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Hypocalcaemic seizures : sign of intestinal disease ?

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Abstract

We describe a baby admitted with convulsions, fever, low protein level and coagulation abnormalities where congenital intestinal lymphangiectasia was confirmed by endoscopy and histology. Treatment with a low fat diet, supplemented with medium chain triglycerides (MCT), resulted in a disappearance of the symptoms and normal growth. When confronted with seizure-like attacks, electrolyte disturbances and hypo-albuminemia one should consider the possibility of protein losing enteropathy. (Acta gastroenterol. belg., **2006**, 69, **243-244**).

Key words : hypocalcaemic seizures, hypoalbuminaemia, intestinal lymphangiectasia.

Introduction

Infantile seizures are caused by a broad variety of underlying conditions. Electrolyte disturbances narrow the differential diagnostic spectrum. Hypocalcaemic seizures usually evoke hormonal (1), nutritional (2), genetic (3) or iatrogenic causes (4). However it should be kept in mind that gastrointestinal disease can cause the same symptoms.

Case

The boy was born after an uncomplicated pregnancy and received breastfeeding. Because of failure to thrive, he was switched to an infant formula at the age of 1 month. He continued to have a poor weight gain, vomited regularly and had diarrhoea.

A 5-month-old boy was admitted in emergency with a first episode of tonic-clonic seizures, followed by irritability. A second episode shortly after admittance was treated with Phenobarbital, Diazepam and Clonazpam. He had fever (39°C) and a striking oedema. A lumbar puncture showed increased white blood cells (533/µL) and normal protein (0,2 g/L) in the liquor. He was treated with Ceftriaxone and Acyclovir intravenously. As he remained in coma (> 12 h), he was referred to our centre.

On admittance blood results revealed an extremely low protein level (3,09 g/dL (normal value 6-7,6 g/dL)) originating from a decrease of albumin (2,5 g/dL (3,4-4,8 g/dL)), immunoglobulins (IgG 0,5 g/L (3,4-7,6 g/L)) and transporting proteins as transferrin ((0,64 g/L (2,01-3,94 g/L)), and caeruloplasmin (0,115 g/L (0,22-0,61 g/L)). There was no urinairy protein loss. The electrolytes were normal except for calcium (5,8 mg/dL (7,8-11,2 mg/dL), confirmed by a low ionised calcium (1,02 mg/dL (1,12-1,32 mg/dL)) and magnesium (1,02 mg/dL (1,7-2,55 mg/dL)). Liver enzymes, bilirubin, ureum and creatinin were normal. Vitamin K dependant coagulation disturbances were observed. Viral and bacterial cultures of blood, urine, stools and cerebrospinal fluid remained negative. CT scan of the brain and EEG were normal.

Albumin infusions had only a temporal effect. There were no arguments for a disturbed liver function since the coagulation studies returned to normal after a single IV gift of 10 mg vitamin K. The continuing need of albumin infusions pointed towards an intestinal problem. To differentiate between absorption problems or extreme losses in the stools additional examinations were performed. The sweat test was repeatedly normal. Additional blood examinations revealed a decrease of fat-soluble vitamins : D (6,6 ng/dL), E (0,26 mg/dL (0,3-0,9 mg/dL)) and A (5,5 µg/dL (20-43 µg/dL)), a CD4/CD8 (0,56 (normal ratio 1,7-3,9)) inversion and low cholesterol (58 mg/dL (114-203 mg/dL)) but normal triglycerides (35 mg/dL). Stool examination showed no increased fat loss, a normal stool pH of more than 6 but a markedly increased α_1-antitrypsin (12,6 mg/g (< 1,6 mg/g)).

Adding up the important hypoproteinemia coming from hypoalbuminemia and hypoimmunoglobulinemia with a decreased calcium, inversed CD4/CD8 ratio and decreased fat soluble vitamins resulted in the hypothesis of intestinal lymphangiectasia. Endoscopy (4 hours after his last bottle feeding) revealed white opaque spots in the duodenum, indicating dilated lacteal vessels. Histology confirmed the presence of dilated lacteals and villus blunting (Fig. 1). Computer tomography and ultrasound excluded diseases known to cause intestinal lymphangiectasia.

Since then the boy received a predominant MCT formula (Caprilon, SHS international, fat 3.6 g/100 ml (MCT 2.7 g/100 ml ; linoleic acid 0.44 g/100 ml ; a-linolenic acid 0.06 g/100 ml)) and started to show a catch-up growth. The weekly albumin infusions were necessary the first 6 weeks of treatment. The oral vitamin supplements (vitamin A, E, D and K) were stopped

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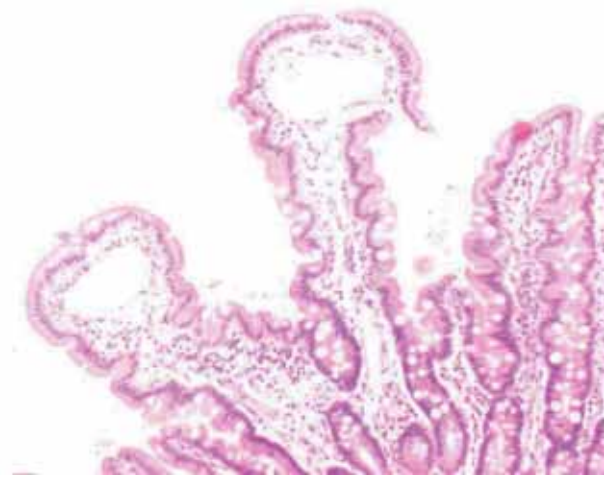

Fig. 1. — Intestinal biopsy confirming the presence of dilated lacteals and villus blunting.

3 months after diagnosis. The baby had a catch-up growth within 2 weeks and a normal neurological development since then. Since the age of 7 months his diet has been diversified with low fat containing industrial baby food, and he still drinks about 600-700 ml MCT enriched formula. With this treatment he has at the age of 5.5 year, normal total protein, immunoglobulin and electrolytes.

Discussion

We describe a baby presenting with seizure-like attacks with fever where congenital intestinal lymphangiectasia was confirmed by endoscopy and histology. An infectious cause could however not be retained. The neurological symptoms are probably due to the hypocalcaemia at diagnosis. Other neurological symptoms due to vitamin E deficiency have also been described in these patients (5). Treatment was complicated by a prolonged sub-consciousness due to the decreased protein binding of the anti-convulsive drugs. These symptoms disappeared after correction of albumin and electrolytes. All the disturbances observed in our case, can be caused by the intestinal lymphangiectasia.

Intestinal lymphangiectasia is a tricky disease (6,7). It can present with the classic malabsorption syndrome with oedema at any age (8,9) or be mistaken for an immune deficiency (10) or a protein losing enteropathy (11-12). This disease is characterised by obstruction of lymph drainage from the small intestine and lacteal dilatation (13). It should not be mistaken with intra-abdominal lymphangioma (14). The elevated lymphatic pressure leads to lymph leakage into the intestine. This causes increased protein but also fat-soluble vitamin and lymphocyte losses. It was suggested by the excessive concentration of a_1-antitrypsine in the stool and confirmed by endoscopy and histology. This baby did not have any disease known to cause secondary lymphangiectasia. Some reports have documented improvement after resection of the affected part (6,15). In this boy radiology suggested a diffuse ectasia of the enteric lymphatics. Due to the pressure decrease in the lacteols when starting a MCT diet, the intestinal losses of protein, fat-soluble vitamins and lymphocytes decreased dramatically. However in some cases parenteral nutrition or treatment with octeotride can be necessary to reverse the process (16,17).

Conclusion

Although the clinical expression of intestinal lymphangiectasia is primarily gastrointestinal, neurological symptoms can be the presenting symptom due to electrolyte disturbances or vitamin deficiencies. It should therefore be included in the differential diagnosis of hypocalcaemic seizure and oedema.

References

1. COX R.E. Hypoparathyroidism : an unusual cause of seizures. *Ann. Emerg. Med.*, 1983, **12** : 314-315.
2. BLOOM E., KLEIN E.J., SHUSHAN D., FELDMAN K.W. Variable presentations of rickets in children in the emergency department. *Pediatr. Emerg. Care*, 2004, **20** : 126-130.
3. LYNCH B.J., RUST R.S. Natural history and outcome of neonatal hypocalcemic and hypomagnesemic seizures. *Pediatr. Neurol.*, 1994, **11** : 23-27.
4. ALI F.E., AL-BUSTAN M.A., AL-BUSAIRI W.A., AL-MULLA F.A. Loss of Seizure Control Due to Anticonvulsant-Induced Hypocalcemia. *Ann. Pharmacother.*, 2004, **38** : 1002-5.
5. GUTMANN L., SHOCKOR W., GUTMANN L., KIEN C.L. Vitamin E-deficient spinocerbellar syndrome due to intestinal lymphangiectasia. *Neurology*, 1986, **36** : 554-556.
6. VARDY P.A., LEBENTHAL E., SHWACHMAN H. Intestinal lymphagiectasia : a reappraisal. *Pediatrics*, 1975, **55** : 842-851.
7. ROBERTS S.H., DOUGLAS A.P. Intestinal lymphangiectasia : the variability of presentation. A study of five cases. *Q J Med.*, 1976, **177** : 39-43.
8. SALVIA G., CASCIOLI C.F., CICCIMARRA F., TERRIN G., CUCCHIARA S. A case of protein-losing enteropathy caused by intestinal lymphangiectasia in a preterm infant. *Pediatrics*, 2001, **107** : 416-417.
9. PROUJANSKY R. Protein losing enteropathy. *In* : WALKER W.A., DURIE P.R., HAMILTON J.R., WALKER-SMITH J.A., WATKINS J.B. (eds). Pediatric gastrointestinal disease, 1996, Mosby, St Louis, pp. 973-975.
10. HERESBACH D., RAOUL J.L., GENETET N., NORET P., SIPROUDHIS L., RAMEE M.P., BRETAGNE J.F., GOSSELIN M. Immunological study in primary intestinal lymphangiectasia. *Digestion*, 1994, **55** : 59-64.
11. BELAICHE J., LOUIS E. Diagnosis of small bowel malabsorption syndromes in adults. *Acta Gastroenterol. Belg.*, 2006, **69** : 31-37.
12. SEMPOUX C. Role of the pathologist in the differential diagnosis of malabsorption. *Acta Gastroenterol. Belg.*, 2006, **69** : 49-51.
13. FAUL J.L., BERRY G.J., COLBY T.V., RUOS S.J., WALTER M.B., ROSEN G.D., RAFFIN T.A. Thoracic lymphangiomas, lymphangiectasis, lymphangiomatosis, and lymphatic dysplasia syndrome. *Am. J. Respir. Crit. Care Med.*, 2000, **161** : 1037-1046.
14. DE BAST Y., HOSSEY D., BOON L., DUTTMANN R., THEUNIS A., CHAMBERS S., NYST M., MENDES DA COSTA P. Intra-abdominal lymphatic malformation. *Acta Gastroenterol. Belg.*, 2006, **69** : 209-212.
15. MISTILIS S.P., SKYRING A.P. Intestinal lymphangiectasia. Therapeutic effect of lymph venous anastomosis. *Am. J. Med.*, 1966, **40** : 634-41.
16. AOYAGI K., IIDA M., MATSUMOTO T., SAKISAKA S. Enteral nutrition as a primary therapy for intestinal lymphangiectasia : value of elemental diet and polymeric diet compared with total parenteral nutrition. *Dig. Dis. Sci.*, 2005, **50** : 1467-70.
17. FILIK L., OGUZ P., KOKSAL A., KOKLU S., SAHIN B. A case with intestinal lymphangiectasia successfully treated with slow-release octreotide. *Dig. Liver Dis.*, 2004, **36** : 687-90.