Intestinal lymphangiectasia secondary to neuroblastoma

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RM REIFEN, PM SHERMAN. Intestinal lymphangiectasia secondary to neuroblastoma. Can J Gastroenterol 1994;8(1):49-51. An eight-month-old infant presented with a 10-day history of vomiting and diarrhea, and a one-week history of swelling of the lower extremities. Laboratory evaluations revealed hypoproteinemia and lymphocytopenia due to protein-losing enteropathy. Peroral small bowel biopsy showed intestinal lymphangiectasia. Subsequent onset of unexplained ecchymosis and obstructive jaundice resulted in additional studies which revealed an omental neuroblastoma as the underlying etiology of the infant's symptoms. This report emphasizes the importance of considering secondary, obstructive causes for lymphangiectasia and protein-losing enteropathy.

Key Words: Intestine, Lymphangiectasia, Malabsorption, Neuroblastoma, Protein-losing enteropathy

Lymphangiectasie intestinale secondaire à un neuroblastome

RÉSUMÉ : Un nourrisson de huit mois a présenté un épisode de dix jours de vomissements et de diarrhée et un oedème d'une semaine des membres inférieurs. Les analyses de laboratoire ont révélé une hypoprotéinémie et une lymphocytopenie dues à une entéropathie avec déperdition protéique. La biopsie perorale de l'intestin grêle a révélé une lymphangiectasie intestinale. La survenue sub-séquente d'ecchymoses non expliquées et d'un ictère obstructif ont nécessité d'autres analyses qui ont révélé la présence d'un neuroblastome omental comme cause sous-jacente des symptômes de ce nourrisson. Ce rapport souligne l'importance de réfléchir aux causes obstructives secondaires possibles dans les cas de lymphangiectasie et d'entéropathie avec déperdition protéique.

PROTEIN-LOSING ENTEROPATHY refers to a symptom complex of hypoproteinemia, hypoalbuminemia and lymphocytopenia in which there is excessive loss of plasma proteins into the lumen of the gastrointestinal tract

(1). Protein-losing enteropathy occurs in a wide variety of diseases involving different regions of the gastrointestinal tract (2).

Lymphangiectasia is a common cause of protein-losing enteropathy,

characterized by dilated lymphatics in the lamina propria, submucosa and subserosa of the intestine (1). In this report, we present an infant with protein-losing enteropathy and intestinal lymphangiectasia due to an unusual cause: obstruction of intestinal lymphatics by a neuroblastoma present in the omentum.

CASE PRESENTATION

An eight-month-old girl of Greek heritage presented with a two-day history of vomiting and diarrhea (10 to 12 watery stools daily) 10 days prior to admission to the hospital. She was treated with clear fluids and rectal suppositories containing an antiemetic. For the seven days prior to evaluation, increasing swelling of the feet and legs was observed.

Maternal pregnancy and the delivery were unremarkable. The child's birth weight was 3100 g. The neonatal and past histories were unremarkable. The family history was unremarkable except for a maternal history of atopy. There were no other siblings. The parents were not related other than by marriage.

The child was irritable but alert and well hydrated. Height and weight were both at the 50th percentile for age. There was evidence of perianal erythema and a scaly rash in the antecubital fossae. Heart sounds were regular and easily auscultated. The chest was clear to auscultation. The abdomen was distended with an everted umbilicus and a soft liver edge palpable 3 cm

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Received for publication May 13, 1993. Accepted June 24, 1993

Figure 1 Small bowel biopsy showing blunted villi with distension of lymphatics (arrows). Original magnification X25

below the right costal margin. There were no palpable splenomegaly or masses. Bowel sounds were normal.

Initial laboratory values included: hemoglobin, 140 g/L (age-specific reference range 110 to 140); white blood cell count, 5.4×10^9 /L (polymorphonuclears, 2.8×10^9 /L; lymphocytes, 0.81×10^9 /L [range 4 to 10]; eosinophils, 0.16×10^9 /L; platelet count, 409×10^9 /L (range 150 to 400); and erythrocyte sedimentation rate, 3 mm/h (normal less than 20 mm/h). Serum electrolytes were (in mmol/L): sodium, 132; potassium, 4.2; chloride, 98; and bicarbonate, 22. Total protein (in g/L, normal

range in brackets) was 44 (54 to 75); albumin, 18 (32 to 48); immunoglobulin (Ig) G, 1.75 (2.73 to 16.60); IgM, 0.97 (0 to 2.16); and IgA, 0.10 (0 to 1.00). Liver function tests included (normal range in brackets): alanine aminotransferase, 23 IU/L (less than 40); aspartate, 111 IU/L (less than 40); alkaline phosphatase, 103 IU/L (185 to 555); total bilirubin, 18 μ mol/L (less than 18); and prothrombin time, 12.3 s (10.5 to 13.5). Serum calcium was (in mmol/L, normal range in brackets) 1.99 (2.25 to 2.74) and phosphate was 1.11 (1.3 to 2.20). Triglyceride was (in mmol/L, normal range in brackets)

1.05 (0.34 to 1.58) and cholesterol was 2.90 (less than 4.91). Urinalysis was unremarkable without evidence of proteinuria. A chest radiograph, electrocardiogram and two-dimensional echocardiogram were normal. A barium meal was normal without evidence of malrotation. Stool samples examined by culture and ova-and-parasite analysis were negative. The alpha-1 antitrypsin clearance was 40 mL/day (normal range less than 22).

A peroral duodenal biopsy documented lymphangiectasia (Figure 1), and the child was placed on a medium-chain triglyceride containing infant formula as therapy.

However, the child subsequently developed periorbital ecchymosis and jaundice accompanied with abnormal liver enzyme tests and platelet count of 311×10^9 /L. Further investigations included a 24 h urine collection for excretion of vanilmandelic acid – 127 μ mol/day (normal value for age younger than 12 months) and homovanillic acid – 65 μ mol/mol creatinine (normal less than 20). Computerized axial tomography of the abdomen demonstrated a mesenteric and omental mass with calcifications that extended into the retroperitoneal space (Figure 2). A cholecystocholangiogram showed the omental mass impinging on the ex-

Figure 2 Computerized axial tomography scan of the abdomen showing a retroperitoneal mass with calcifications (arrows) extending anteriorly into the root of the mesentery

Figure 3 Cholecystocholangiogram showing a complete obstruction of the common bile duct (arrow)

tra-hepatic biliary tract with obstruction to flow (Figure 3). A bone scan showed retro-orbital metastatic lesions. A laparotomy was performed to provide a histological diagnosis. Histological review of the biopsy showed a neuroblastoma with features of early differentiation consistent with the 'stroma-poor' classification of Shimada et al (3). The protein-losing enteropathy resolved with successful treatment of the tumour.

DISCUSSION

Enteric losses of protein in our patient were consistent with intestinal lymphangiectasia, and this diagnosis was confirmed by the presence of dilated lymphatic channels in the mucosa and submucosa of the duodenum. Intestinal lymphangiectasia is characterized by dilated intestinal submucosal and subserosal lymphatics, protein-losing enteropathy, hypoalbuminemia, hypoproteinemic edema and lymphocytopenia. The disease can vary widely in both the clinical spectrum of manifestations and its severity. Lymphangiectasia can be limited to the

intestine or involve multiple organs, such as occurs in Noonan syndrome, Turner syndrome and Milroy disease (4). When confined to the intestinal tract, lymphangiectasia can be due to primary or secondary causes. Primary lymphangiectasia is presumed to be due to a congenital lymphatic anomaly (1).

Secondary cause of intestinal lymphangiectasia are related to obstruction of mesenteric lymph nodes and lymphatic channels as is seen, for example, in malrotation (5). Protein-losing enteropathy has also been reported in association with malignant tumours – usually primary tumours of the gastrointestinal tract as well as in lymphosarcoma and Hodgkin's disease (6). Protein-losing enteropathy and lymphangiectasia due to lymphatic obstruction by the tumour mass of a neuroblastoma have been reported previously in two other children (7,8). Neuroblastoma, a common tumour of infants less than one year of age (9), originates from amine precursor uptake and decarboxylation cells in the neural crest (10). Metastases from neuroblastoma characteristically migrate along

paravertebral lymph nodes (10), which potentially could obstruct the lymphatic flow. Over the past 10 years, seven children were diagnosed with intestinal lymphangiectasia at The Hospital for Sick Children in Toronto, Ontario. The only child with secondary lymphangiectasia in this group was the presented patient.

CONCLUSIONS

This case report emphasizes that small bowel biopsy, considered a definitive diagnostic procedure for intestinal lymphangiectasia (6), does not differentiate primary causes from secondary etiologies. Therefore, distinction of primary, from secondary, causes of lymphatic obstruction should be part of the evaluation of all patients presenting with protein-losing enteropathy due to lymphangiectasia. In children, additional investigations (in the authors' estimation) should include measurement of urinary catecholamine levels, abdominal ultrasonography, a barium meal to localize the ligament of Treitz and, possibly, computerized tomography of the abdomen.

ACKNOWLEDGEMENTS: P. Sherman is the recipient of a Career Scientist Award from the Ontario Ministry of Health.

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