A Female Neonate with Hirschsprung's Disease and Ichthyosis

Erez Nadir MD, Shmuel Yerman MD and Michael Feldman MD

Neonatal Intensive Care Unit, Hillel Yaffe Medical Center, Hadera, Israel

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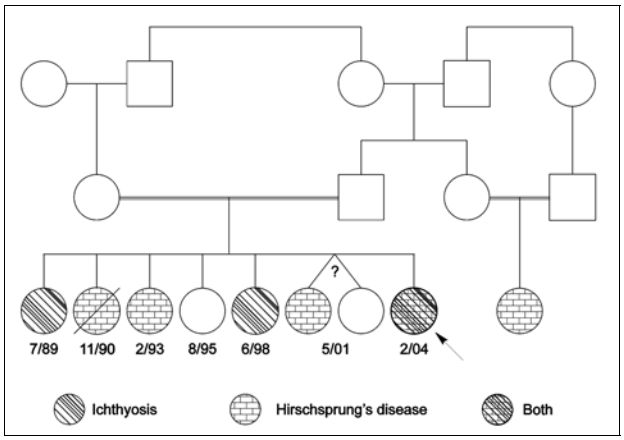
Hirschsprung's disease is a congenital absence of ganglion cells in the distal colon, resulting in a functional obstruction. Ichthyosis refers to a relatively uncommon group of skin disorders characterized by the presence of excessive amounts of dry surface scales and caused by a disorder of keratinization or cornification. We report a female neonate with Hirschsprung's disease and ichthyosis.

Patient Description

A singleton female baby was born in our hospital in February 2004 in the 40th week of her mother's eighth pregnancy. Birth weight was 3,170 g (appropriate for gestational age) and Apgar score was 9 (at 1 minute) and 10 (at 5 minutes). The mother was 36 years old and the father 35 years old, and they are first-degree cousins. Their previous children included seven daughters but no sons. Three of their seven daughters previously had Hirschsprung's disease, and one of them died from the disease. Two of the seven girls had ichthyosis. The family had undergone genetic consultation, but without results. During the current pregnancy, wide bowel loops were seen on ultrasound.

On admission the baby was alert, pink, with good tonus, and cried loudly. Skin turgor was good. The skin of her entire body was desquamated, and she had left pes plannovalgus. The rest of the examination was within normal limits.

The baby was breathing room air spontaneously, was stable hemodynamically, and had no neurologic deficit. Due to vomiting in the first days of life and in view of the family history, a rectal biopsy was performed. Hirschsprung's disease was diagnosed. Left extended hemicolectomy with appendectomy, and colostomy were performed. Ichthyosis was diagnosed by dermatologic examination. Left pes plannovalgus was treated with physiotherapy. The baby was discharged home at the age of 29 days, and conclusive surgery was planned.



The family tree

The family

The mother, S.M., born in 1968, is married to her first cousin (the son of her father's sister). Her husband has a sister who is also married to a first cousin (the son of her father's sister). They too have a daughter with Hirschsprung's disease [Figure].

The first daughter of S.M. was born in July 1989. She had mild ichthyosis that resolved with local treatment. She was discharged from hospital at age 2 days.

The second daughter was born in November 1990 and was also discharged after 2 days. She was readmitted due to vomiting when she was 4 days old. Laparotomy was performed due to bowel obstruction, with partial ileectomy and end-to-end anastomosis. Pathologic examination revealed ganglions. After about 2 weeks there was a leakage from the anastomosis and an ileus. Another laparotomy was performed, with resection of part of the ileum and the cecum, side-to-end anastomosis, and colostomy. Sweat test was negative. When she was 7 months old the colostomy was closed. The part of colon that was resected was found to contain ganglions. About 3 weeks later, a third laparotomy was performed with partial colectomy and ileectomy and a new colostomy. While ganglions were found in the ileum part, this time there were no ganglions in the colon part. The colostomy was closed when she was 10 months old, and a new colostomy was undertaken a month later. During the next year and half, she was on total parenteral nutrition at least part of the time, which caused jaundice and hepatitis. She died at age 2 years 2 months.

The third daughter was born in February 1993. A laparotomy was performed due to enterocolitis, with double ileostomy and appendectomy. There were no ganglions in the colon. Definitive surgery was conducted when she was 9 months old. When she was 1 year 9 months old, a laparotomy was performed because of adhesions.

The fourth daughter was born in August 1995, and was discharged at age 2 days.

The fifth daughter was born in June 1996. Examination revealed ichthyosis. She was discharged at age 2 days.

The sixth and seventh girls are twins born in May 2001. One of them was healthy. The other had bowel obstruction. On biopsy there were no ganglions in the colon. Total colectomy with colostomy was performed when she was 2 months old. The colostomy was closed after 6 months.

The eighth daughter is the case reported here.

Comment

There are no specific published data in the Statistical Abstract of Israel, but extrapolation of the published data [1] showed that the prevalence of families with eight children is about 1–1.5% of families in the Israeli population. Assuming a 50% chance for having a girl at every birth, families with eight girls are much rarer. Probably, all male fetuses aborted, which most likely occurred very early during pregnancy since the mother reported no delay in her menstrual cycle.

Hirschsprung's disease is thought to be due to a disturbed rostrocaudal migration of neural crest cells through the gastrointestinal tract during its development. It occurs in around 1 in 5,000 live births, with a male predominance of about 4:1. Hirschsprung's disease also occurs in association with other syndromes and anomalies, such as congenital central hypoventilation syndrome (Ondine's course), 22q11 deletion syndrome, and in a variant of Shah-Waardenburg syndrome. These conditions primarily involve abnormalities in systems developmentally related to the neural crest. Hirschsprung's disease has a strong genetic component, with increased intrafamilial risk, of 4% for siblings compared to 0.02% in the general population [2].

Ichthyosis that has its onset at birth is lamellar. Lamellar ichthyosis type I occurs in 1:200,000 to 300,000 live births. Most cases are due to a mutation in the transglutaminase 1 gene mapped to locus 14q11.2. This enzyme is thought to be responsible, at least in part, for the assembly of cornified cell envelope precursor protein to form a cornified cell envelope [3]. Lamellar ichthyosis type II is mapped to locus 2q33-35. In neither locus has a form of Hirschsprung's disease been mapped.

A Medline search disclosed only one report of ichthyosis and Hirschsprung's disease occurring in the same patient. The authors contend that their patient likely represents a case of keratosis, ichthyosis and deafness syndrome [4].

In conclusion, we report a family with no boys, eight girls, some of whom had Hirschsprung's disease, and some ichthyosis. This may be an unusual coincidence, but it could also be an interesting association, where all the males aborted, and some of the females have either Hirschsprung's disease, or ichthyosis, or both.

References

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Correspondence: Dr. E. Nadir, Neonatal Intensive Care Unit, Hillel Yaffe Medical Center, Hadera 38100, Israel.
Phone: (972-4) 630-4379
Fax: (972-4) 630-4323
email: premature@hillel-yaffe.health.gov.il