The Turkish Journal of Pediatrics 340 107 - 109, 1992

NEUROBLASTOMA PRESENTING AS PROTEIN – LOSING ENTEROPATHY*

*Turgay Coşkun MD***, Hasan Özen MD***, Münevver Büyükpamukçu MD**** Gülsev Kale MD*****

SUMMARY: Coşkun T, Özen H, Büyükpamukçu M, Kale G. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Neuroblastoma presenting as protein - losing enteropathy. Turk J Pediatr 34: 107-109, 1992.

Protein - losing enteropathy is often reported to be associated with malignancies such as Hodgkin's disease, non - Hodgkin's lymphoma, and mesenteric mesenchymoma, but it seldom complicates neuroblastoma. In this report, we describe a case of neuroblastoma presenting as protein - losing enteropathy in which neurohumoral mechanisms were involved. *Key words: neuroblastoma, protein - losing enteropathy.*

Protein - losing enteropathy (PLE) is characterized by loss of plasma proteins from the gastrointestinal tract and the eventual development of hypoproteinemia[1]. Cardiac failure, nephrotic syndrome and various neoplasms may cause PLE as well as primary diseases of the digestive system which may involve any part of the gastrointestinal tract[2].

Neuroblastoma, which is one of the most common malignant tumors of childhood, seldom causes chronic diarrhea[3, 4]. In this report, we describe a case of neuroblastoma which appeared as PLE, and we wish to emphasize that malignant tumors should also be considered among the diseases causing protein - losing chronic diarrhea.

Case Report

A 2½ –month –old female infant was admitted to our hospital for evaluation of mild edema of the feet and watery diarrhea containing no blood and/or mucus which had developed one month prior to admission. She had been breast - fed until the onset of the diarrhea. She had no history of vomiting or fever and had lost 300 g within a period of one month.

Physical examination revealed an infant weighing 5,900 g with acidotic respiration. The temperature was 36 °C, pulse rate 120/min and respiratory rate 40/min.

* From the Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.
** Associate Professor of Pediatrics, Hacettepe University Faculty of Medicine.
*** Resident in Pediatrics, Hacettepe University Institute of Child Health.
**** Professor of Pediatrics and Pediatric Oncologist, Hacettepe University Institute of Oncology.
***** Professor of Pediatrics and Pediatric Pathologist, Hacettepe University Faculty of Medicine.

The liver was palpable 4 cm below the right costal margin and mild pretibial edema was detected.

Initial laboratory studies revealed hemoglobin 14.4 g/dl, white blood cells 10,700/µl with 55 % neutrophils, 37 % lymphocytes, 7 % monocytes and 1 % eosinophils, and platelet count 310,000/µl. Prothrombin time was 20 seconds and partial thromboplastin time 45 seconds. Other studies indicated serum sodium 128 mEq/L, potassium 1.8 mEq/L, chloride 98 mEq/L, CO_2 8.2 mEq/L, SGOT 117 IU/L, SGPT 56 IU/L, alkaline phosphatase 134 IU/L, total protein 2.5 g/dl, and albumin 1.4 g/dl. Routine urinalysis, chest x-ray and bone marrow examination were negative. Urine sodium, potassium and protein concentrations were within normal limits.

The patient had three episodes of tachycardia, in addition to diaphoresis, peripheral cyanosis and hypertension during follow - up. Generalized edema developed. On a repeat examination, a mass was detected upon deep palpation of the epigastric region. Contrast radiography revealed slight slurring of the large curvature of the stomach which implied external pressure. Ultrasound examination confirmed the presence of a 34 x 25 mm solitary mass in the right lobe of the liver. Scintigraphic studies of the liver using 90^m Tc - sulphur colloid showed a solitary nodule at the same site with irregular uptake of radioactivity. Vanyl mandelic acid was positive in a spot urine sample.

An exploratory laparotomy revealed a lobulated 3 x 4 x 3 cm mass alongside the large curvature of the stomach which involved the right adrenal gland and extended into the pancreas and duodenum. There were multiple metastases in the liver. The diagnosis of neuroblastoma was arrived at from biopsies of the mass and the liver. Chemotherapy was instituted. The diarrhea abated and the hypoproteinemia improved in three weeks after the onset of treatment.

Discussion

There are two para-neoplastic syndromes which may coexist with neuroblastoma in childhood. One is myoclonic encephalopathy with opsoclonus, myoclonus, and cerebellar ataxia, while the other is a clinical syndrome of chronic diarrhea, hypokalemia and achlorhydria or more often hypochlorhydria. The latter is caused by oversecretion of vasoactive intestinal polypeptides (VIP)[4]. This syndrome is observed not only in neuroblastoma, but also in other neoplasms of the sympathetic nervous system which secrete VIP[5]. VIP is a peptide of 28 - amino acids mainly synthesized in the duodenum. It acts as a neurotransmitter not only in the gastrointestinal tract, but also in neural tissue elsewhere and shows a wide range of biologic activity such as relaxation of smooth muscles, stimulation of intestinal water and electrolyte excretion, and an increase in the secretion of insulin, glucagon and various hormones of adenohypophysis. VIP is synthesized

from a precursor (pro - VIP) in neuroblastoma cells and the synthesis of pro - VIP is stimulated by Bt_2 cAMP[3].

Although PLE is reported to be more frequently associated with such malignancies as non - Hodgkin's lymphoma, Hodgkin's disease, and mesenteric mesenchymoma, it seldom complicates neuroblastoma[2]. Neoplasms cause PLE mainly by two mechanisms. The first is the direct protein loss from the ulcerated or inflamed mucosa like that seen in primary neoplasms of the gastrointestinal tract, while the second is secondary lymphangiectasia caused by lymphatic obstruction which in turn results in the loss of protein and lymphocytes[1]. Intestinal lymphangiectasia and PLE were reported by Gerdes et al[6] in an 8-month-old baby and by Schusseim[1] in two 3-year-old children with neuroblastoma.

In our case, there was no proteinuria evidenced. The hypoproteinemia was thought to be caused by losses from the gastrointestinal tract. Lymphopenia, which is expected in cases of lymphangiectasia, was not observed and neither was there any external pressure detected during surgery performed on the intestinal wall. Since there was no evidence of lymphangiectasia, intestinal protein loss was attributed to neurohumoral mechanisms. This view was supported by the amelioration of diarrhea and the normalization of the serum protein and albumin levels after the intiation of chemotherapy.

REFERENCES

1. Schussheim A. Protein-losing enteropathies in children. *Am J Gastroenterol* 58:124, 1972.
2. Waldmann TA. Protein-losing enteropathy. *Gastroenterology* 50:422, 1966.
3. Hayakawa Y, Obata K, Itoh N, et al. Cyclic AMP regulation of pro-vasoactive intestinal polypeptide/PHM - 27 synthesis in human neuroblastoma cells. *J Biol Chem* 259:9207, 1984.
4. Bousvaras A, Kirks DR, Grossman H. Imaging of neuroblastoma: an overview. *Pediatr Radiol* 16:89, 1986.
5. Rescorla FJ, Vane DW, Fitzgerald JF, et al. Vasoactive intestinal polypeptide-secreting ganglioneuromatosis affecting the entire colon and rectum. *J Pediatr Surg* 23:635, 1988.
6. Gerdes JS, Katz AJ. Neuroblastoma appearing as protein-losing enteropathy. *Am J Dis Child* 136:1024, 1982.