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SLC29A3 Pathogenic Variants Resulting in Dural Based Fibroinflammatory Mass Lesions and H Syndrome Treated With Cobimetinib

A Case Report

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Abstract

Objectives

Pathogenic *SLC29A3* variants are known to cause autosomal recessive disease with a spectrum of systemic involvement. We sought to expand on the spectrum of *SLC29A3* variants and describe potential treatment.

Methods

We describe a case of newly diagnosed *SLC29A3*-related disorder, also known as H syndrome or familial histiocytosis, associated with CNS inflammatory pseudotumor and spinal cord compression.

Results

We present a 25-year-old man with recurrent dural based masses resulting in spinal cord and brain compression, hyperpigmented skin patches, proptosis, short stature, and elevated serum and spinal fluid inflammatory markers. Panel genetic testing revealed homozygous pathogenic variant c.1309G>A in the *SLC29A3* gene resulting in a missense alteration (p. Gly437Arg). The patient was treated with cobimetinib with clinical, serologic, and radiographic improvement at 1-month follow-up.

Discussion

SLC29A3 variant may cause fibroinflammatory lesions involving the dura resembling the clinical spectrum of Rosai-Dorfman disease. Patients with *SLC29A3* disease and neurologic signs or symptoms should undergo screening MRI for CNS involvement. MEK inhibition represents a novel treatment for this disorder.

PRACTICAL IMPLICATIONS

SLC29A3-related disorder can result in inflammatory pseudotumor of the dura that may respond to cobimetinib.

Introduction

Biallelic pathogenic variants in the *SLC29A3* gene, which encodes human equilibrative nucleoside transporter 3 (hENT3), have been known to cause a spectrum of diseases with multisystem involvement.[1] Limited data are available regarding the neurologic spectrum of this disease.[2] In this article, we present a case of a patient with homozygous pathogenic

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variants in the *SLC29A3* gene resulting in extensive dural based masses clinically resembling a Rosai-Dorfman phenotype, expanding on the current available literature of *SLC29A3* disease, and providing a perspective on treatment.

Methods

This study was approved by the institutional review board of Mayo Clinic, MN (IRB ID: 08-006647); the patient gave consent for the passive use of his record for research.

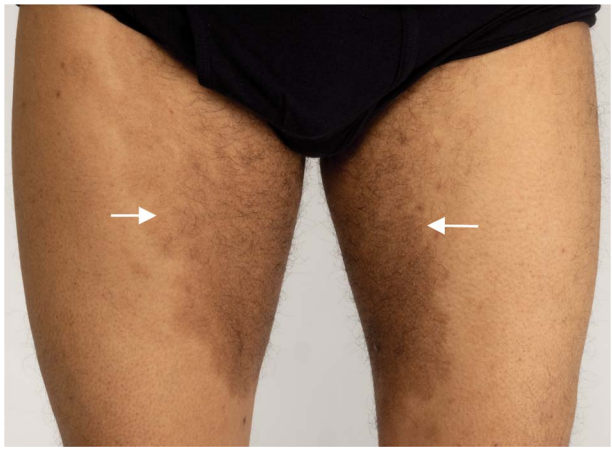
Results

A man in his 20s from Saudi Arabia presented with recurrent idiopathic inflammatory pseudotumor involving the pachymeninges with onset in his teenage years. Family history was notable for parents being consanguineous (first cousins) and a maternal first cousin with a similar skin lesion to this patient (Figure 1). The proband is the only child between his mother and father.

The patient's birth was complicated by a left brachial plexus injury, with resulting paresis in the left hand and joint contractures. At age 9, the patient developed headaches and right eye proptosis. As a teenager, he developed hyperpigmented patches on the thighs and legs with associated hypertrichosis (Figure 1).

As a teenager, he developed bilateral leg weakness and walking difficulty. A thoracic spine MRI revealed dorsal extra-axial dural based mass with associated compression of the spinal cord (Figure 2, A and B). Full-body PET-CT at the time revealed no other systemic involvement. Owing to spinal cord compression, he underwent surgical debulking and laminectomy from T3-T8 and he received one cycle of hyper-CVAD regimen (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) for suspected lymphoma with minimal improvement. The pathology was reported to show an extensive lymphoid infiltrate, felt to represent a reactive response. Extensive workup was otherwise notable for elevated C-reactive protein to 49.3 mg/L (normal ≤5 mg/L). A diagnosis of idiopathic inflammatory pseudotumor was made, and no specific treatment was recommended.

Figure 1 Dermatologic Examination Findings in the Patient With Pathogenic *SLC29A3* Variant



As a teenager, the patient developed large approximately 15–20 cm patches with hyperpigmentation and hypertrichosis on his medial thighs (arrows), with smaller patches on the buttocks, hips, and legs.

Five years later, in his 20s, he developed severe right-sided headaches with intermittent double vision when looking to the right. He was started on acetazolamide with improvement. Lumbar puncture was performed after initiation of acetazolamide, and opening pressure was normal.

Three years later, he developed new bilateral leg weakness. Thoracic spine MRI showed recurrence of the dural based mass with extensive intracranial involvement (Figure 2, D and E). Surgical resection revealed thickened dura with fibrosis and chronic inflammation without diagnostic features of histiocytic or lymphoid neoplasm (Figure 3). Specifically, no Rosai-Dorfman–type histiocytes were identified. Neurologic examination was notable for mild myelopathic findings, gaze-evoked nystagmus, with no evidence of papilledema. Skin examination revealed large approximately 15–20 cm symmetric hyperpigmented patches on the medial thighs, and smaller 5–10 cm patches on the buttocks, hips, and legs with associated hypertrichosis (Figure 1). Lumbar puncture demonstrated normal opening pressure; 11 total nucleated cells per microliter, with a lymphocytic predominance; protein 59 mg/dL (normal <35); and no CSF (CSF) unique oligoclonal bands. C-reactive protein was elevated at 89.5 mg/L. Serum cytokine analysis showed elevations in total tumor necrosis factor (TNF) (35.5 pg/mL, normal <10), interleukin (IL) 6 (5.6 pg/mL, normal <5), soluble IL-2 receptor alpha (1,135 pg/mL, normal <959), and IL-18 (743 pg/mL, normal <468). Pituitary, gonadal, and adrenal functional testing was normal. Skin punch biopsy from the left medial thigh revealed undulating mild acanthosis with basilar hyperpigmentation, mild hyperkeratosis, and minimal perivascular lymphocytic inflammation.

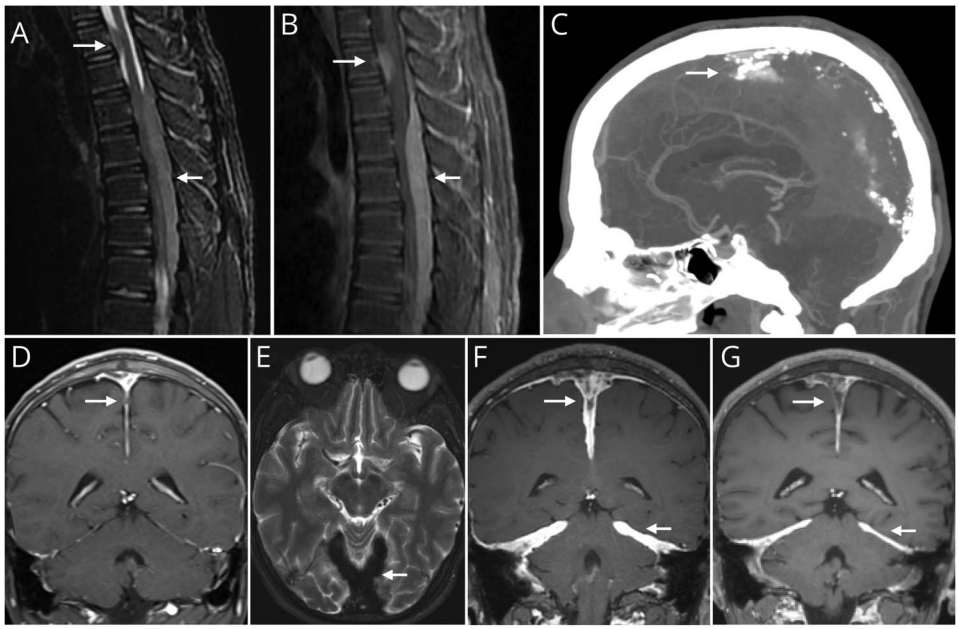
Next-generation sequencing demonstrated a germline homozygous pathogenic variant, specifically named c.1309G>A in the *SLC29A3* gene resulting in a missense alteration. The patient was initiated on cobimetinib.

At follow-up after 1 month on cobimetinib, patient's gaze-evoked nystagmus had resolved on examination. Bloodwork revealed normal C-reactive protein (<3 mg/L), normal TNF (<10 pg/mL), IL-6 (<5 pg/mL), soluble IL-2 receptor alpha (495 pg/mL), and lower IL-18 (653 pg/mL). MRI revealed notable reduction in severity of dural thickening and enhancement along the falx and tentorium (Figure 2G).

Discussion

This case describes a patient with recurrent inflammatory pseudotumor with involvement of the spinal and intracranial

Figure 2 Dural Based Lesions in a Man With *SLC29A3* Pathogenic Variant



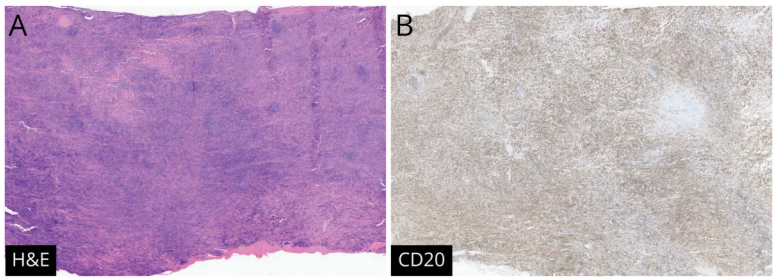
As a teenager, he developed myelopathy secondary to extra-axial compression from dural based lesions. MRI demonstrated homogeneous enhancement on sagittal T1 postgadolinium fat-saturated sequences of the spine (A, arrows) with spinal cord compression, and isointense signal on T2 (B, arrows). Eight years later, the CT venogram demonstrated extensive dural sinus occlusion secondary to dural disease with extensive dural calcification (C, arrow). As a teenager, the coronal T1 postgadolinium sequence showed enhancing dural thickening intracranially (D, arrow), that worsened 8 years later (F, arrows). The dural thickening had an intensely dark appearance on T2 (E, arrow), no diffusion restriction was seen (not shown). Brain parenchyma was otherwise normal (not shown). The radiographic differential diagnosis was broad and included meningiomatosis, dural lymphoma, and metastatic disease; the intensely dark T2 appearance made histiocytosis, IgG4-related disease, neurosarcoidosis, infiltrative pseudotumor, desmoid tumor, and other fibrotic tumors a stronger consideration. Subsequently, genetic testing revealed a homozygous pathogenic variant c.1309G>A in the *SLC29A3* gene, and he was started on cobimetinib. After 1 month on cobimetinib, follow-up MRI revealed reduced dural thickening (G, arrows) and normalization of CRP.

dura and associated mass effect secondary to homozygous *SLC29A3* missense variants. This patient also had related hyperpigmented skin patches, exophthalmos, short stature, inflammatory serum and CSF testing, joint contractures possibly related to congenital brachial plexopathy, and a family history notable for consanguinity and a first cousin with similar skin patches.

In our review, there has only been 1 prior report of dural involvement with biallelic *SLC29A3* variants. The prior case described a 42-year-old woman who presented with a similar appearing dural based mass with secondary compression of the spinal cord,[2] and she received corticosteroids and tocilizumab with stabilization of the mass but no curative response. The authors described this as an Erdheim-Chester disease-like presentation; however, in our experience, dural based lesions are more frequently seen in Rosai-Dorfman disease.[3] It is important to note that the pathology in our case did not reveal any features diagnostic of either Erdheim-Chester disease or Rosai-Dorfman disease, despite the clinical phenotype. Regarding other involvement of the CNS, hydrocephalus has been reported in a 4-year-old[4] and 16-year-old,[5] noted on CT without further details available.

There have been many names given to the syndromes associated with biallelic *SLC29A3* variants, now more inclusively named *SLC29A3*-related disorders, including H syndrome, familial Rosai-Dorfman disease, Faisalabad histiocytosis, and

Figure 3 Pathology of Dural Lesion



Pathology from the thoracic extramedullary dural based mass showed markedly thickened dura with chronic inflammation in a densely fibrotic background. The infiltrate included numerous CD20-positive B cells (A, hematoxylin and eosin stain; B, CD20 immunoperoxidase stain [×20]). Immunoperoxidase stains revealed a mixture of small CD3-positive T cells and CD20-positive B cells; bland-appearing histiocytes expressing CD163 were seen, and no diagnostic features of histiocytic (negative OCT2, cyclin D1) or lymphoid neoplasm were present.

pigmented hypertrichosis with insulin-dependent diabetes mellitus syndrome.[6] *SLC29A3*-related disorders are inherited in an autosomal recessive pattern. The phenotype can vary greatly in affected individuals and may include massive cervical lymph node enlargement resembling Rosai-Dorfman disease, fever, leukocytosis, elevated inflammatory markers, cutaneous hyperpigmentation and hypertrichosis, hepatosplenomegaly, heart anomalies, hypogonadism, hearing loss, short stature, insulin-dependent diabetes, proptosis, eyelid swelling, and camptodactyly.[6] Prior reports of biopsied tissue (skin, lymph node, and eyelid) showed similar pathologic changes to Rosai-Dorfman disease,[7] although our case did not.

SLC29A3 encodes hENT3, which is involved in lysosomal trafficking[8] and T-cell survival and proliferation.[9] In individuals with biallelic *SLC29A3* variants, there is loss of function of hENT3 resulting in decreased pH in the lysozyme, increased toll-like receptor expression, and activation of the mitogen-activated protein-kinase (MAPK) pathway resulting in pro-proliferative signals and subsequent development of inflammatory pseudotumor.[10]

Patients with *SLC29A3*-related disorders have been previously treated with tocilizumab, a humanized interleukin-6 (IL-6) receptor antibody. Previously published cases reported a reduction in acute phase markers, skin changes, and hearing loss, despite normal serum circulating IL-6 levels prior to treatment.[11-13] Notably, the only previously reported case with dural involvement was treated with tocilizumab without improvement of their neurologic disease.[2] There has been 1 patient reported to be treated with trametinib with H syndrome. This patient had dramatic response to skin lesions with tocilizumab and, however, had a persistent large maxillary sinus tumor that also failed to respond to steroids and methotrexate. Trametinib, a MEK inhibitor, resulted in slow resolution of the tumor, that was sustained 2 years after discontinuation of treatment.[10] MEK inhibitors have been used to successfully treat histiocytic disorders,[14,15] and cobimetinib is thought to have better bioavailability in the CNS, which is the reason it was recommended in this case. If the patient does not have continued response to cobimetinib, tocilizumab will be trialed.

This case presents a rarely described manifestation of *SLC29A3* disease. Patients who are identified with variants in this gene who develop neurologic signs and symptoms should be screened for involvement of the pachymeninges with MRI. Cobimetinib represents a novel therapy in this disease.

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Appendix 1 *(continued)*

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Appendix 2 *(continued)*

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References

1. Noavar S, Behroozi S, Tatarcheh T, Parvini F, Foroutan M, Fahimi H. A novel homozygous frame-shift mutation in the SLC29A3 gene: a new case report and review of literature. *BMC Med Genet*. 2019;20(1):147. doi:10.1186/s12881-019-0879-7
2. Lequain H, Gerfaud-Valentin M, Emile J-F, et al. H syndrome mimicking Erdheim Chester disease: new entity and therapeutic perspectives. *Haematologica*. 2023; 108(8):2255-2260. doi:10.3324/haematol.2022.282040
3. Banks SA, Sartori Valinotti JC, Go RS, et al. Neurological manifestations of histiocytic disorders. *Curr Neurol Neurosci Rep*. 2023;23(6):277-286. doi:10.1007/s11910-023-01272-4
4. Avitan-Hersh E, Mandel H, Indelman M, Bar-Joseph G, Zlotogorski A, Bergman R. A case of H syndrome showing immunophenotye similarities to Rosai–Dorfman disease. *Am J Dermatopathol*. 2011;33(1):47-51. doi:10.1097/DAD.0b013e3181ee547c
5. Rossbach HC, Dalence C, Wynn T, Tebbi C. Faisalabad histiocytosis mimics Rosai-Dorfman disease: Brothers with lymphadenopathy, intrauterine fractures, short stature, and sensorineural deafness. *Pediatr Blood Cancer*. 2006;47(5):629-632. doi: 10.1002/pbc.20605
6. Morgan NV, Morris MR, Cangul H, et al. Mutations in SLC29A3, encoding an equilibrative nucleoside transporter ENT3, cause a familial histiocytosis syndrome (Faisalabad histiocytosis) and familial Rosai-Dorfman disease. *PLoS Genet*. 2010;6(2): e1000833. doi:10.1371/journal.pgen.1000833
7. Moynihan LM, Bundey SE, Heath D, et al. Autozygosity mapping, to chromosome 11q25, of a rare autosomal recessive syndrome causing histiocytosis, joint contractures, and sensorineural deafness. *Am J Hum Genet*. 1998;62(5):1123-1128. doi: 10.1086/301824
8. Kang N, Jun AH, Bhutia YD, Kannan N, Unadkat JD, Govindarajan R. Human equilibrative nucleoside transporter-3 (hENT3) spectrum disorder mutations impair nucleoside transport, protein localization, and stability. *J Biol Chem*. 2010;285(36): 28343-28352. doi:10.1074/jbc.M110.109199
9. Wei C-W, Lee C-Y, Lee D-J, et al. Equilibrative nucleoside transporter 3 regulates T cell homeostasis by coordinating lysosomal function with nucleoside availability. *Cell Rep*. 2018;23(8):2330-2341. doi:10.1016/j.celrep.2018.04.077
10. Shiloh R, Lubin R, David O, et al. Loss of function of ENT3 drives histiocytosis and inflammation through TLR-MAPK signaling. *Blood*. 2023;142(20):1740-1751. doi: 10.1182/blood.2023020714
11. Rafiq NK, Hussain K, Brogan PA. Tocilizumab for the treatment of SLC29A3 mutation positive PHID syndrome. *Pediatrics*. 2017;140(5):e20163148. doi:10.1542/peds.2016-3148
12. Jacquot R, Jouret M, Valentin MG, et al. H syndrome treated with Tocilizumab: two case reports and literature review. *Front Immunol*. 2023;14:1061182. doi:10.3389/fimmu.2023.1061182
13. Gunderman LM, Valika T, Carol H, Khojah A. Improvement of SLC29A3 spectrum disorder-related sensorineural hearing loss after initiation of IL-6 inhibitor. *BMJ Case Rep*. 2022;15(6):e249191. doi:10.1136/bcr-2022-249191
14. Abeykoon JP, Rech KL, Young JR, et al. Outcomes after treatment with Cobimetinib in patients with Rosai-Dorfman disease based on KRAS and MEK alteration status. *JAMA Oncol*. 2022;8(12):1816-1820. doi:10.1001/jamaoncol.2022.4432
15. Acosta Medina AA, Zanwar S, Ruan G, et al. Efficacy of MEK inhibitors in Erdheim Chester disease. *Blood*. 2022;140(Supplement 1):9733-9734. doi:10.1182/blood-2022-163674