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Interstitial Lung Disease and Colorectal Cancer, a case report

Ivan Hernández-Betancor[1]*, Emilio González-Reimers[1], Sonia García-Hernández[2], Marina Fernandez-Nierto[3], Francisco Santolaria-Fernández[1], Helena Hernández-Rodríguez[4], Maria J. Sánchez-Pérez[1].

[1]Departament of Internal Medicine, Hospital Universitario de Canarias, La Laguna, Santa Cruz de Tenerife, Canary Islands. Spain.
[2]Departament of Pathological Anatomy, University of La Laguna (ULL).
[3]Nursing Departament, Hospital Universitario de Canarias, La Laguna, Santa Cruz de Tenerife, Canary Islands. Spain
[4]Departament of Thoracic Surgery, Hospital Universitario de Canarias, La Laguna, Santa Cruz de Tenerife, Canary Islands. Spain. Ofra s/n 38320 La Laguna. Tenerife. Canary Islands (Spain)
*Correspondence: ivanhbet@gmail.com

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Summary

Interstitial Lung Disease and Colorectal Cancer, a case report.

Diffuse interstitial lung disease encompasses a wide spectrum of entities. The most frequently observed are those related to diverse forms of lung fibrosis, some of them associated with inmmune disorders. Rarely a bronchioloalveolar carcinoma may mimic the radiological appareance of an interstitial lung disease. There are three different histological patterns of bronchioloalveolar carcinoma: mucinous, nonmucinous and mixed mucinous and nonmucinous or indeterminate form. This last form may raise differential diagnosis with colonic adenocarcinoma. Distinction between these two processes may be difficult, even with the aid of immunohistochemistry.

We here present the case of a 79-years old male patient, affected by arterial hypertension, who was admitted to our unit complaining dyspnea and swollen legs; after appropriate therapy the radiological pattern was consistent with pulmonary fibrosis, leading to lung biopsy, which results strongly suggest metastatic colon adenocarcinoma.

Keywords: interstiticial lung disease, colorectal cancer, lung fibrosis, inmunohistochemistry.

Resumen

Enfermedad pulmonar intersticial y cáncer colorrectal, a propósito de un caso.

Las enfermedades pulmonares intersticiales comprenden un amplio espectro de entidades. La forma mas frecuente de ellas es la fibrosis pulmonar, algunas de ellas van asoacidas con trastornos autoinmunes. Raramente, un carcinoma bronquioalveolar puede tener la apariencia radiológica de una enfermedad intersticial pulmonar. Existe tres diferentes patrones histológicos de carcinoma bronquioalveolar: mucinoso, no mucinoso y una forma indeterminada. Esta última forma puede dificultar el diagnóstico de cancer colorrectal.. La distinción entre estos procesos puede llegar a ser tan dificultosa que incluso, en ocasiones, se hace necesario técnicas de inmunohistoquimia.

Se presenta el caso de un paciente de 79 años de edad, varón, afecto de hipertensión arterial que fue ingresado en el Servicio de Medicina Interna aquejando disnea y edemas en miembros inferiores. Después de un adecuado tratamiento el patrón radiológico mostró fibrosis pulmonar, llevando a la biopsia pulmonar con resultados compatibles con adenocarcinoma colorrectal metastásico.

Palabras clave: enfermedad pulmonar intersticial, cancer colorrectal, fibrosis pulmonar, inmuno-histoquinia.

Case report

A 79 year old man with a history of 50 years smoker, long-time hypertension, hyper-cholesterolemia, atrial fibrillation (on dicumarinics), ischemic heart disease with two-vessel disease, inferior acute myocardial infarction in 2003 with transluminal percutaneous angioplasty in the proximal right coronary artery presents in our Hospital's Internal Medicine station with a month history of inferior limb oedema, progressive dyspnea, nocturnal paroxysmal dyspnea and isolated episodes of white-yellowish expectoration. The patient had recent changes for his usual heart failure medication and the case was initially oriented as congestive heart disease due to suboptimal treatment and a respiratory tract infection. In the admission chest radiography bilateral reticular-nodular infiltrates resembling pulmonary fibrosis could be seen (figure 1).

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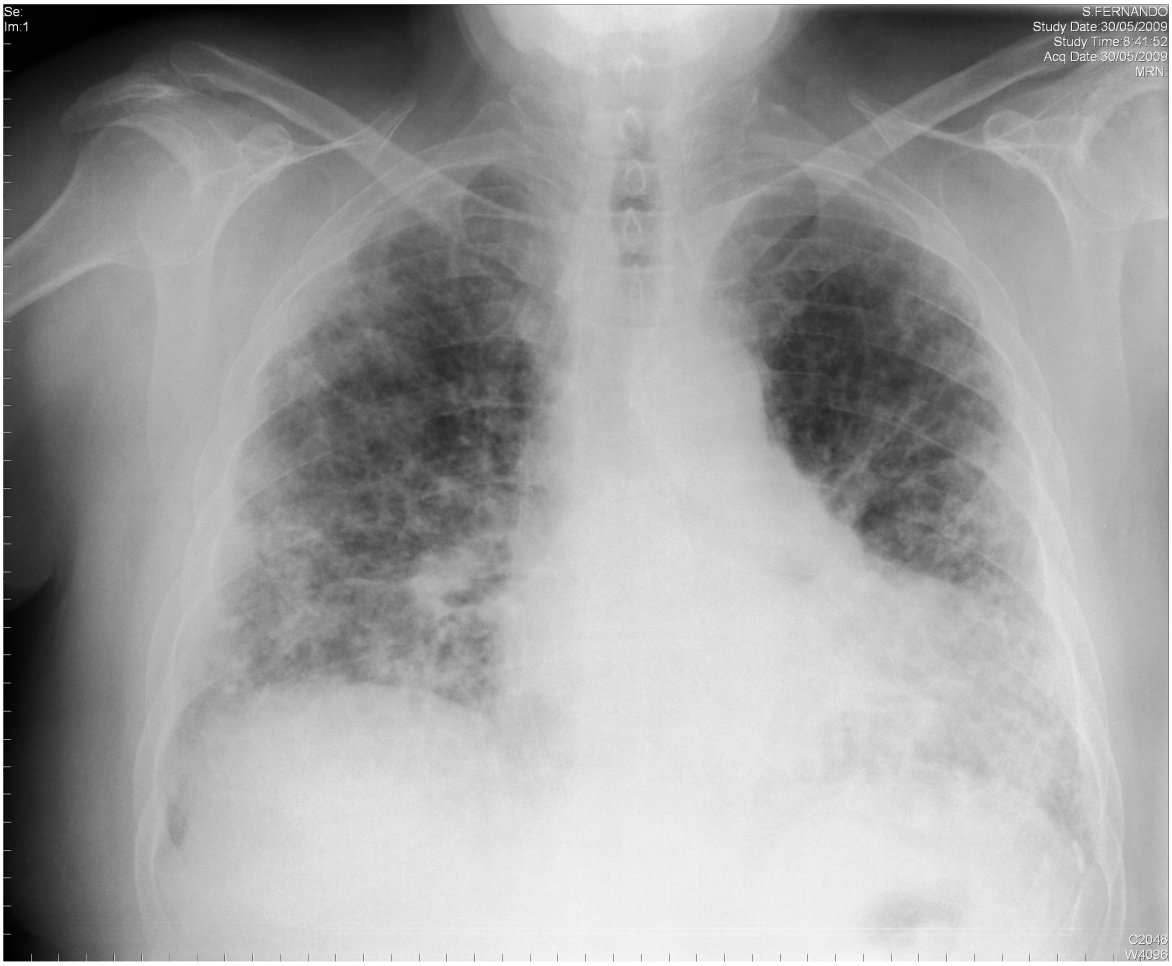

Figure 1. Bilateral reticulo-nodular pattern.

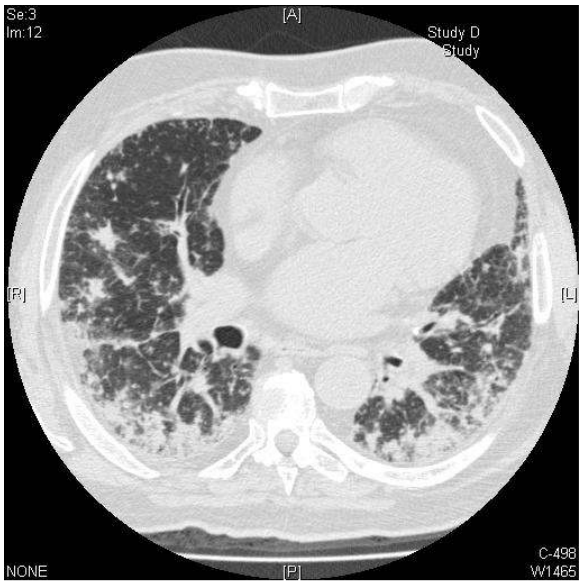

Figure 2. CT pattern of pulmonary fibrosis

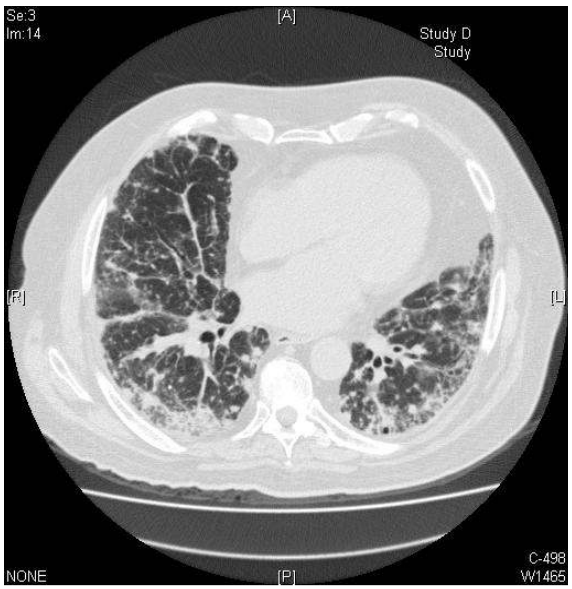

Figure 3. CT pattern of pulmonary fibrosis

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After re-evaluating the patient he reported having taken amiodarone (Trangorex®)for two months approximately years ago. Thus, a CT scan of the chest was performed under the suspicion of the development of pulmonary fibrosis due to the use of this drug. The study was informed as bilateral, Corticosteroids were initiated without improving the patient's condition. Thus, further exams were performed in order to clear out the case's ethiology. Functional respiratory tests were performed, revealing a mixed pattern (with a more important restrictive component) with neither air trapping nor diffusion alteration (FEV: 53.5 %; FEV1: 57.3 %; FEV1/FVC: 104.4 %; TLCO: 45 %). The walking test was mainly limited because of dyspnea and the patient's severe drop in pulse oximetry (from a basal 91% to 83% after 150 metres).

Given the lack of improvement in the patien status a bronchoscopy was performed, revealing an area in the anterior segment of the inferior left lobe suggestive of aspergiloma. However, cultures and diffuse, poor delimited, subpleural nodular and lineal parenchimal opacities with patchy ground glass neumonitis and subpleural areas of parenchimal consolidation resembling chronic eosinophilic pneumonia but not discarding other interstitial lung diseases (figure 2,3).

galactomanan tests were repeatedly negative. After 4 weeks of hospitalization under high dose corticoid treatment and hardly improvement a lung biopsy was performed. The procedure revealed stiff fibrotic looking lung parenchyma with nodular areas, especially in the left inferior lobe. An atipic lingula segment resection was performed. In the pathologic study coalescent grid forming glanduloid structures with central necrosis were seen (figure 4). The epithelium was of glandular intestinal type with local stroma presenting limphoplasmocitoid inflammatory infiltrates. The inmunohistochemical analyses showed CK20 (figure 5) and CEA positivity without CK7 expression (figure 6).

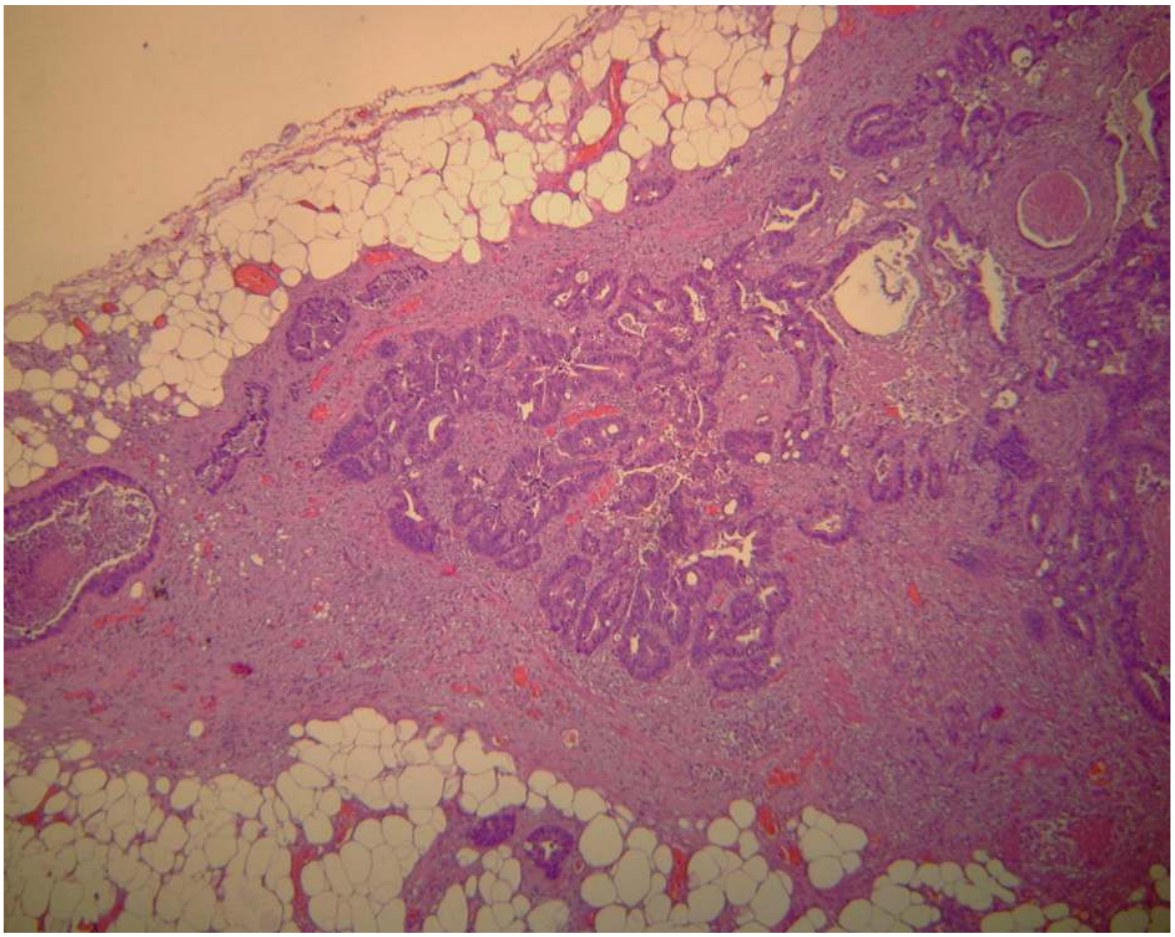

Figure 4. Hematoxylin-eosin stain showing pictures of structures that tend to be arranged glanduloides together by adopting a cribriform pattern with areas of central necrosis with glandular epithelium of intestinal type lining with surrounding stroma showing fibrosis and lymphoplasmacytic inflammatory infiltrates. However, BAL was negative in our patient, something rarely observed. Bronchioloalveolar carcinoma can be divided into three histologic subtypes: mucinous, nonmucinous, and a mixed mucinous and nonmucinous or indetermite form [4].

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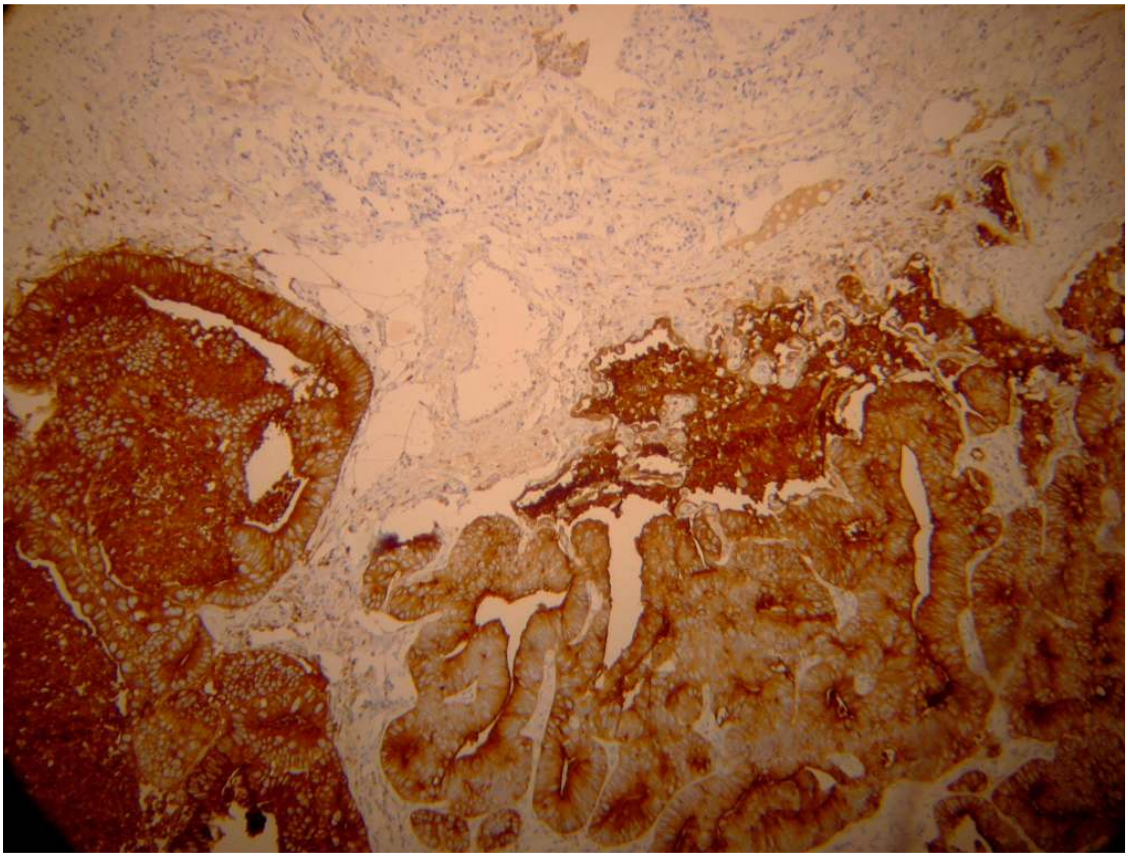

Figure 5. Positive immunohistochemical staining for CK20.

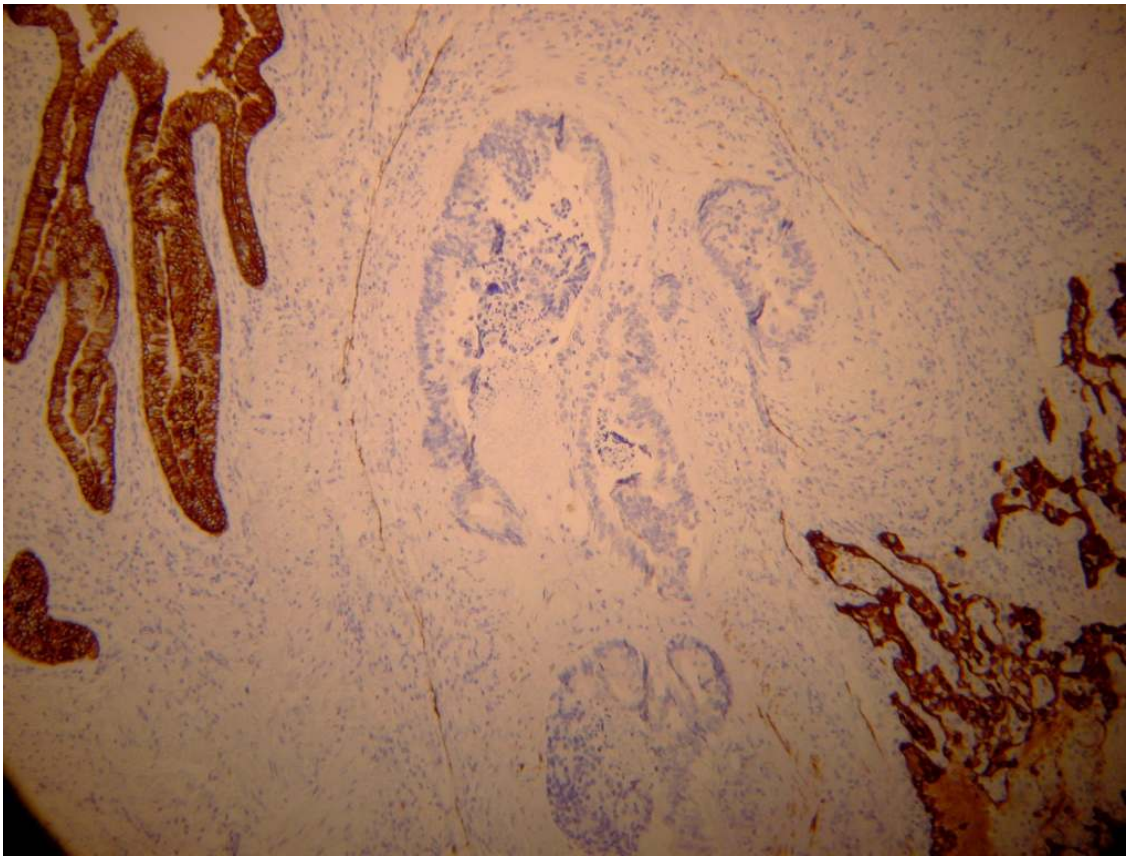

Figure 6. Negative immunohistochemical staining for CK7.

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Discussion

There are several aspects of this case which are noteworthy. At first the patient presented with a clinical picture fully compatible with heart failure, which was interpreted in relation with the long-standing hypertension. Even the radiological picture at admission sustained the clinical diagnosis, but after initial resolution of the dyspnea and edema there still remained a diffuse interstitial pattern wich prompted us to perform a CT scan. The radiological appeareance of the scanner was fully compatible with an intersticial lung disease, but there was also an image compatible with aspergilloma. This finding led us to perform bronchoscopy and bronchioloalveolar lavage, which was negative for both fungi and malignancy. Based on this we placed the patient on prednisone 40 mg/day without any improvement. Only lung-open biopsy provided a diagnosis of malignancy, something which explains the poor response of the patient to steroids. Also inmunohistochemistry stainings the soli aid in cases like this, in which there is a discordance between clinical and histological findings. In adittion, in this case illustrates the importance to perform lung biopsy as a diagnostic procedure. In interstitial lung disease, normal procedures TC, BAL and which were both negative. Considering malingnance as an option, the first diagnosis in this case should be bronchioloalveolar carcinoma.

• **Cytokeratin 7** (**CK7**) - In multiple studies, staining for the CK7 marker was positive in more than 90 percent of all lung adenocarcinomas, including those with bronchioloalveolar carcinoma. In patients with metastatic colonic adenocarcinoma CK7 was positive in only 23 percent of cases [2, 3] (figure 6).

• **Cytokeratin 20** (**CK20**) - Staining for CK20 has given mixed results in patients with bronchioloalveolar carcinoma. CK20 was positive in more than 95 percent of patients with metastasic colorectal cancer [1,3] (figure 5).

• **CDX2** - Distinguish between mucinous bronchioloalveolar carcinoma and primary colon cancer may be particularly difficult, as well as our case, even with staining for CK7, CK20 markers. Immunohistochemical staining for CDX2 (*caudal-related homeobox 2*) is an excellent marker to identify adenocarcinoma of gastrointestinal origin. In one series, staining for CDX2 was positive in 97 percent of colorectal adenocarcinomas, while it was negative in all patients with bronchioloalveolar carcinoma [3] (figure 7).

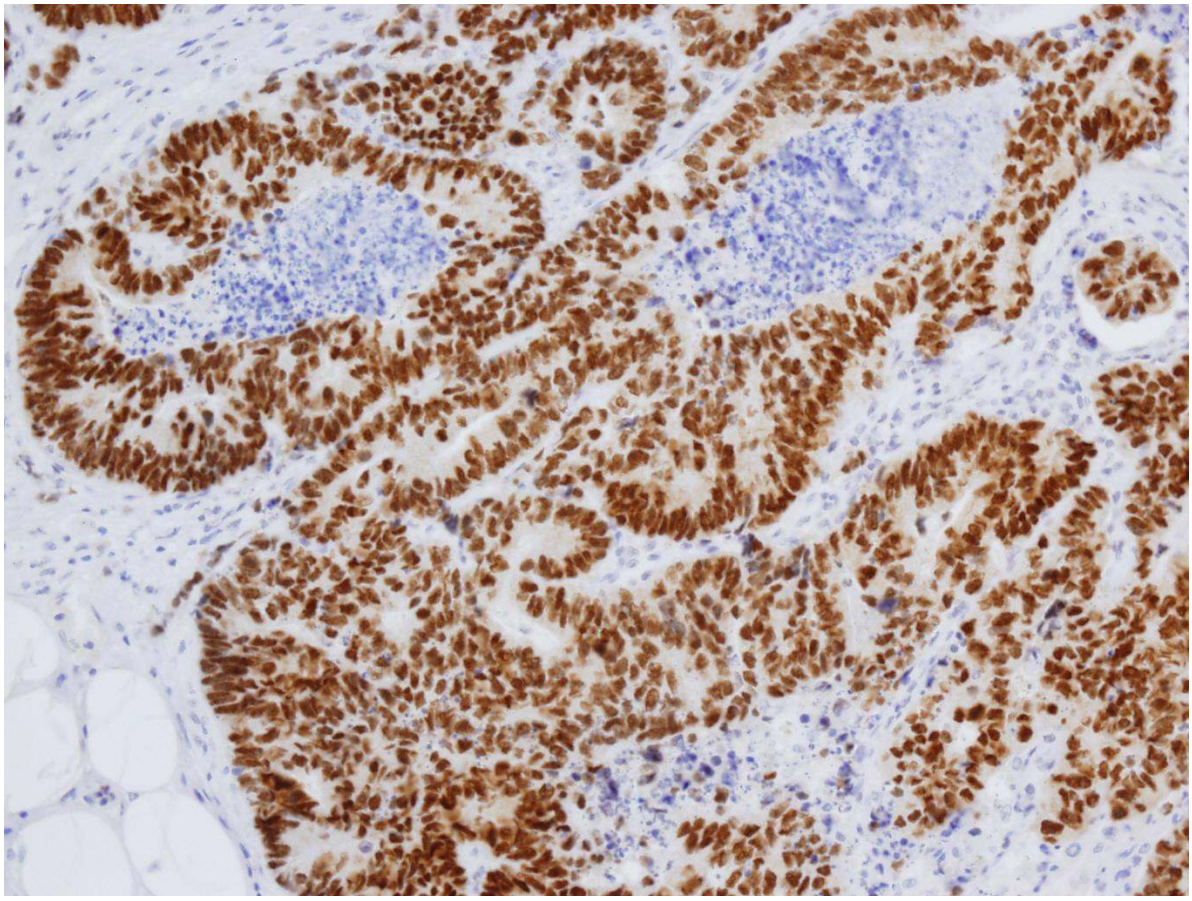

Figura 7. Positive immunohistochemical staining for CDX2.

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Unfortunately our patient died short after the diagnostic procedure, due to respiratory insufficiency. Therefore, we had no chance to perform colonoscopy, but it is noteworthy the total abscence or any clinical complaint regarding colonic neoplasm.
Thus, this case illustrates the importance to perform lung biopsy as a diagnostic procedure.

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