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MRI IMAGING IN GRISCELLI SYNDROME

[1]Dr. Tushar Kalekar MD and [2]Dr. Gopal Khadse MD

[1]Assistant Professor, Department of Radiology, B J Medical College, Pune.
[2]Professor and Head of Department of Radiology, B J Medical College, Pune.

***Corresponding Author: Dr. Tushar Kalekar MD**

Assistant Professor, Department of Radiology, B J Medical College, Pune.

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ABSTRACT

Griscelli syndrome was first described by Griscelli and Siccardiin in 1978 at Paris[1]. It is a rare autosomal recessive disorder resulting in pigmentary dilution of the skin and hair, presence of large clumps of pigment in hair shafts and accumulation of melanosomes in melanocytes. It results in silver-grey hair along with variable cellular immunodeficiency or severe neurological impairment or both. Three types of Griscelli syndromes have been presented so far. All types of Griscellies syndrome reveal large-irregularly distributed melanin aggregates in the hair under light microscope. In Type 1, there is severe neurologic impairment but immune deficiency and hemophagocytosis is usually absent. In Type 2, patients have precise immune deficiency and hemophagocytosis, neurologic impairment is not primarily seen but due to the lymphocytic infiltration of brain, it may be seen as secondary manifestation. In type 3, there are no neurological and immunological impairment without any hemophagocytosis. In most cases diagnosis occurs between the ages of 4 months to 7 years.

KEYWORDS: Griscelli syndrome, pigmentary dilution, CNS involvement.

INTRODUCTION

Our study is a case series of nine children whow were siblings of third degree consanguineous marriage born to healthy parents after an uncomplicated pregnancies and deliveries. The children had normal neuro- psychomotor development during the first year of age. These siblings presented with different primary neurological complaints at different age groups.

MATERIALS AND METHODS

This is retrospective study and imaging was carried in all the clinically diagnosed patients of Griscelle's syndrome. Study was perfomed on 1.5 T SIEMEN'S MRI scanner.
Imaging protocol
Plain multiplanar MRI performed using
Axial T1, Axial T2, Coronal T2, Sagital T1, spin echo images, Axial GRE images with 5mm slice thickness and 1mm interslice gap.
Diffusion weighed imaging with B value of 1000 used
Post gadolinium enhanced SE T1 images acquired in axial, coronal and sagital images in all patients

OBSERVATIONS AND RESULTS

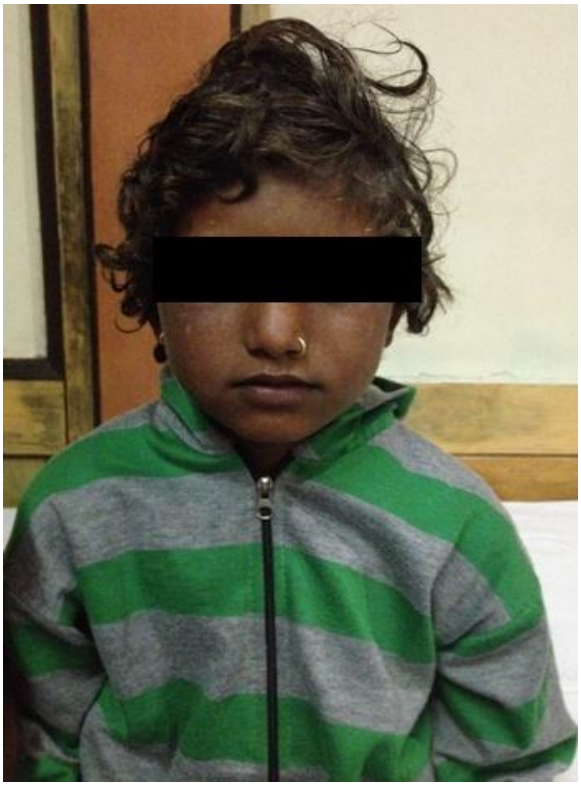

Figure 1: case 2 with silver grey hair and hypo pigmentation of skin.

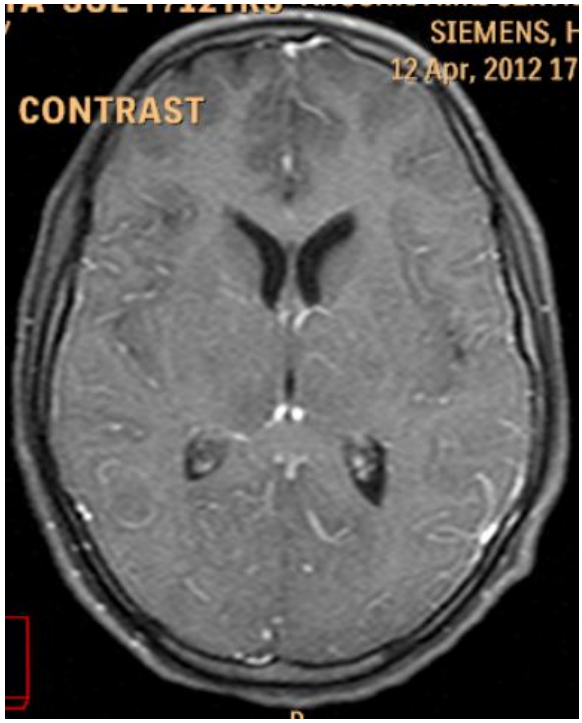

Figure 2: Post contrast axial image showing diffuse leptomeningitis with early hydrocephalus

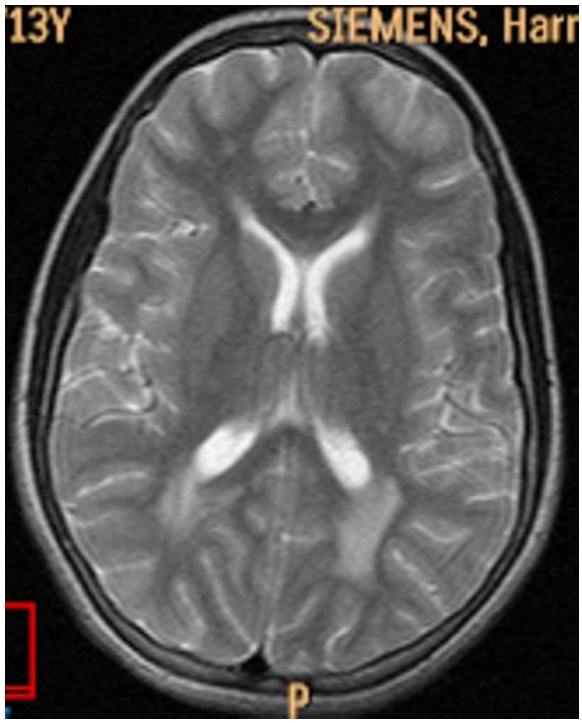

Figure 3: T2-weighted axial image showing ill-defined confluent hyperintensities in the bilateral supra-tentorial peri-ventricular, deep white matter regions.

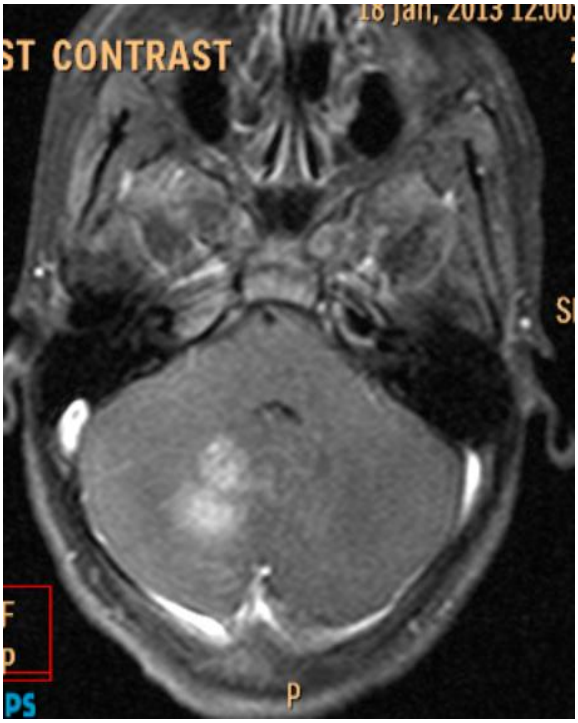

Figure 4: Post contrast axial image showing extensive ill-defined enhancing areas involving bilateral cerebellar hemispheric white matter regions, more extensive on right side.

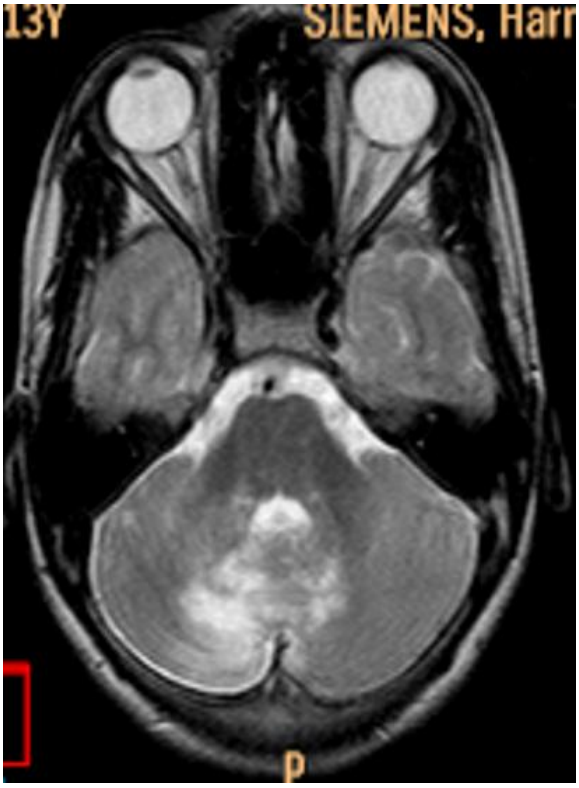

Figure5: T2 w and FLAIR axial images showing gliotic changes in bilateral cerebellar white matter areas, more extensive in the right cerebellar white matter and superior vermis.

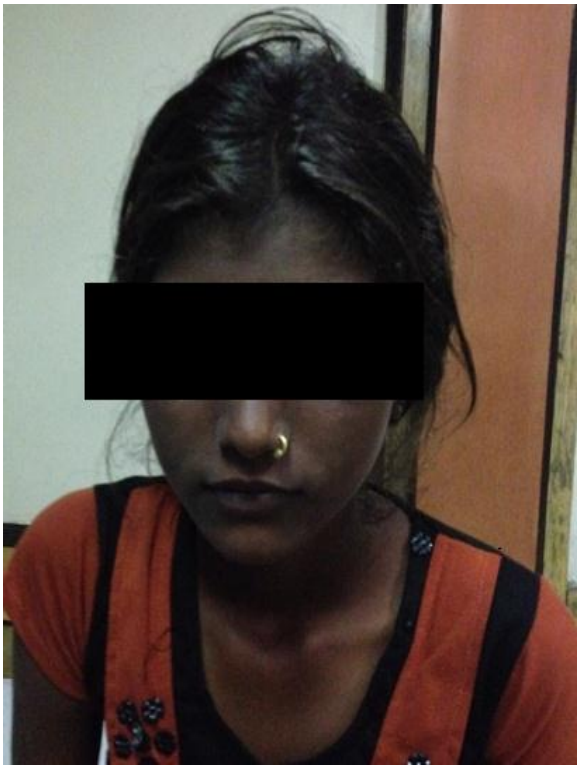

Figure 6: case 3 with silver grey hair and hypo pigmentation of skin.

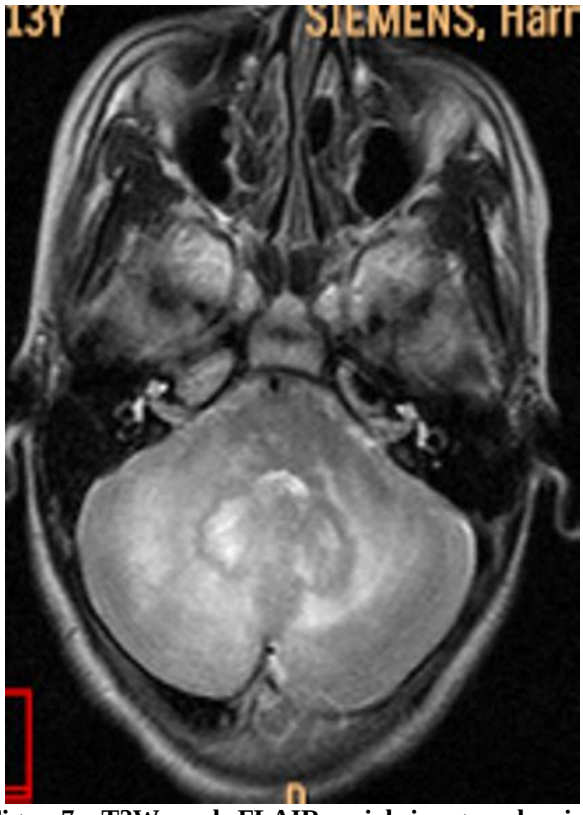

Figure7: T2W and FLAIR axial images showing gliotic changes involving cerebellar hemispheres, vermis with significant atrophy.

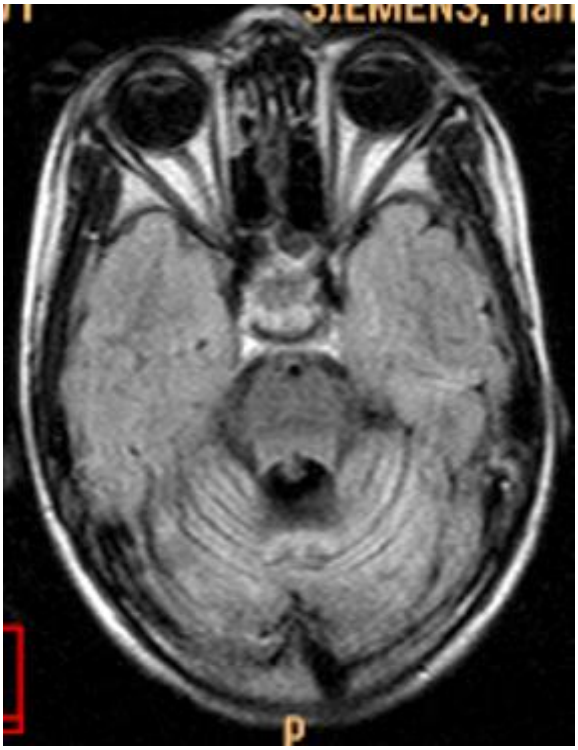

Figure8(a): T2W and FLAIR axial images showing atrophy of bilateral cerebellar hemispheres and vermis.

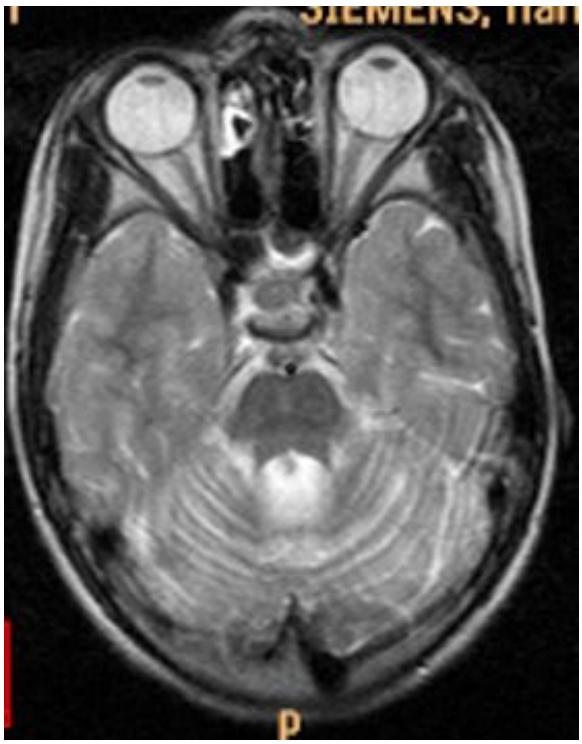

Figure8(b): T2W and FLAIR axial images showing atrophy of bilateral cerebellar hemispheres and vermis

Case 1
A 5yrs old child presented with complaints of fever and convulsions. He had silvery-grey hair on examination. He had history of multiple hospital admissions with same complaints. His imaging details are not available. He expired at the age of 12yrs.

Case 2
A 13-year-old girl presented with a history of headache, nausea of 3-4 days duration, generalized tonic clonic seizures with up-rolling of eye balls and frothing from mouth. These convulsions lasted for 5 to 10mins. She had similar complaints one year back. She also has history of goiter since 20 months. On examination she was pale, had silvery-grey hair (Fig 1). Neurologically she had normal tone in both limbs with power of 3/5 on both sides. Reflexes were normal. She had ataxia. Rest of the systemic examination was normal. A complete blood count showed anaemia. Renal function tests and liver function tests were within normal limits. CSF examination showed 100 nucleated cells/ cmm, (90% lymphocytes, 10% monocytes), Proteins 49mg%, sugar 50mg%, chlorides 695mg%. On Zeihl Neelsen stain, no acid fast bacteria were detected. Ultrasonography examination of abdomen was normal. Her first MRI brain examination showed diffuse leptomeningitis with early hydrocephalus (Fig 2). She also had non-enhancing hyperintensity in left superior frontal gyrus, which was highly suggestive of focal cerebritis with diffuse cerebral edema and tonsilar herniation. Follow up MRI brain revealed extensive ill-defined enhancing lesions in cerebellar white matter (Fig 4, 6). Few non enhancing gliotic areas were seen in supra-tentorial white matter (Fig 3, 5). This time CSF examination was normal. Recent follow up MRI scan shows significant resolution of signal abnormalities and gliotic changes in cerebellar lesions (Fig 7, 8).

Case 3
This 8-year-old younger sibling presented with a history of left sided focal convulsions. She had similar complaints in the past and was started on valparoate 1 year back. She never had headache, urinary or bowel complaints, bleeding from any part of the body. She had delayed developmental mile stones. On clinical examination she was pale, had silvery-grey hair (Fig 9). Her vital parameters were normal. Neurologically she has normal tone in both limbs, power of 3/5 on both sides. Reflexes were normal. She has ataxia. Rest of the systemic examination was normal. A complete blood count showed mild anaemia (Hb10.8g/dl). Renal and liver function tests were within normal limits. Ultrasonography of abdomen was within normal limits. On present MRI brain study reveals gliotic changes involving cerebellar hemispheres, vermis with significant atrophy. Mild atrophy of supra-tentorial neuroparenchyma is also noted (Fig 10).

Case 4
This is 7 yr old girl with history of repeated convulsions since two yrs and was on antiepileptic medications. She had delayed developmental mile stones, pale and gray colored hairs. Neurological examinations was normal. Bochemical studies were also within normal limits. MRI revealed generalised cerebral atrophy with dilated CSF spaces and ventricles (fig.11).

Case 5
A 10-year-old girl presented with a history of weight loss, few episodes of vomiting and past history of generalized tonic clonic seizures with up-rolling of eye balls six months back. On examination she was pale, had silvery-grey hair . Neurologically she had normal tone in both limbs with power of 4/5 on both sides.. Ultrasonography examination of abdomen showed mild hepatomegalyl. Her first MRI brain examination showed non-enhancing hyperintensities in periventricular and subcortical white matter with cerebral atrophy.

Case 6
A 6yrs old child presented with complaints of fever and convulsions. He had silvery-grey hair on examination. He had history of multiple hospital admissions with same complaints. Neurological examinations was normal. Bochemical studies were also within normal limits. MRI study reveals mild cerebral atrophy, no other abnormality seen

Case 7
This is 11 yr old girl with delayed development and history of repeated convulsions since four yrs and was on antiepileptic medications. She had delayed mile stones, pale colored brittle hairs. Neurological examinations was normal. Bochemical studies were also within normal limits. MRI revealed dilated CSF spaces and ventricles with few scattered subcortical white matter abnormalities on FLAIR.

Case 8
A 13-year-old girl presented with vomitting and nausea of 8 days, generalized tonic clonic seizures with up-rolling of eye balls and frothing from mouth. She had similar complaints 6 month back. On examination she had pale and grey hair Neurologically she had normal tone in both limbs with power of 4/5 on both sides. Reflexes were normal. Lab investigations reveald mild iron deficiency anemia. MRI brain examination showed non-enhancing hyperintensity in bilateral frontal and parietal hyperintensities in gray and subcortical white matter with few areas of gliosis. The CSF examination was normal.

Case 9 This is 10 yr old girl presented with focal convulsions since two yrs and delayed development . Neurological examinations was normal. Hairs were pale coloured. Bochemical studies were also within normal limits. MRI revealed no significant abnormality

DISCUSSION

Griscelli syndrome (GS) is a rare autosomal recessive disorder. It is caused by mutation in the MYO5A (GS1, Elejalde), RAB27A (GS2) or MLPH (GS3) genes. Common features of all three subtypes of this disease include pigmentary dilution of the hair and skin with silvery-gray hair. GS1 is characterized by primary neurological impairment, whereas the GS2 patients have severe immunological deficiencies that lead to recurrent infections and hemophagocytic syndrome. GS3 is characterized by the pigmentation dysfunction only. All our patients presented with neurological dysfunctions and has no features of immunological deficiencies and hemophagocytic syndrome. The close differential diagnosis for griscellies syndrome is Chediak-Higashi syndrome (CHS), Elejalde syndrome. Chediak-Higashi syndrome is characterized by neurologic and immunologic impairment .Presence of giant lysosomes / endosomes (inclusion bodies) in leukocytes or giant melanosomes in melanocytes is characteristics of CHS and, conversely, the absence of giant granules in leukocytes but the presence of a large accumulation of normal mature melanosomes within the melanocytes are typical features of GS (8).Patients with Elejalde syndrome (ES) are also being compared with GS. The distinctive clinical feature of ES is the absence of recurrent accelerated phases, a hallmark of GS and CHS. Elejalde syndrome differs further by the presence of PAS positive lysosomal inclusions in fibroblasts and by electron microscopy of the skin (8).

A very few cases had been presented as type 1Griscelli syndrome.

NazanSarperGu¨ r Akansel et al[1] presented a 7 month old baby with silvery-gray hair and areas of increased T2 signal involving the genu and posterior limb of the right internal capsule, posterior aspects of both thalami, pars compacta of the substantianigra bilaterally, patchy areas in both parietal lobes, peri aqueductal white matter, external and extreme capsules and frontal subcortical white matter on the right side.

Masriet al[2] presented a 6-year old boy from Jordan with silvery-gray hair, fever and focal seizures. In MRI brain there were hyperintense signal in the periventricular cerebral white matter and left thalamus without any atrophic changes in the posterior fossa and cerebral hemispheres.

Rajadhyax et al[3] reported a 32 months old girl with hydrocephalus unaccompanied by haematological abnormalities, organomegaly or hemophagocytic coagulopathy.

Brismar and Harfi[4] reported 4 patients with Griscelli syndrome, all had white matter changes, which progressed from the posterior fossa to the supratentorial periventricular white matter with addition to severe brain atrophy, but none of them had immune deficiencies and hematologic abnormalities. Similar findings are seen in second case of our study.

The prognosis and treatment of GS depend on the type of condition. GS is most commonly diagnosed between the ages of 4 months and 7 years (7). There is no cure for GS1 and the lives of the patients depend on the severity of the neurological impairment. The treatment of choice for GS2 is bone marrow transplantation (BMT), which should be done as early as possible. GS3 does not need treatment since it involves altered pigmentation only.

Our cases are also presented with only neurological symptoms (type 1GS) without any hemophagocytosis. Among three siblings first child has expired at the age of 15 years. The second child has recurrent neurological impairments with low IQ for age. The third child is relatively well with recurrent episodes of focal convulsions with normal IQ for age.

CONCLUSION

We present the case series of Griscelli syndrome in three siblings of Indian family. Primary neurological deficiency marked by profound cerebellar atrophy is associated to GS1 (Elejalde). Neuroimaging with brain MRI is a successful tool in the evaluation of central nervous system abnormalities. Griscelli syndrome should always be suspected in any child with silvery hair because early bone marrow transplantation might offer a chance for survival.

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