

7. Alla V, Abraham J, Siddiqui J, Raina D, Wu GY, Chalasani NP, et al. Autoimmune hepatitis triggered by statins. *J Clin Gastroenterol.* 2006;40:757–61.
8. Castiella A, Zapata E, Lucena MI, Andrade R. Drug-induced autoimmune liver disease: A diagnostic dilemma of an increasingly reported disease. *World Journal of Hepatology.* 2014;6:160–8.
9. Stephens C, Castiella A, García-Romero EM, Otazua P, López-Nebot MÄ, Zapata E, et al. Autoantibody presentation in drug-induced liver injury and idiopathic autoimmune hepatitis: the influence of human leucocyte antigen alleles. *Pharmacogenet Genomics.* 2016;26:414–22.
10. Stine JG, Nothup PG. Autoimmune-like drug-induced liver injury: a review and update for the clinician. *Exp Opin Drug Metab Toxicol.* 2016 Jul 21:1–11 [epub ahead of print].

Mara Sánchez^a, Agustín Castiella^{b,*}, Eva Zapata^b, Leire Zubiaurre^b, Josu Pérez-Yebóles^c, Leire Mendibil^a, Arantxa Iribarren^a

^a *Medicina Familiar y Comunitaria, Hospital de Mendaro, Mendaro, Spain*

^b *Servicio Digestivo, Hospital de Mendaro, Mendaro, Spain*

^c *Servicio Endocrinología, Hospital de Mendaro, Mendaro, Spain*

*Corresponding author.

E-mail address: agustincastiella@yahoo.es (A. Castiella). 2444-3824/

© 2017 Elsevier España, S.L.U. All rights reserved.

Protein-losing enteropathy resolved after ventral abdominal hernia repair[☆]



Enteropatía pierde-proteínas resuelta tras la reparación de una eventración abdominal

Protein-losing enteropathy (PLE) is characterised by an excessive loss of serum proteins through the gastrointestinal tract, primarily causing hypoproteinaemia with hypoalbuminaemia and oedema. When a patient has hypoalbuminaemia with oedema, other causes of decreased serum protein levels, such as malnutrition, kidney disease with proteinuria or liver impairment with alteration in protein synthesis, should first be ruled out.¹

There are different causes of PLE, including metabolic, intestinal, inflammatory and infectious disorders, and alterations in lymphatic drainage, such as occurs in intestinal lymphangiectasia.¹

We report the case of a 57-year-old woman who had two episodes of idiopathic acute pancreatitis in less than a year. In that year, the patient developed palpebral and lower extremity oedema with persistent hypoalbuminaemia, with serum albumin levels <2 g/dl (normal 3.30–5.20), a decrease in the concentration of γ -globulins and short half-life proteins, without diarrhoea. In the investigations performed at that time, faecal elastase and faecal fat tests were normal. Alpha-1-antitrypsin clearance was 797 ml/24 h (normal 0.00–12.50) and the bacterial overgrowth test, stool cultures and stool analysis for parasites were negative. Nephrotic syndrome was also ruled out as a cause of hypoalbuminaemia.

The patient subsequently had a further episode of acute pancreatitis with splenic vein thrombosis for which she

was started on anticoagulation; treatment was also started with corticosteroids, as autoimmune pancreatitis was suspected despite normal IgG4. She showed no improvement but instead had another exacerbation of pancreatitis. A hypercoagulability study was performed with factor V Leiden, proteins c and S, antithrombin III, homocysteinaemia and prothrombin 20210, which were all within normal limits. A month later, positron emission tomography scan showed an increase in uptake in the tail of the pancreas, suspected to be of malignant origin. In the end, a distal pancreatectomy with splenectomy was performed via laparotomy; pathology was compatible with chronic pancreatitis (inflammation and fibrosis associated with areas of necrosis).

As the hypoalbuminaemia persisted, the patient was started on parenteral nutrition, leading to a slight improvement in blood test parameters (serum albumin 2.6 g/dl) and improvement clinically. Upper gastrointestinal endoscopy identified duodenal and jejunal lymphangiectasia. Causes of secondary lymphangiectasia were ruled out, except for chronic pancreatitis, which the patient already had. Colonoscopy was also performed, showing mucosa with normal appearance. One year after starting the parenteral nutrition, the patient developed pancreatic pain resistant to first- and second-step analgesics, with no diarrhoea or weight loss. MRI and endoscopic ultrasound showed severe chronic calcifying pancreatitis in the head of pancreas and a cyst measuring 35 mm in the wall of the duodenum. She was started on octreotide and FNA confirmed the inflammatory nature of the contents of the cyst. In view of the poor pain control, a coeliac plexus block was performed, which provided pain control for a year. After that same period of time, an abdominal CT detected a subcostal incisional hernia related to the surgical wound (Fig. 1). The hernia was repaired laparoscopically, after which the patient experienced an improvement in her pain. At the same time, her serum albumin levels improved and she was able to stop the parenteral nutrition. Six months after the intervention, serum albumin was 4.21 g/dl and alpha-1-antitrypsin clearance was 37.96 ml/24 h.

Resolution of PLE following laparoscopic hernia repair is not a common event. In our case, intestinal lymphangiectasia was caused by chronic pancreatitis and aggravated by the subcostal hernia. This event, secondary to distal

[☆] Please cite this article as: Aguilera Castro L, Téllez Villajos L, López San Román A, Botella Carretero JI, García García de Paredes A, Albillos Martínez A. Enteropatía pierde-proteínas resuelta tras la reparación de una eventración abdominal. *Gastroenterol Hepatol.* 2018;41:313–315.

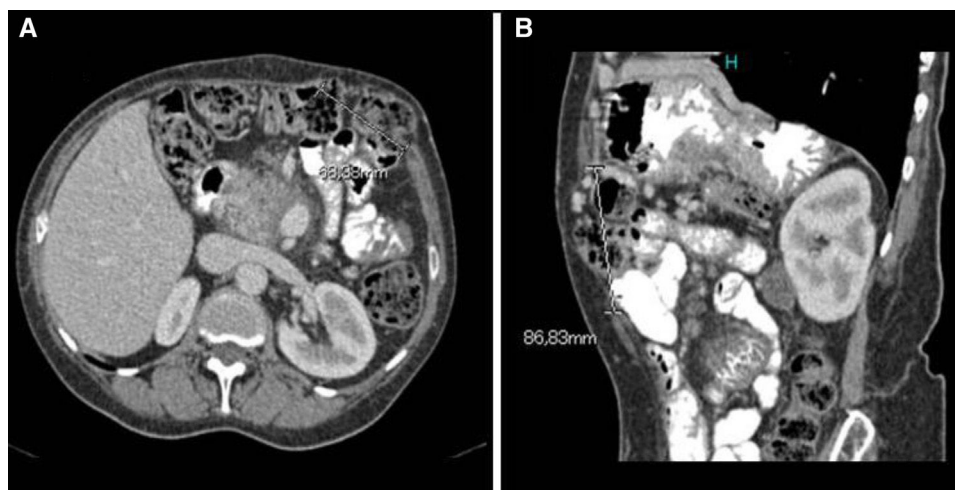


Figure 1 Axial (A) and parasagittal (B) view of abdominal CT: subcostal hernia before repair.

pancreatectomy with splenectomy, caused lymphatic congestion, which led to leakage of lymph with a large amount of proteins into the intestinal lumen. However, following the hernia repair and the consequent decrease in abdominal pressure and lymphatic congestion, the condition resolved both clinically and analytically. The fact that the diagnosis of PLE was previous to the development of the hernia suggests that this was a factor added to the chronic pancreatitis.

Intestinal lymphangiectasia can be primary or secondary; the first affects children and is characterised by ectasia of the intestinal lymph vessels in the mucosa or submucosa, with disorders in the lymphatic system in other parts of the body.² In secondary intestinal lymphangiectasia, the lymph vessels become dilated either due to obstruction in the lymphatic system or high lymphatic pressure resulting from high venous pressure. The obstruction may be associated with heart disease, which is the most common cause, Budd-Chiari syndrome, liver cirrhosis, enterolymphatic fistulas, cardiac surgery such as the Fontan procedure, inflammatory bowel disease, sarcoidosis, lymphoma or chronic pancreatitis.

The most characteristic symptoms are peripheral oedema, ascites, pleural or pericardial effusion and diarrhoea.³ For the diagnosis of intestinal lymphangiectasia it is important to first confirm the excessive loss of proteins in the gastrointestinal tract, where a useful marker is the clearance of alpha-1-antitrypsin. A clearance >28 ml/24 h without diarrhoea or >57 ml/24 h with diarrhoea is abnormal.¹ Once the loss of proteins is confirmed, the definitive diagnosis of lymphangiectasia requires endoscopic assessment with duodenum and/or jejunum biopsies.

There are very few cases in the literature discussing any link between abdominal hernia or eventration and PLE.⁴⁻⁶ In 2005, Tainaka et al. described the case of a girl with PLE caused by a paraduodenal hernia whose serum proteins and albumin returned to normal after surgery.⁴ In our case, it

was a subcostal hernia after open abdominal surgery. Hernia is a common complication of abdominal surgery, with an incidence that varies from 2% to 20%.^{7,8} The incidence in pancreatic debridement is even higher, reaching 42%.⁹ The signs and symptoms vary from none at all to abdominal pain with complications such as incarceration. As far as treatment is concerned, in most cases, it involves repair of the wall with placement of non-absorbable prosthetic mesh.¹⁰

References

1. Umar SB, Dibaise JK. Protein-losing enteropathy: case illustrations and clinical review. *Am J Gastroenterol.* 2010;105:43–9.
2. Ingle SB, Hinge Ingle CR. Primary intestinal lymphangiectasia: minireview. *World J Clin Cases.* 2014;2:528–33.
3. Freeman HJ, Nimmo M. Intestinal lymphangiectasia in adults. *World J Gastrointest Oncol.* 2011;3:19–23.
4. Tainaka T, Ikegami R, Watanabe Y. Left paraduodenal hernia leading to protein-losing enteropathy in childhood. *J Pediatr Surg.* 2005;40:E21–3.
5. Cohen AM, Maran R, Gelvan A, Fireman Z, Lurie B. Malabsorption due to a ventral hernia. *Neth J Med.* 1992;41:24–7.
6. Evans JD, Perera MT, Pal CY, Neuberger J, Mirza DF. Late post liver transplant protein losing enteropathy: rare complication of incisional hernia. *World J Gastroenterol.* 2013;19:4409–12.
7. Le Huu Nho R, Mege D, Ouassiss M, Sielezneff I, Sastre B. Incidence and prevention of ventral incisional hernia. *J Visc Surg.* 2012;149:e3–14.
8. Burger JW, Lange JF, Halm JA, Kleinrensink GJ, Jeekel H. Incisional hernia: early complication of abdominal surgery. *World J Surg.* 2005;29:1608–13.
9. Al-Azzawi HH, Kuhlenschmidt H, Howard TJ, Bermes AM, Bishop SN, Nakeeb A, et al. The burden of incisional hernia in necrotizing pancreatitis: how can we improve? *Am J Surg.* 2010;199:310–4.
10. Kingsnorth A. The management of incisional hernia. *Ann R Coll Surg Engl.* 2006;88:252–60.

Lara Aguilera Castro^{a,*}, Luis Téllez Villajos^a,
Antonio López San Román^a,
José Ignacio Botella Carretero^b,
Ana García García de Paredes^a, Agustín Albillos Martínez^a

^a *Servicio de Gastroenterología y Hepatología, Hospital Universitario Ramón y Cajal, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Universidad de Alcalá, Madrid, Spain*

^b *Servicio de Endocrinología y Nutrición, Hospital Universitario Ramón y Cajal. CIBER de Fisiopatología de la Obesidad y la Nutrición (CIBERObn), Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Universidad de Alcalá, Madrid, Spain*

*Corresponding author.

E-mail address: laraaguilera88@hotmail.com
(L. Aguilera Castro).
2444-3824/

© 2017 Elsevier España, S.L.U. All rights reserved.

Unusual presenting manifestation of a rare polyposis, Cowden syndrome[☆]



Manifestación inicial atípica de una poliposis poco frecuente, el síndrome de Cowden

Cowden syndrome (CS) is a rare genetic disease characterised by the development of hamartomas that can affect multiple organs, with an increased risk of different types of cancer. Although hamartomatous polyps are common, it is less common to find intestinal ganglioneuromas as the first sign.^{1,2}

We present the case of a patient with ganglioneuromatous polyposis in whom the final diagnosis of CS was arrived at through the other extra-intestinal manifestations.

This was a 39-year-old man who was referred for colonoscopy with a history of a first-degree relative having died of colorectal cancer (CRC). Colonoscopy showed more than 100 polyps, distributed throughout the colon, but more predominant on the left side. Following the resection of several of these polyps, the histology showed a diffuse mesenchymal proliferation of spindle cells with scattered ganglion cells in lamina propria, all compatible with ganglioneuromatous polyps (Fig. 1). In view of these findings, we requested a gastroscopy which showed an extensive glycogenic acanthosis in the oesophagus and more than 100 polyps in the second part of the duodenum, mostly millimetric in size, corresponding to tubular adenomas with moderate dysplasia.

On questioning about his previous medical history, the patient reported having had a hemi-thyroidectomy for adenoma and the resection of a collagen fibroma in his right flank. On examination, we found obvious macrocephaly (studied in childhood and attributed to rickets) and the presence of brownish pigmented macules on his penis.

After confirming from all these findings that the patient met clinical criteria for CS,³ complete sequencing of the *PTEN* gene study was performed, obtaining a pathogenic mutation (p.Arg130Gln) in exon 5 associated with CS. Further tests ruled out an association with type II multiple endocrine neoplasia.

Ganglioneuromatosis is caused by hyperplasia of the myenteric plexuses and enteric nerve fibres. Clinically, there are three distinct types: (1) polypoid ganglioneuromatosis, which consists of few isolated ganglioneuromas; (2) generalised ganglioneuromatosis, which is associated with multiple endocrine neoplasia type IIb and von Recklinghausen neurofibromatosis; and (3) ganglioneuromatous polyposis, without associated systemic disease, in which category our case falls into.²

CS is a hereditary disease, with autosomal dominant transmission, due to germline mutation in the *PTEN* tumour-suppressor gene. Its prevalence is estimated at one case per 200,000–250,000 population.⁴

Initially, diagnostic criteria were proposed that included major and minor pathognomonic criteria.⁵ Because of their lack of specificity, Pilarski et al. proposed alternative criteria which have been adopted by the National Comprehensive Cancer Network. One of the main differences is that gastrointestinal hamartomas, including ganglioneuromas, are included as major criteria (Table 1).³

Mucocutaneous lesions (98%), macrocephaly (93%), gastrointestinal polyps (93%) and benign lesions of the breast (74%) and thyroid (71%) are the most common manifestations.⁶ In the gastrointestinal tract, one of the most common manifestations is glycogenic acanthosis of the oesophagus. Despite their non-specificity, it has been proposed that oesophageal acanthosis and colon polyposis should be considered as pathognomonic criteria for CS. Gastrointestinal polyps have been described in 67–100%, the majority hamartomatous and hyperplastic, but also adenomas. As far as involvement of the colon is concerned, 92% have polyps, varying from a few to countless. What is interesting is the coexistence of multiple histological types, which include hamartomas, hyperplastic polyps, ganglioneuromas and adenomas.⁷

However, the most important factor is the risk of malignant tumours. Several studies have reported the same increased risk of cancer of the breast

[☆] Please cite this article as: Adán Merino L, Aldegue Martínez M, Álvarez Rodríguez F, Barceló López M, Plaza Santos R, Valentín Gómez F. Manifestación inicial atípica de una poliposis poco frecuente, el síndrome de Cowden. *Gastroenterol Hepatol*. 2018;41:315–317.