spur (osseous or fibrous), usually symptomatic, and type II: single dural sac containing both hemicords, usually paucisymptomatic.[4]

Diastematomyelia represents an intriguing congenital malformation due to a lack of notochord development.[4,9] The most accepted theory argues that an abnormal adhesion between the ectoderm and endoderm creates a neurenteric duct leading to two hemicords.[4,9]

Although diastematomyelia is rare, it occurs worldwide.[4,9] The mean age at presentation is 3.5–6.7 years and has female gender predominance (5/3–1.5/1).[4,9] The vast majority of diastematomyelia cases are sporadic.[4,9] Family history has been occasionally described.[8,9] Most diastematomyelia patients are symptomatic. Patients with mild type II may be asymptomatic (like our patient).[4,9]

Finally, a genetic study (including *PTCH1* gene analysis) is recommended in all patients with suspected GGS.[1,2] However, it is unnecessary if two major criteria or one major criterion and two minor criteria are fulfilled (Table 1),[1,2] as occurs in our case and the previous similar reported case.[3] Besides, performing was impossible because of a lack of financial resources.

4 | CONCLUSIONS

This is the first reported GGS case with headache as presenting manifestation unveiling diastematomyelia. Further studies analyzing the causal association between GGS and diastematomyelia are warranted. Headache and diastematomyelia should be included as possible associations with GGS. MRI of the spinal cord performance in all GGS cases could help establish an early diagnosis and appropriate management of diastematomyelia.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest from the authors of this manuscript.

DATA AVAILABILITY STATEMENT

The data supporting this study's findings are available in the references.

INFORMED CONSENT

Written informed consent was obtained from the patient to publish this case report and any accompanying images.

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