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2444-3824/

Shadow cells in a cutaneous epidermoid cyst: Searching for a polyposis syndrome☆

Quiste epidermoide cutáneo con células sombra: a la búsqueda de un síndrome polipósico

We present the case of an asymptomatic 69-year-old man with a prior history of removed retroauricular epidermoid cyst. Histology revealed foci of intraluminal shadow cells, a finding consistent with Gardner's syndrome. He did not exhibit any other associated extraintestinal manifestations and had no family history of gastrointestinal disease. The panendoscopy revealed multiple millimetric oesophageal polyps, the histology of which did not indicate adenomatous changes. The colonoscopy showed six polyps of between 2 and 20 mm, which were resected. The histological study was consistent with tubular adenoma, with low-grade dysplasia observed in three of them and high-grade dysplasia in the other three. In addition, a 15-mm ulcerated neoformation was identified in the rectosigmoid junction, the biopsies of which were consistent with adenocarcinoma. Five days after the colonoscopy, the patient had low-grade fever and pain in the right iliac fossa. A CT scan was ordered that revealed findings suggestive of acute appendicitis, which was initially managed conservatively. Neoadjuvant radiotherapy was started and the follow-up CT scan revealed a focal hepatic injury. Surgery was performed, consisting of lower anterior rectal resection, liver metastasectomy and appendectomy, finding adenocarcinoma with lymph node involvement, adenocarcinoma liver metastasis and appendiceal goblet cell carcinoid tumour with free edges in the histological study, respectively. The genetic study for the *APC* mutation was negative. Adjuvant chemotherapy with fluorouracil and oxaliplatin was then administered, with no evidence of tumour recurrence to date.

Shadow or ghost cells are keratinised eosinophilic cells with an unstained central area at the site of the shadow of the lost nucleus. Their presence is an indication of an aborted attempt to form hair shafts (Fig. 1). They are a characteristic, albeit nonspecific, histological finding of pilomatricoma and pilomatrical carcinoma.[1] Familial adenomatous polyposis is an autosomal dominant disorder secondary to the mutation of the *APC* tumour suppressor gene and is characterised by the development of multiple premalignant adenomatous colon polyps. There are numerous variants of this disease, one of which is Gardner's syndrome, which is defined as the association of colonic polyposis with the onset of various extraintestinal manifestations.[2] Of these, the most common are epidermoid cysts and skin fibromas, osteoma of the face and long bones, hypertrophy of the retinal pigment epithelium, dental abnormalities and desmoid tumours of the abdominal and intra-abdominal wall, as well as the development of malignant tumours at various sites (thyroid, duodenal, ampullary, pancreatic, gastric, etc.).[3] Some of these extraintestinal manifestations may occur years before the onset of gastrointestinal symptoms.

Epidermoid cysts occur in 50–60% of all cases of Gardner's syndrome compared to 9–10% in the general population.[2] They generally develop before puberty, may be the first sign of the disease and carry no risk of malignancy. Accumulations of shadow cells and foci of matrix keratinisation inside these cells have been reported, similar to what occurs in pilomatricoma.[4] Although they constitute a common finding in the physical examination of patients

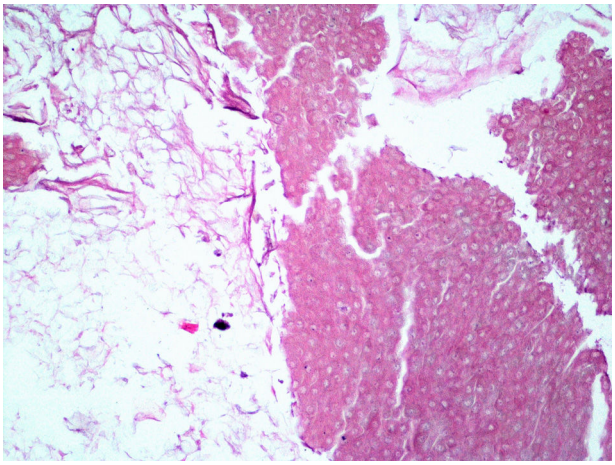

Figure 1 (H&E, ×40) Cyst contents comprising sheets of flaky keratin and masses of shadow cells.

☆ Please cite this article as: García de la Filia Molina I, Crespo Pérez L, Ríos León R, Barbado Cano A, Moreno García del Real C, Aburto Bernardo A, et al. Quiste epidermoide cutáneo con células sombra: a la búsqueda de un síndrome polipósico. Gastroenterol Hepatol. 2019;42:386–387.

with Gardner's syndrome, they are not specific to the disease and have been associated with other conditions like *MUTYH*-associated adenomatous polyposis (germline mutations) and with somatic mutations in the catenin beta 1 gene (*CTNNB1*).[5] Familial adenomatous polyposis associated with *MUTYH* mutations is an autosomal recessive disorder characterised by the appearance in adult age of multiple adenomatous polyps with an increased risk of developing colorectal cancer. In the event of histological findings consistent with pilomatricoma in a patient with multiple adenomatous polyps, the differential diagnosis should include more conditions than just Gardner's syndrome, and potentially test for genetic mutations responsible for attenuated polyposis syndromes, like the *MUTYH* gene, and not exclusively associated with the *APC* gene.

In conclusion, the identification of shadow cells in cutaneous epidermoid cysts may be the first finding to generate suspicion of polyposis syndromes like Gardner's syndrome. In our patient, the detection of shadow cells inside a removed cutaneous cyst guided us to this potential diagnosis. Although it ultimately did not meet the characteristic endoscopic or genetic criteria for this syndrome, these findings led to a colonoscopy being requested, which identified colorectal cancer. The onset of post-colonoscopy appendicitis led to the diagnosis of an appendiceal goblet cell tumour.

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2444-3824/

Pulmonary aspergillosis in a Crohn's disease patient receiving adalimumab and steroid therapy☆

Paciente con enfermedad de Crohn en tratamiento con adalimumab y esteroides que desarrolla aspergilosis pulmonar

We present the case of a 41-year-old male patient diagnosed with ileocolic Crohn's disease (CD) in 1999 (A2 L3 B1+p), with ileocaecal resection in 2006, on treatment with mercaptopurine for prevention of recurrence. He subsequently developed a complex perianal fistula, which was initially treated with infliximab before switching to adalimumab in 2013 due to a sensitivity reaction, with good response and withdrawal of mercaptopurine. In 2016, adalimumab (80–80–80 mg/week) was reintroduced due to loss of response with perianal and luminal activity. Due to the patient's lack of improvement, steroids were added (1 mg/kg = 80 mg). One month after starting the treatment, the patient reported a three-day history of weight loss, cough and expectoration. The chest X-ray revealed several cavitated nodular images in both lung fields consistent with pulmonary tuberculosis. The study was broadened to include CT scan, blood panel, Mantoux test and bronchoscopy. The chest CT scan (Fig. 1) showed bilateral cavitated nodular images, the Mantoux test was negative and the blood tests only revealed a slight increase in CRP (15 mg/l) and fibrinogen (520 mg/dl). The bronchoscopy was normal, samples were taken for culture and bronchoalveolar lavage was performed. The microbiological study for mycobacteria was negative (AAFB and culture in Löwenstein medium). The microbiological study was broadened and multiple *Aspergillus* spp. colonies were isolated. Adalimumab was withdrawn and treatment with intravenous voriconazole, imipenem and cilastatin was started. After three months of treatment, the patient had no pulmonary or intestinal symptoms, together with radiological improvement, so adalimumab was reintroduced.

Patients with inflammatory bowel disease (IBD) are particularly susceptible to opportunistic infections thanks to the use of immunosuppressants, particularly if several

☆ Please cite this article as: Ferrer Bradley I, Maroto Arce N, Mora Escrig M, Hinojosa del Val J. Paciente con enfermedad de Crohn en tratamiento con adalimumab y esteroides que desarrolla aspergilosis pulmonar. Gastroenterol Hepatol. 2019;42:387–388.