# Glycogen Storage Disease 1a with Piebaldism

**BHASWATI GHOSHAL, NIRMALYA SARKAR, MALA BHATTACHARJEE AND RABINDRA BHATTACHARJEE**
*From the Departments of Pediatrics and Cardiology, Calcutta National Medical College, Kolkata, India.*

*Correspondence to:*
*Bhaswati Ghoshal, Assistant Professor, Department of Pediatric Medicine, Calcutta National Medical College Hospital, Kolkata, India.*
*bhaswatighoshalmailme@yahoo.com*
*Received: March 09, 2010;*
*Initial review: May 10, 2010;*
*Accepted: November 03, 2010.*

A 3½ years old male child born by consanguineous marriage presented with white forelock and symmetric hypopigmented areas present since birth, similar to his mother and elder sister. Hepatomegaly was noticed at one year of age. Liver biopsy revealed enlarged pale hepatocytes distended with glycogen. Skin biopsy revealed absence of melanin pigment in white depigmented skin. *G727T* gene splice mutation was diagnosed in exon 5 of 17q21 chromosome.

**Key words:** *Child, Glycogen storage disease, India, Piebaldism.*

Piebaldism is a autosomal dominant disorder of localized amelanotic patches as a result of permanent localized absence of melanocytes. GSD1a is autosomal recessive disorder of carbohydrate metabolism characterized by deficiency of Glucose-6-phosphatase. We herein report a rare case of GSD type1a with piebaldism.

## CASE REPORT

A 3½-year old male child was admitted with history of gradual distention of abdomen since one year of age. The child had localized hypopigmented areas over anterior scalp, both elbows, knees, over abdomen since birth, which were similar to those in his mother and elder sister (***Fig.*1**). Second degree consanguinity was present in parents. The maternal grandparents also had 2nd degree consanguinity. At around 9 months of age, the child had an episode of convulsion on overnight fasting. Three more convulsions were reported later. Child had overwhelming hunger, poor growth, frequent lethargy and difficult arousal from overnight sleep. There was no history of recurrent infections or muscle weakness. On examination, the child had doll like face, fat cheeks, short stature, relatively thin extremities, protuberant abdomen, delayed milestones. Deafness was absent. He was underweight and stunted. There was no family history of protuberant abdomen or hepatomegaly. Liver span was 13 cm and firm. Spleen was not palpable. Laboratory workup revealed haemoglobin 10g/dL, complete blood count including differential count, platelet count, bleeding time and coagulation profile were within normal limits. Random blood glucose level was 46 mg/dL. Liver enzymes and uric acid were within normal limits. Serum cholesterol was 186 mg/dL (Normal 155 mg/dL), triglyceride was 320 mg/dL (Normal 56 mg/dL). Lactate-creatinine ratio was estimated in urine which was 0.9 mmol/mmol. USG revealed hepatic enlargement. Blood gas analysis revealed metabolic acidosis with respiratory compensation. EEG and MRI brain were within normal limits. Percutaneous liver biopsy revealed enlarged pale hepatocytes distended with glycogen, compressing sinusoids and giving a mosaic pattern. Intracellular glycogen was demonstrated with periodic acid Schiff reaction, readily digested by diastase. Slender periportal fibrous band was present. Histological features were consistent with liver glycogenosis. Genetic sequencing was done for all exons of *17q21* gene. A *G727T* gene splice mutation was diagnosed in exon 5 of *17q21* gene. The child was homozgyous for the mutation. Genetic analysis of parents for GSD1a could not be arranged. Punch biopsy of piebald skin revealed absence of melanocytes and melanin pigment in white depigmented area by Manson Fontana stain. The case was diagnosed as a case of Glycogen storage disease 1(a) with piebaldism.

After starting dietary therapy, the fasting blood sugar increased to 80-85mg/dL, urinary lactate-creatinine ratio was 0.07 mmol/mmol. Annual USG surveillance and sunprotective measures were advised. Skin grafting for repigmentation of piebald skin is also planned.

## DISCUSSION

GSD1(a) is an autosomal recessive disease caused by mutations at loci 17q21 [1]. This patient have G727T splice mutation which may be manifested due to second degree consanguinity among parents and maternal grand parents. G727T mutation is a common reported mutation

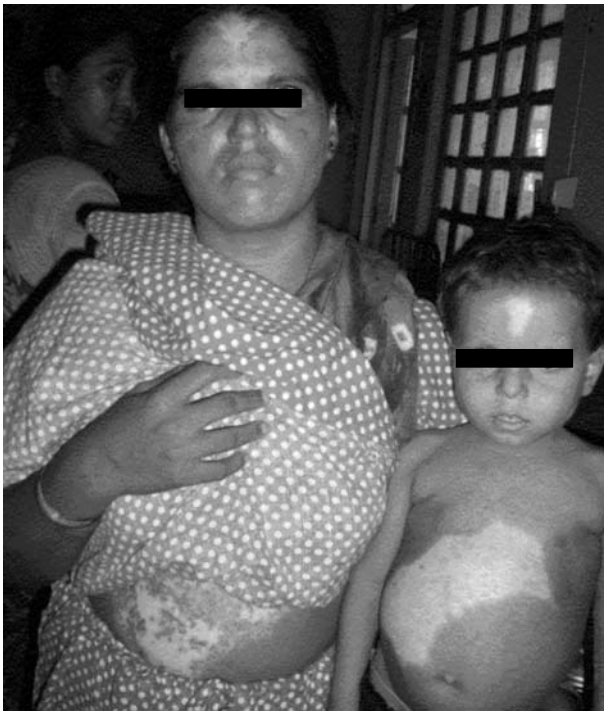

**FIG.1** *Piebaldism seen in patient and mother*.

in Japanese and Chinese patients [2]. In Indian children, this mutation is relatively rare. In GSD1a cases, stringent genotype phenotype relation is not found [3]. The piebald skin have mutation of KIT gene inherited in a autosomal dominant manner. These two mutations appears to be unrelated and a chance finding. Histological features in liver glycogenoses include documented fatty change, nuclear hyperglycogenation and fibrosis [4]. We could demonstrate glycogen in hepatocytes in our patient with slender periportal fibrosis. Our patient has responded to uncooked cornstarch feeding to maintain the blood sugar level. Young infants need continuous nasogastric feed with sucrose free low lactose formula enriched with maltodextrine for this purpose [5].

The differential diagnosis of Piebaldism are Addison disease, albinism, vitiligo, Vogt koyanagi Harada syndrome, Waardenburg Syndrome, etc. The nonprogressive nature of the hypopigmentation and absence of associated features rules out the other possibilities. Piebaldism is one of the cutaneous signs of Waardenburg syndrome, along with heterochromia of iris, lateral displacement of inner canthi, and deafness [6]. The present case did not have deafness or facial features of Waardenburg syndrome. The KIT mutation in vicinity of codon 20 of 4q12 chromosome leads to the usual phenotype of static piebaldism [7]. The depigmented skin in piebaldism is unresponsive to medical and light treatment. Autologous punch grafting for repigmentation in piebaldism may be considered [8].

*Contributors*: MB and RB diagnosed the case. BG and NS prepared the manuscript and managed the case.
*Funding*: None; *Competing interests*: None stated.

## REFERENCES

1. Brody LC, Abel KJ, Castilla LH, Couch FJ, McKinley DR, Yin G, *et al*. Construction of a transcription map surrounding the BRCA1 locus of human chromosome17. Genomics. 1995; 25:238-47.
2. Okubo M, Aoyama Y, Kishirmoto M, Shishiba Y, MuraseT. Identification of point mutation (G727T) in the glucose 6 phosphatase gene in Japanese patients with glycogen storage disease type1a and carrier screening in healthy volunteers. Clin Genetics. 1997;51:179-83.
3. Chou JY, Mansfield BC. Mutations in the glucose 6 phosphatase-á (G6PC) gene that cause type1a glycogen storage disease. Hum Mutation. 2008;29:921-30.
4. Hasan Ö. Glycogen storage diseases: New perspectives. World J Gastroenterol. 2007; 13:2541-53.
5. Rake JN, Visser G, Labrune P, Leonard VJ, Ullrich K, Smit GP. Guidelines for management of glycogen storage disease type 1-European Study on Glycogen Storage Disease type 1(ESGSD-1). Eur J Pediatr. 2002;161:112-9.
6. Jan JA, Stroedter L, Haq AU. Association of Shah Waardenburg syndrome: a review of 6 cases. J Pediatr Surg. 2008;43:744-7.
7. Ward KA, Moss C, Sanders DS. Human piebaldism: relationship between phenotype and site of kit gene mutation. Br J Dermatol. 1995;132:929-35.
8. Garg T, Khaitan BK, Manchanda Y. Autologous punch grafting for repigmentation in piebaldism. J Dermatol. 2003;30:849-50.