CASE REPORT

Cerebellar involvement of Griscelli syndrome type 2

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SUMMARY

Griscelli syndrome type 2 is characterised by partial albinism and primary immunodeficiency. We present a case of a 3-year-old girl diagnosed with cerebellar involvement of Griscelli syndrome type 2. Neurological complications may accompany Griscelli syndrome, however, to the best of my knowledge there are only a few case reports of cerebellar involvement of Griscelli syndrome type 2 in the literature.

BACKGROUND

Griscelli syndrome (GS) was first described by Griscelli *et al*¹ as partial albinism associated with different degrees of pancytopenia in 1978. Its main clinical features include silvery-grey hair and immunological dysfunction. GS is classified into three subtypes. type 1 (GS1) is caused by a mutation in the MYO5A gene and accompanying severe primary neurological impairment in addition to pigmentation defects.² The second type (GS2) is caused by a mutation in the RAB27A gene. It is associated with primary immunodeficiency due to an impairment of T cell and natural killer cytotoxic activity, leading to haemophagocytic syndrome or haemophagocytic lymphohistiocytosis (HLH), which is usually triggered by viruses. HLH is characterised by fever, hepatosplenomegaly and pancytopenia. Only type 2 GS has been associated with HLH.^{3, 4} On the other hand, the third type (GS3) is caused by a mutation in the melanophilin gene (MLPH) and its clinical features are restricted to hypopigmentation of skin and hair.⁵

We report a case of a 3-year-old girl diagnosed with GS2 and treated for HLH but who expired due to the cerebellar involvement of the disease 9 months after the diagnosis. To the best of my knowledge there are only a few case reports of cerebellar involvement of GS type 2 in the literature.

CASE PRESENTATION

A 3-year-old girl was referred to the neurology department of our hospital for ataxia of 2 weeks duration and frequent generalised seizures with status epilepticus. Her physical examination revealed ataxia and silvery-grey hair. Her seizures were controlled with phenytoin, levetiracetam and valproic acid. In her history it was learned that she was diagnosed with GS by evaluation, under light microscopy, of her hair, which established irregular pigmentations about 9 months earlier. Moreover, at the same time she was also diagnosed with haemophagocytic syndrome by bone marrow aspiration demonstrating several histiocytes with haemophagocytosis; she was treated at another centre. She

was Caucasian and the second child of a consanguineous (first cousins) marriage and born from healthy parents after an uncomplicated pregnancy and delivery. Since her family screening was negative for an appropriate bone marrow donor, she was on a waiting list for a suitable donor for about 9 months.

INVESTIGATIONS

Her laboratory examinations including complete blood count, liver and renal function tests and blood electrolyte levels were normal.

DIFFERENTIAL DIAGNOSIS

- Chediak-Higashi syndrome
- Elejalde syndrome (Griscelli type 1)
- Hermansky-Pudlak syndrome

TREATMENT

On the fourth day of hospitalisation her symptoms improved with phenytoin, levetiracetam and valproic acid treatment and she was well.

OUTCOME AND FOLLOW-UP

However, on the sixth day of hospitalisation her general condition worsened and her neurological examination revealed ataxia, dyssynergia and dysmetria. Brain MRI revealed multiple hyperintense lesions in T2-weighted images in the cerebellum, which were presumed to be caused by lymphocytic infiltration ([figure 1](#)). Despite intensive care support the patient expired on the 10th day of hospitalisation. Her family refused an autopsy. Based on the previous diagnosis of GS2 and MRI findings, her clinical picture was considered to be lymphohistiocytic infiltration of the cerebellum.

Figure 1 Brain MRI revealing multiple hyperintense lesions in T2-weighted images of the cerebellum.

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DISCUSSION

GS type 2 is a rare autosomal recessive disease and most commonly diagnosed with clinical suspicion and the light microscopic evaluation of hair shafts. However, molecular diagnosis is now available and in some regions is even the standard. The defects of adaptive immunity owing to the absence of giant granules in the peripheral leucocytes are the mainstay of the disease while granulocyte and lymphocyte counts and functions are generally normal.⁶ The gene associated with GS2, the RAB27A gene, is not expressed in neuronal cells, so the neurological symptoms reported in GS2 cases are attributed to histolytic infiltration of the central nervous system. Mishra *et al*⁷ described two brothers who had GS2 with clinically diverse manifestations; one of the siblings was diagnosed with GS2 and cerebral lymphohistiocytic infiltration. Similarly Arushi *et al* have also reported a cerebellar involvement of GS2 in a

3-year-old boy based on MRI findings.⁸ Rajadhyax *et al*⁹ reported a GS2 case presented with obstructive hydrocephalus and infiltrative lesions in the brain unaccompanied by other features of accelerated phase; biopsy of these lesions demonstrated sinus histiocytosis. Ashrafi *et al*¹⁰ reported bilateral basal ganglia involvement in a GS2 case who was admitted to the hospital with seizures and stupor.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- ▶ Griscelli syndrome (GS) type 2 is characterised by partial albinism and primary immunodeficiency.
- ▶ The prognosis of GS2 is poor and death is usually due to haemophagocytic lymphohistiocytosis, which should be suspected, diagnosed and treated promptly.
- ▶ The rates of autosomal recessive diseases are higher in areas where the rate of consanguinity is greater.
- ▶ Clinicians should be aware of different clinical pictures and complications of these rare diseases in order to treat patients as early as possible. Neurological complications and cerebellar involvement may accompany GS2 and may deteriorate the clinical picture.

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