A RARE CASE OF TYPE II GRISCELLI SYNDROME:

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ABSTRACT

Griscelli syndrome type II (GS type II) is a rare autosomal recessive disorder that presents with hypo-pigmentation of the skin and hair, immunodeficiency and neurological impairment.It is caused by a mutation in RAB27A gene responsible for vesicular trafficking and is often associated with hemophagocyticlymphohistiocytosis (HLH). We present a case of a one-and-a-half-year-old patient having hypo-pigmented silver gray hair of the scalp, eyebrows and eyelashes. Labs were suggestive of inflammatory etiology. MRI imaging revealed edematous changes in the brainstem, basal ganglia and cerebellar hemispheres. Although the initial neurological exam was normal, patient later developed fits, which was suggestive of autoimmune or infectious etiology in the central nervous system, and the rapidly deteriorating condition implied aggressive disease.

Case Presentation

A one-and-a-half-year-old girl presented with complains of irritability for 10 days, low grade fever for 10 days and drooling from mouth since 2 days. She had hypo-pigmented silver gray hair of the scalp, eyebrows, and eyelashes. Heart rate, breathing rate as well as temperature was all normal. On neurological examination, she had normal tone, power and reflexes. Plantar was up-going. There was no neck stiffness, no involuntary movement. Anterior fontanelle was normal with no bulging noted. Brudzinki s and Kernig s signs were absent. Accessible cranial nerves II, III, IV, VI, VII, IX, X, XII were intact. On respiratory examination, trachea was central, normal shape, symmetrical with equal movements, respiratory rate was 54 bpm, with signs of labored breathing. Resonant percussions were noted. On auscultation,equal breath sounds were heard. On palpation, chest expansion was symmetrical with no swelling, tenderness or

Figure 1: Patient having hypopigmented, silver-gray hair of the scalp and eyebrows.

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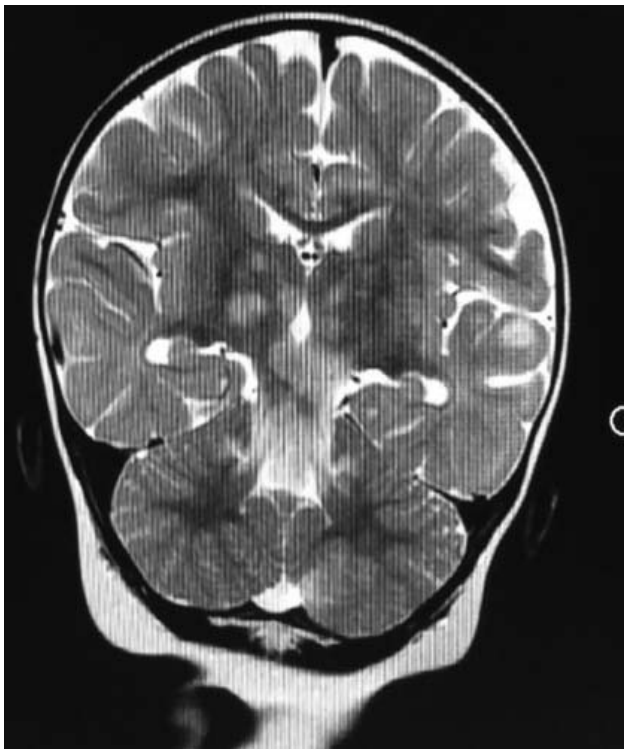

Figure 2: MRI Brain showing T2/ FLAIR hyper intense signals bilaterally, involving bilateral thalami, basal ganglia, grey white matter junction and cerebellar hemispheres.

crepitus. Abdomen was soft and nontender. There was mild hepatomegaly. Liver was palpable 4 cm below costal margin. Tip of spleen was also palpable. On CBC, TLC was slightly elevated and ESR was also increased. RBCs were normocytic normochromic. Atypical lymphocytes were seen. Blood, tracheal and urinary cultures were negative for any microbes. Patient was intubated in pediatric ICU on account of her respiratory distress. She was kept on ventilator support. IV line was maintained, and the patient was sedated and relaxed. On day 3 her GCS deteriorated to 2/10, pupils become grade 1 non reactive. She had fits and was managed with anti-epileptic medications.

MRI brain was performed. There was evidence of multiple supra and infra tentorial T2/ FLAIR hyper intense signals bilaterally which were involving bilateral thalami, basal ganglia grey white matter junction and cerebellar hemispheres bilaterally. There was extensive involvement of brain stem which was resulting in significant surrounding edema, these lesions were showing enhancement on post contrast sequences. Based on MRI, differentials involved demyelinating disease such as acute disseminated encephalomyelitis or encephalitis. Methylprednisolone was started, but no significant improvement was seen. Hair microscopy examination was performed. Whole mount examination of hair under light microscopy showed large clumps of pigment in the medulla in contrast to normal hair, confirming the diagnosis of Griscelli syndrome.

Discussion

GS type II is a rare, autosomal recessive disorder consisting of immunodeficiency, hypo-pigmented skin and hair as well as HLH (Hemophagocytic lympho-histiocytosis). It is caused by mutations in the RAB27A gene.[1] RAB27A is present within the genome of multiple cells, especially melanocytes. This gene interacts with other loci and increases the tendency for patients to develop HLH, which in itself is a potentially fatal condition.[2]

Patients presenting with seizures indicate central nervous system involvement of hemophagocytosis, and this was the case with our patient, as stated in the above case presentation. MRI was essential in detecting central nervous system involvement. Although other findings such as hypo-pigmentation of the skin and hair are more common, neurological presentation can also be seen.[3]

HLH is a commonly seen presentation for patients with GS type II. HLH is a disorder in which multiple organs of the body become inflamed. This is due to undue activation of antigen presenting cells, which involve macrophages and histiocytes. These cells are recruited to the inflamed area as a series of self amplifying reactions, and cause excessive tissue damage.[4]

The diagnosis of HLH is established by fulfilling one of the following 2 criteria:

Molecular diagnosis consistent with HLH (PRF mutations, SAP)

Presence of 5 of following 8 symptoms, signs, or laboratory abnormalities:

Fever, spenlomegaly, cytopenia, hypertriglyceridemia/ hypofibrinogemia, hemophagocytosis in bone marrow, low or absent natural killer cell cytotoxicity, hyper-

ferritinemia, elevated soluble CD25.[5]
Treatment for Griscelli Syndrome type II is hematopoietic stem cell transplantation, however it is not possible without complications, including veno-occlusive disease, chronic graft versus host disease, as well as the introduction of Epstein Barr virus.[6]
Treatment of HLH involves the HLH-94 protocol. This includes immunochemotherapy drugs, namely epipodophyllotoxinsand corticosteroids which were the standard drugs before the release of the said protocol. This protocol however, introduced cyclosporine A in the therapy, and suggests a successive bone marrow transplant.[7] HLH-94 has proved to be ground-breaking for patients with HLH, and has improved survival rate, especially in children.[8,9] Another protocol, HLH-2004 was introduced, which intensified the therapy by introducing cyclosporine A in advance. However, HLH-94 still proved to be more effective than HLH-2004 and is the standard therapy.[10]

Conclusion

The major challenge in combating GS type II is HLH, and the HLH-94 protocol has brought major improvement in survival rate of patients with the said disease process, especially children. However, further advancements remain the need of the hour.

Conflict of Interest: Authors mentioned no financial or institutional COI

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