Severe Form of Primary Intestinal Lymphangiectasia in an One-Year-Old Child

ABSTRACT

Primary intestinal lymphangiectasia (Waldmann syndrome) is a congenital abnormality of the lymphatic system in children – a disease that occurs infrequently. There are about 80 published descriptions of this pathology in infants. The main clinical manifestation of intestinal lymphangiectasia is a syndrome of malabsorption: diarrhoea, nausea, vomiting, abdominal pain and peripheral oedema. In some cases, steatorrhoea of varying severity occurs. Long lasting of the disease, no effect on the therapy leads to such complications as chylous ascites and chylothorax. This paper presents a clinical case of an early debut primary intestinal lymphangiectasia in a 6-month-old child, complicated by development of concomitant immunodeficiency. The final diagnosis was set after the histological examination of biopsy material in jejunum. Substitution therapy with albumin had no positive effect. Because of the constant hypoproteinaemia that had not been corrected with either albumin or ongoing corticosteroid therapy, it was decided to start the sandostatin therapy. With improvement in the patient’s condition, he was transferred from intensive care to the department of somatic pathology. Transfusions of albumin have been cancelled. The protein level increased up to 53 g/l, swelling disappeared, but general sponginess of the tissue remained. The patient was discharged from the hospital with recommendations to continue the combined therapy including sandostatin and compulsory monitoring of the concentration of immunoglobulins.

KEYWORDS intestinal lymphangiectasia, malabsorption syndrome, hypoproteinemia, immunodeficiency, sandostatin

INTRODUCTION

Primary intestinal lymphangiectasia (Waldmann syndrome) is a congenital abnormality of the lymphatic system in children – a disease that occurs infrequently. There are about 80 published descriptions of this pathology in infants\(^1\)-\(^3\). Presumably, the bases for the development of this disease are genetic disorders, and the type of inheritance is autosomal recessive. However, in the literature there are no data about the genetic mutations associated with the development of the indicated anomalies. The intestinal lymphangiectasia is characterized by abnormal enlargement of the lymph vessels in the submucosal and mucosal layers of the colon. Pressure in the lymphatic system increases as a result of impaired lymph drainage and the lymph penetrates into the intestinal lumen\(^1\)-\(^3\). Consequently, the lymph so lost – containing the main immune cells and immunoglobulins – contributes to the emergence of secondary immunodeficiency, characterized by increased susceptibility to infectious diseases\(^4\)-\(^6\). In addition, the process of intestinal absorption of fats, proteins and minerals disrupts, which leads to hypoproteinaemia, hypolipidaemia, hypocalcaemia, often reduced content of iron and copper in the blood and malabsorption syndrome\(^1\)-\(^3\). Primarily, loss of proteins results in the essential decrease of proteins with a long half-life (albumin, ceruloplasmin, immunoglobulins M, G and A), while the concentration of proteins with short half-lives (immunoglobulin E, coagulation factors, prealbumin, transferrin) does not change significantly. If the usual consumption of albumin is 6–10% per day, then albumin loss from intestinal enteropathy increases to 60%. Despite the ability of the liver to synthesize albumin, its activity is not enough to restore a normal level of this protein\(^7\)-\(^8\).

The main clinical manifestation of intestinal lymphangiectasia is a syndrome of malabsorption: diarrhoea, nausea, vomiting, abdominal pain and peripheral oedema. In some cases, there is steatorrhoea of varying severity.
In spite of persistent course, however, no effect on the therapy leads to such complications as chylous ascites and chylothorax.

In the treatment of the most severe cases of intestinal lymphangiectasia, sandostatin is used. Sandostatin is a synthetic cyclic octapeptide, a derivative of endogenous somatostatin with similar pharmacological effects and much longer effect duration. Somatostatin is synthesized by cells of the central and peripheral nervous system, the hypothalamus, the islet cells of the pancreas (β-cells), glandular and neuronal cells of the stomach and intestines, and functions as a neurotransmitter. It is also produced by inflammatory and immune cells, and has autocrine, paracrine and endocrine effects. Further, it controls a large number of physiological functions: the transmission of nerve impulses, cell secretion and proliferation, muscular contractility, intestinal motility, nutrient absorption and function of the immune cells. Its effects are implemented through its interaction with specific somatostatin receptors (SSTRs). Sandostatin is an inhibitor of the endocrine and exocrine secretion of the pancreas, a modulator of intestinal motility, absorption of electrolytes and nutrients, secretion of the stomach and pancreas. It reduces the arterial blood supply to the visceral organs and portal blood flow, inhibits pathologically increased secretion of growth hormone, as well as peptides and serotonin, produced in the gastrointestinal endocrine system. The injection of sandostatin is not accompanied by the phenomenon of hypersecretion of hormones by the mechanism of ‘negative feedback’.

In patients, sandostatin reduces vegetative-vascular reactions, apparently due to its effect on blood vessels and visceral blood flow. Consequently, the hypovolemia associated with the loss of fluids through the intestines is reduced. However, in turn, the reduction of hypovolemia decreases the release of vasoactive substances (serotonin, histamine, catecholamines) that cause vegetative-vascular reactions.

**OBSERVATION**

Patient A: In February 2015, at the age of 6 months he was diagnosed with acute respiratory viral disease, accompanied by rise of temperature up to 38°C. He was treated as an outpatient, and ampicillin was prescribed. For the first time, his mother noticed the swelling on the face, then, during breastfeeding atonic seizures with reduction of albumin (50% of the reference), hypocalcaemia (1.57 mmol/l). Analysis on protein fractions showed a decrease of albumin (292.4 mg/l within 2 days) and hypocalcaemia (1.99 mmol/l). Analysis on protein fractions showed a decrease of albumin (50% of the reference), α₁-globulins were within normal limits, α₂-globulins were decreased by 50% from the normal, β₁-globulins reduced by 28%, β₂-globulins showed a decline of 80% and γ-globulins were reduced by 98% from the normal content.

Clinical signs: the temperature rose up to 38°C, restlessness, single vomiting and bloating.

Oesophagogastroduodenoscopy study: mucosa of the duodenum and jejunum was moderately oedematous, while coating was observed on the walls of the intestine.

Histological examination of the jejunum biopsy: examination of the biopsy of the jejunum mucosa revealed that brush border is visualized throughout. Villi of varying heights and the accumulation of net eosinophilic masses were visualized; further, consolidate friable surface epithelium with the formation of cystic cavities, thereby deforming the villi, were also visualized. Dilated lymphatic vessels were also revealed (Figs. 1, 2). Crypts are not changed, and the number of goblet cells was within the permissible norm. Panett cells had a moderate amount of azurophilic granules. Lymphoplasmocytic infiltrations were revealed in the stroma.

Conclusion: intestinal lymphangiectasia. Chronic atrophic eyeunit without exacerbation.

The results of immunological examination: the total number of leucocytes was within the permissible norm, with absolute lymphopenia. The ratio of cell subpopulations was severely disrupted due to the decrease of the absolute number of T-helper lymphocytes. The content of activated T- and B-lymphocytes increased. Severe hypogammaglobulinemia of all the classes was observed. Immunologist’s opinion: concomitant...
immunodeficiency manifested by infectious syndrome due to the underlying disease.

The doctors, taking into account the age of the infant patient, the presence of massive, symmetrical and peripheral oedema, absence of factors that trigger the occurrence of secondary lymphangiectasia, as well as based on data of histological examination, arrived at the final diagnosis of primary intestinal lymphangiectasia syndrome (Waldmann syndrome), with secondary immunodeficiency.

Treatment at the initial stage of the therapy was as follows: transfusion of the albumin to restore protein levels, antibacterial drugs to prevent infectious processes, Octagam to restore the concentration of antibodies, prednisone for anti-inflammatory effect, as well as drugs for the correction of electrolyte disturbances. Positive effect was detected, and the child’s condition had remained with moderate severity without deterioration. The concentration of serum protein after albumin transfusions increased up to 40–42 g/l for a short period. Because of the constant hypoproteinaemia, which was not corrected by albumin and ongoing corticosteroid therapy, a decision to start sandostatin therapy in the dosage of 1 mg/kg was made.

Cyanosis of the extremities and restlessness appeared 2 h after injection, but these side effects were levelled in the next hour. Biochemical analysis showed the increase of the protein level up to 46 g/l. With the improvement of the health status, the child was transferred from the intensive care to the department of somatic pathology. Two days after therapy with sandostatin, transfusions of albumin were cancelled. During the treatment, the protein level increased up to 53 g/l, swelling disappeared, but general sponginess of the tissue still remained (Fig 3). The patient was discharged with recommendations for the permanent sandostatin therapy and compulsory monitoring of immunoglobulins’ levels.
DISCUSSION

Intestinal lymphangiectasia should be suspected in every patient with obscure symptoms of hypoalbuminemia, especially in the background of steatorrhoea and/or lymphocytopenia.

Thus, this clinical case has the following interesting features:

1. A rare occurrence pathology
2. Uncommon early onset
3. The severity of developed immunodeficiency
4. Manifested infectious syndrome that made difficult to diagnose the underlying disease
5. Rare use of sandostatin in children in the first year of life

REFERENCES