End-stage Renal Disease in Griscelli Syndrome

Sir,

We report a previously unknown renal manifestation of Griscelli syndrome (GS). A 7-year-old developmentally normal male child, second product of a non-consanguineous marriage, presented with pallor and failure to gain weight and height. His elder sister had partial albinism and chronic kidney disease (CKD). She died at age of 11 years awaiting renal transplant. On examination, the index child had pallor, frontal bossing, oculocutaneous albinism, short stature (height- 108 cm), and stage-1 hypertension (BP = 110/60 mmHg). Eye evaluation showed eyelashes and iris hypopigmentation. Rest of the systemic examination was normal. His hemogram revealed microcytic hypochromic anemia and normal leukocyte count without platelet clumping or abnormal vacuolated granules on peripheral blood film (PBF). Electron microscopy confirmed normal leukocytes and platelets. Blood gas showed normal anion gap metabolic acidosis. Renal functions indicated nonoliguric renal failure (blood urea/serum creatinine-112/2.3 mg/dL). Estimated glomerular filtration rate was 21.2 mL/min/1.73 m^2, suggestive of grade-4 CKD. Vitamin D-deficiency rickets (25(OH) D- 14.9 ng/mL) with hyperphosphatemia was present. Complement levels were reduced (C3- 80.2 mg/dL, C4- 8.6 mg/dL). His urine analysis, antinuclear antibody, immunodeficiency workup, viral markers, glycosylated hemoglobin, and thyroid function tests were normal.

In view of oculocutaneous albinism, strong family history, and CKD, hair light microscopy was done, which showed abnormal pigmentation with uneven clusters of melanin pigment in the center of the hair shaft, confirmatory of GS [Figure 1]. Skin biopsy showed epidermis and dermis negative for IgG, IgM, IgA, and C3. Ultrasound abdomen showed left kidney 6.3 cm and right kidney 5.5 cm with bilateral raised cortical echogenicity consistent with bilateral renal parenchymal disease. Dimercapto succinic acid (DMSA) scan showed global impairment in renal function (left kidney 29%, right kidney 71%). Renal biopsy was withheld in view of bilateral small kidneys. He was started on CKD treatment, which included sodium bicarbonate, activated vitamin D, calcium carbonate, and erythropoietin. He is under follow-up while awaiting renal transplant.

GS, a rare autosomal recessive disorder which results in pigmentary dilution of the skin, silver-gray shiny hair, and presence of large clumps of pigment in hair shafts due to abnormal accumulation of melanosomes in melanocytes. Three main types of GS are caused by mutations of the tripartite complex comprising Rab27a, melanophilin (Mlph), and Myosin Va genes. The tripartite complex helps in vesicle transport and membrane trafficking in the melanosome transport pathway. Any defect in the pathway results in impaired melanosome transport manifesting as albinism. Our case fits in Type 3 GS, which is due to a defect in Mlph gene on chromosome 2q37.3 and presents with partial albinism without any immunological or neurological involvement.[1] Close differentials include Chediak–Higashi syndrome (CHS) and Hermansky–Pudlak syndrome (HPS). There is abnormal vacuolation in the granulocytes on PBF in CHS, with the hair shaft containing evenly distributed regular melanin granules.[2] In GS, the clusters of melanin pigment in the hair shaft are larger than in CHS and are distributed in the center of the hair shaft, as was typically seen in our case. In HPS, there is platelet clumping and absent dense bodies on electron microscopy, giving it a butter cookie appearance with reduced pigment in the hair shaft, but no abnormal clumping.[3] As treatment and prognosis differ among various types, genetic diagnosis is required early in life.

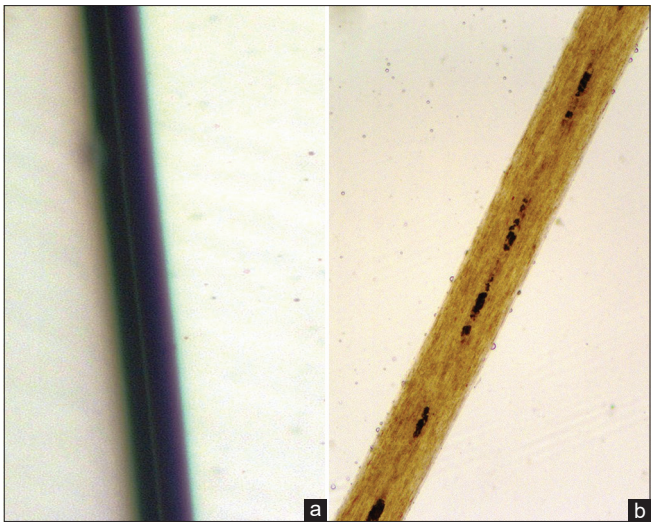

Figure 1: Hair light microscopy showing (a) normal hair pigmentation and (b) abnormal pigmentation in the index case with uneven clusters of melanin in the center of the hair shaft, pathognomonic of Griscelli syndrome

Authors' contributions

Vidushi Mahajan clinically managed the patient, wrote the first draft, and approved the final manuscript. Shivanjali Sood did literature search, assisted in writing the draft and, approved the final manuscript. Reena Das did hair shaft microscopy and reported hemogram, including electron microscopy, and approved the final manuscript.

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Conflicts of interest

There are no conflicts of interest.

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