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ORIGINAL ARTICLE

Intestinal failure and transplantation in microvillous inclusion disease☆

B. Fernández Caamaño[a,*], M.J. Quiles Blanco[a], L. Fernández Tomé[a], E. Burgos Lizáldez[b], J. Sarría Osés[a], M. Molina Arias[a], G. Prieto Bozano[a]

[a] *Servicio de Gastroenterología, Hospital Universitario La Paz, Madrid, Spain*
[b] *Servicio de Anatomía Patológica, Hospital Universitario La Paz, Madrid, Spain*

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KEYWORDS
Microvillus inclusion disease;
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Abstract
Introduction: Microvillous inclusion disease is a rare autosomal recessive condition, characterized by severe secretory diarrhoea that produces a permanent intestinal failure and dependency on parenteral nutrition. It usually begins in the neonatal period, and the only treatment at present is intestinal transplantation.
Patients and methods: A retrospective review was conducted on 6 patients (three males and three females) diagnosed with microvillous inclusion disease between 1998 and 2013.
Results: All debuted in the first month of life, with a median age of three days (range, 3–30 days), and had secretory diarrhoea dependent on parenteral nutrition, with fasting faecal volume of 150–200 ml/kg/day. Light microscopy of duodenal biopsy samples showed varying degrees of villous atrophy without cryptic hyperplasia, accumulation of PAS positive material in the cytoplasm of enterocytes brush border, and anti-CD10 immunostaining was suggestive of intracytoplasmic inclusions. Diagnostic confirmation was performed with electron microscopy. Two of them had a genetic study, and showed mutations in MYO5B gene. Three died and three are alive; two of them with an intestinal transplantation and the third waiting for a multivisceral transplantation.

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* Corresponding author.
E-mail address: beatrizfdezcaamano@gmail.com (B. Fernández Caamaño).

PALABRAS CLAVE
Enfermedad por inclusiones microvellositarias;
Distrofia microvellositaria;
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Trasplante intestinal;
Nutrición parenteral

Fracaso intestinal y trasplante en la enfermedadpor inclusiones microvellositarias

Resumen
Introducción: La enfermedad por inclusiones microvellositarias es una entidad rara, de herencia autosómica recesiva y caracterizada por una diarrea grave de carácter secretor que produce un fracaso intestinal permanente dependiente de nutrición parenteral. Habitualmente se inicia en el período neonatal y el único tratamiento posible en el momento actual es el trasplante intestinal.
Pacientes y métodos: Se revisa, de forma retrospectiva, a 6 pacientes (3 varones y 3 mujeres), diagnosticados entre 1998 y 2013 de enfermedad por inclusiones microvellositarias.
Resultados: Todos comenzaron en el primer mes de vida, con una mediana de edad de tres días (rango: 3-30 días) y presentaron diarrea secretora dependiente de nutrición parenteral, con un volumen faecal en ayunas de 150-200 ml/kg/día. La microscopia óptica de muestras biópsicas duodenales mostró grados variables de atrofia vellositaria sin hiperplasia críptica, con acumulación de material PAS positivo en el citoplasma de los enterocitos del borde en cepillo y la inmunotinción anti-CD10 fue indicativa de inclusiones intracitoplasmáticas. La confirmación diagnóstica se realizó con microscopia electrónica. En 2 de ellos se realizó estudio genético que demostró mutaciones en el gen MYO5B. Evolutivamente, 3 fallecieron y 3 se encuentran vivos; 2 de ellos portadores de trasplante intestinal y el tercero en espera de trasplante multivisceral.

Introduction

Microvillous inclusion disease (MVID) or congenital/familial microvillous atrophy is due to a congenital disorder of the epithelial cells of the bowel. The literature has reported multiple mutations in the MYO5B gene that encodes myosin Vb that are associated with the development of this disease. It usually manifests in the neonatal period with severe diarrhoea that persists despite fasting, with children becoming permanently dependent on parenteral nutrition (PN). Its histological features consist in the absence or altered appearance of the enterocyte brush border membrane along with the presence of characteristic microvillous inclusions. The treatment of MVID includes PN and intestinal transplantation.

Patients and methods

We performed a retrospective review of the patients diagnosed with MVID in our hospital in a 15-year period (1998–2013). We analyzed epidemiological, clinical, diagnostic, treatment and patient outcome variables. Biopsy samples were collected by means of upper gastrointestinal endoscopy for diagnostic confirmation. A conventional histological examination was performed that included a haematoxylin–eosin stain (HE) and a periodic acid-Schiff stain (PAS), as well as immunohistochemical testing with anti-CD10 antibodies and electron microscopy examination. Two of the six patients underwent genetic testing for mutations in the MYO5B gene. Infectious, allergic and autoimmune aetiologies, defects in digestion, absorption and transport of nutrients and other diseases of the intestinal mucosa were ruled out in all patients.

Results

The onset of diarrhoea occurred within four days from birth in five patients, at a median age of 3 days (range, 3–30 days) (Table 1). Three patients were male and 3 were female. Patients 2 and 3 were siblings born to consanguineous parents, and there was no blood relationship between the two parents of the remaining patients. Patient 6 was born to term, while the rest were born at 35–36 weeks of gestational age. All were born with normal weights for their gestational age. Prenatal ultrasonography had shown dilation of bowel loops in half of the patients, with no other significant findings.

All six patients had onset with severe diarrhoea (stool volume ~120–200 ml/kg/day) of the secretory type (sodium in stools >100 mEq/L) and with abundant mucus, which persisted despite fasting. Patient 5 developed renal complications associated with PN and severe electrolyte imbalances, and patient 6 developed intense skin itching as a prominent symptom. None of the patients could tolerate any type of enteral formula, and all required PN to prevent dehydration and metabolic acidosis.

The upper gastrointestinal endoscopy did not show significant macroscopic abnormalities. The diagnosis was made by the histological examination of duodenal biopsies with light and electron microscopy. The presence of mutations in the MYO5B gene was confirmed in patients 5 and 6. The rest of the patients did not undergo genetic testing. All patients received PN in the hospital and at home for prolonged periods of time (3–36 months). Three of the six patients have died (one at age 3 months of septic shock, and the other two of liver complications associated with intestinal failure while they were on the transplant list). Of the three survivors, one is awaiting a multivisceral transplantation