Hirschsprung's Disease with Congenital Hypothyroidism

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We report a female newborn baby who presented with vomiting and abdominal distension on day 21 of life. Examination revealed facial puffiness, open posterior fontanelles, dry skin, cold peripheries and prominent abdominal veins with visible peristalsis. Barium enema revealed dilated proximal colon, empty rectum, funnel like transition zone between proximal dilated and distal constricted bowel. Serum TSH level was >150 µIU/mL. Biopsy revealed aganglionic segment suggesting Hirschsprung's disease, an unusual association with congenital hypothyroidism.

Key words: *Hirschsprung's disease, Hypothyroidism, Neuronal migration.*

Hirschsprung's disease (HD) as well as congenital hypothyroidism can present with functional intestinal obstruction and abdominal distension in neonates [1]. Hirschsprung's disease results from a colonization defect of neural crest cells through the colon and the aganglionic segment presents with obstruction [2]. Thyroid hormone is necessary for neuronal migration and lamination during brain development. Although hypothyroidism impairs colonic motility resulting in pseudo-obstruction, which may be reversed by thyroxine supplementation, the effects of hypothyroidism on neuronal migration through bowel have not been adequately studied. We report a child with co-existence of the two conditions.

CASE REPORT

A 21-day old female infant, product of a consanguineous marriage, presented with vomiting, abdominal distension and passage of small quantity of stool, liquid in consistency, for the previous two weeks. There was an associated history of poor feeding and excessive cry. There was no history of convulsion, feeding abnormality or any other neonatal illness. The baby had been delivered uneventfully with a birth weight of 2.5 kg and a length of 48 cm. There was no history suggestive of any significant maternal illness during pregnancy or in the past. Examination revealed facial puffiness, open anterior and posterior fontanelles, rough dry skin and cold peripheries. There was no neck swelling or umbilical hernia. On abdominal examination, there were prominent veins, visible intestinal peristalsis and mild hepatosplenomegaly. The rest of the systemic examination was normal. The hemogram, serum electrolytes, kidney and liver function tests were normal. Plain abdominal radiograph revealed dilated gas filled bowel loops. Barium enema revealed dilated proximal colon, empty rectum, delayed emptying time, funnel like transition zone between proximal dilated and distal constricted bowel. Her thyroid showed low T3 (36.4 ng/ml), low T4 (1.4 µg/dL) and high TSH (>150 µIU/mL). The maternal thyroid profile was normal. Thyroid scintigraphy (^{99m}Tc) revealed athyrosis. After hemodynamic stabilization, a colonoscopic biopsy and colostomy were done. Histopathology of the biopsy specimen revealed aganglionic segment, confirming the diagnosis of Hirschsprung's disease. The patient's genetic analysis revealed 46XX karyotype without any chromosomal abnormality or any mutations. She was discharged on oral thyroxine replacement. Five months later, the infant weighed 6.3 kg and her length was 108 cm, and underwent a transanal endorectal pull-through operation followed by colostomy closure.

DISCUSSION

Association of HD along with congenital hypothyroidism is rare [3]. Our patient presented with vomiting, abdominal distension with passage of small quantity of liquid stool which are classically seen in HD. Hirschsprung's disease results from the failure of neural crest cell precursors to colonize the gut resulting in absence of myenteric (Auerbach) and submucosal (Meissner) plexuses [4]. The aganglionic segment is limited to the rectosigmoid in 75% of patients; in 10% the entire colon lacks ganglion cells. Total bowel aganglionosis is rare. HD occurs as an isolated trait in 70% of patients; in association with a chromosomal abnormality it exists in 12% of cases [5]. There are eight genomes associated with this disorder, the most common association being RET proto-oncogene [6]. Our patient's genetic analysis revealed a normalwithout any mutations, hence the other associated abnormalities of MEN2 linked with RET mutation were not searched for and no genetic counseling was offered to family members.

Elevated TSH values with athyrosis observed on

thyroid scintigraphy (^{99m}Tc) confirmed the diagnosis of congenital primary hypothyroidism. There are 3 theories linking congenital hypothyroidism with HD. The most commonly accepted theory is that there is a defective cranio-caudal migration of neuroblasts due to thyroid hormone deficiency which is necessary for appropriate neuronal migration and lamination during brain development [7]. However, Cranio-caudal migration of neuroblasts originating from the neural crest occurs much earlier(5-12 wk gestation) than the recreation of thyroid hormones in the fetus (12 wk gestation). Thyroid hormone in the early gestational period is maternally originated, the mother's thyroid hormone status seems more important than that of the fetus in early pregnancy [9]. The other two theories include: defects in the differentiation of neuroblasts into ganglion cells [8] and accelerated ganglion cell destruction within the intestine; situations in which fetal thyroid hormone levels seem more important.

Although hypothyroidism impairs the colonic motility and function [10], the effect of thyroid hormone on neural crest cell migration through the bowel have not been studied yet. Our case highlights the possible role of thyroid hormones in the development of HD. Further studies are needed to establish this.

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