

pressure of oxygen at the new altitude. Avoiding exercise and alcohol during the first 48 h until acclimatization also minimizes the risk. Pre-existing conditions that lead to increased pulmonary blood flow, such as pulmonary hypertension, increased pulmonary vascular reactivity, or a patent foramen ovale, are predisposing factors for the appearance of the HAPE.

The key factor in the pathophysiology of the disease is the initial adaptation to altitude, in which the individual will typically increase ventilation. Activation of the pulmonary and cerebral hypoxic vasoconstriction reflex results in an exaggerated vasoconstriction response, raising pulmonary artery systolic pressure.³ The subsequent transudative capillary leak and the increase in perfusion increase blood pressure and hydrostatic pressure, causing damage to the alveolar–capillary barrier, and ultimately, increased vascular permeability leading to acute, non-uniform pulmonary edema.

Treatment consists of oxygen therapy and descending around 1000 m or to a level where symptoms resolve, minimizing exertion during the descent. Pharmacological treatment mentioned in the literature includes vasodilators, such as nifedipine (dihydropyridinic calcium channel blocker antagonists)⁴ or sildenafil,³ phosphodiesterase inhibitors,⁴ and dexamethasone. Acetazolamide is also used as a treatment because it creates alkalemia, which leads to increased ventilation by increasing the arterial oxygen content of blood, and study is ongoing into its prophylactic use for ascents to more than 2700 m.^{3,6,7} Potential new therapies, such as ibuprofen, nitrates, and intravenous iron supplements are recommended.³

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Paula Isabel García Flores,* Alberto Caballero Vázquez, Ángela Herrera Chilla, Ana Dolores Romero Ortiz

Servicio de Neumología, Hospital Universitario Virgen de las Nieves, Granada, Spain

* Corresponding author.

E-mail address: paulaflores89@gmail.com (P.I. García Flores).

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Pulmonary Necrobiotic Nodules: A Rare Manifestation of Crohn's Disease[☆]



Nódulos necrobióticos pulmonares: una manifestación excepcional de la enfermedad de Crohn

To the Editor,

The most unusual extraintestinal manifestations of inflammatory bowel disease (IBD) are respiratory, and ulcerative colitis (UC) is the most common causative entity. Clinical presentation is variable, ranging from asymptomatic patients to cases that present with cough, dyspnea, and respiratory failure. One peculiar characteristic is that pulmonary involvement does not always occur in parallel to intestinal tract disease, making it difficult to diagnosis. Pulmonary necrobiotic nodules as pulmonary complications of Crohn's disease (CD) are an exceptional manifestation, calling for a differential diagnosis with neoplastic diseases and infectious diseases, characterized by an excellent response to treatment with corticosteroids. Very few cases have been reported in the literature on this entity, and all of them presented with pulmonary symptoms, such as cough and dyspnea. We report the case of a patient with CD without respiratory manifestations, in whom pulmonary necrobiotic nodules were an incidental radiological finding.

A 26-year-old woman consulted for diarrhea, with a 2-year history of 6–10 stools per day of liquid consistency with blood and mucus, abdominal pain, and weight loss. She was a smoker of 10 cigarettes a day and had no other clinical history of interest. Physical

examination revealed poor general condition and painful abdomen on palpation in the epigastrium. Cardiopulmonary auscultation was normal, and no adenopathies or skin lesions were observed. Clinical laboratory tests were significant for hemoglobin 10.5 g/dl and transferrin saturation 5.1%, platelets 393 000/ml, and eosinophils 1000/ml. Chest radiograph was normal. Stool cultures at the time of the study were negative. Ileocolonoscopy showed swollen and erythematous mucosa with crater-like, serpiginous ulcers alternating with normal mucosa. The pathology report was suggestive of CD. Treatment began with oral budesonide 9 mg/day and mesalazine 2 g/day, with clinical improvement.

The patient's digestive symptoms subsequently improved, but lobar pneumonia developed, which was treated with levofloxacin. However, several lung nodules measuring 8–10 mm in diameter were identified in the X-ray performed to monitor radiological progress when the respiratory symptoms had resolved, and confirmed on a chest CT scan (Fig. 1). Bronchoscopy was normal with no tumor cells or pathogens in bronchoalveolar lavage (BAL). Other diagnoses, including metastasis and abscesses, were considered in the differential diagnosis. The diagnosis of pulmonary necrobiotic nodules associated with CD was given, in view of the temporal relationship between the diagnosis and IBD flare-up, and the good condition of the patient. She was treated with systemic corticosteroids, and radiological resolution of the nodules was achieved after 1 month of treatment (Fig. 1).

IBD is a chronic inflammation of unknown etiology, which affects the digestive tract. Pathogenesis is due to a recurrent inadequate response of the mucosal immune system, activated by the presence of normal luminal flora in genetically predisposed individuals. It is histologically characterized by a lymphocytic polymorphonuclear infiltrate with formation of granulomas, ulcers, and fissures in the mucosa. Although it mainly affects the intestine,

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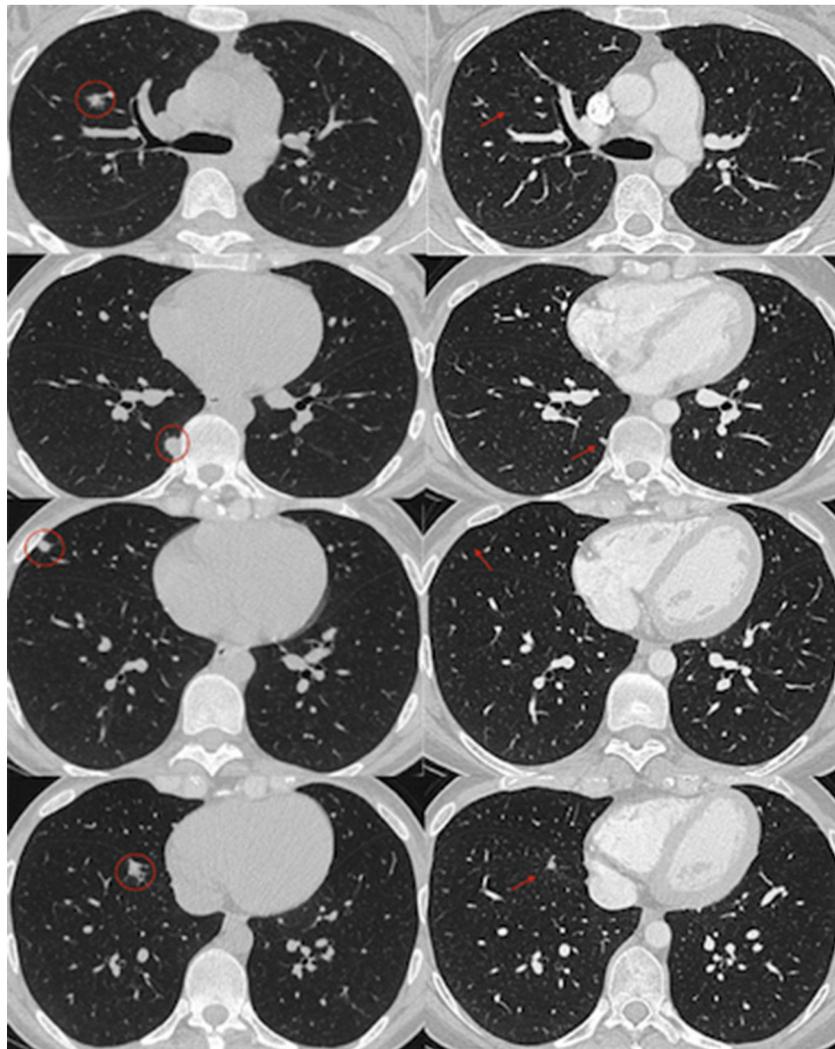


Fig. 1. Chest CT. Pulmonary nodules at diagnosis and after 1 month of treatment. On the left, chest CT images showing lung nodules of varying size (circles) in the right middle and lower lobes and the paravertebral region. On the right, images showing complete resolution of some of the nodules (arrows) after one month of treatment, and others reduced in size.

extraintestinal manifestations are well-known, with a prevalence of 21%–41% that increase as the disease progresses.¹

Pulmonary involvement as an extraintestinal manifestation was first described by Kraft et al. in 1976 after observing 6 patients with a diagnosis of IBD who developed chronic bronchial suppuration.² Different pathogenic mechanisms for the pulmonary involvement in these patients have been described, including the common embryological origin of the airway and the intestine, a similar immune system, and the presence of circulating immune complexes and autoantibodies.³ This is the most unusual extraintestinal manifestation of IBD and is usually seen in patients with UC, distinguishing it from other extraintestinal manifestations. Its real prevalence is unknown because it is sometimes asymptomatic or does not coincide chronologically with the IBD.¹ All these factors make diagnosis difficult in the absence of a high suspicion. However, early identification is important to prevent it progressing to a more disabling condition and to avoid complications.

The most common symptoms are derived from airway inflammation (cough, expectoration, or dyspnea), which manifests in many ways, ranging from asymptomatic disease to involvement of the tracheobronchial tree (bronchitis, bronchiectasis or bronchiolitis), the lung parenchyma, and the pleura.

A distinction must be drawn between pulmonary involvement caused by IBD and that caused by IBD treatment, the latter being the

most frequent. IBD treatment that might cause pulmonary involvement includes the long-term use of sulfasalazine, mesalazine, methotrexate, and anti-tumor necrosis factor (anti-TNF), rather than the underlying disease.

Pulmonary necrobiotic nodules in IBD are an exceptional complication and are more frequent in UC. This presentation was first described in patients with rheumatoid arthritis or pneumoconiosis (Caplan's syndrome). Histologically, necrobiotic nodules are sterile aggregates of neutrophils, which frequently cavitate.⁴

Radiologically, the differential diagnosis must consider pulmonary nodules of infectious origin (tuberculosis, fungi, staphylococci), autoimmune diseases, cancer, etc. In our case, the absence of fever, absence of neoplastic cells in BAL, and absence of eosinophils in BAL ruling out any association with mesalazine, led us to start empirical treatment with corticosteroids, with good response. Based on these findings, lung biopsy was avoided, pending clinical response and response to the new treatment.

Very few cases have been reported in the literature on this entity, and all of them presented with respiratory symptoms, including cough and dyspnea.^{5–9} This makes our patient even more unique, since she did not present respiratory manifestations, and diagnosis was made from an incidental finding.

Although the spontaneous resolution of necrobiotic nodules in IBD has been described, of the 5 cases associated with CD, only 1

resolved spontaneously.⁶ The other patients were treated with oral prednisone, with complete resolution. Infliximab is currently being used for lung nodules that are refractory to systemic steroids.¹⁰

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Laura Larrey Ruiz,^a Cristina Sabater Abad,^{b,*} Laura Peño Muñoz,^a Jose María Huguet Malavés,^a Gustavo Juan Samper^b

^a Servicio de Patología Digestiva, Consorcio Hospital General Universitario de Valencia, Valencia, Spain

^b Servicio de Neumología, Consorcio Hospital General Universitario de Valencia, Valencia, Spain

* Corresponding author.

E-mail address: sabaterabadcristina@gmail.com (C. Sabater Abad).

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Pleural Schwannoma Mimicking Metastatic Rectal Carcinoma[☆]



Schwannoma pleural que simula metástasis pleural de un carcinoma de recto

To the Editor,

Neuroblastoma-like schwannomas or neurilemmomas arising from the Schwann cells of the nerve sheath are extremely uncommon benign tumors, first described by Goldblum in 1994.¹ They mainly affect the head, particularly the jaw and neck, the flexor surface of limbs and the posterior root of the spinal nerve.¹ Tumors tend to be solitary, and in exceptional circumstances occur in the chest wall,² but they can occasionally be multiple in neurofibromatosis type 2 (NF2) or in the entity known as schwannomatosis.³

We report the case of a 57-year-old man with an 80 pack-year smoking history, prostate cancer treated with transurethral resection, and rectal cancer in the lower middle third of the rectum, treated surgically, with subsequent chemotherapy and radiation therapy (RT). The patient was clinically stable and asymptomatic from a respiratory point of view. Chest computed tomography (CT) was performed as part of the extension study, revealing well-defined, nonspecific oval pleural nodular thickening in the posterolateral portion of the 8th right intercostal arch measuring 35×11 mm. The same lesion was visualized on magnetic resonance imaging (MRI). The patient was referred to our clinic to rule out the existence of pleural metastases. We performed a chest ultrasound, which showed a poorly defined, anechoic, homogeneous lesion in the right chest wall, about 4.3 cm long and 1.8 cm thick. No infiltration was observed in the visceral pleura located medially to this lesion. Ultrasound-guided biopsy was performed using 14G Acecut[®] needles with 75 mm and 22 mm penetration depth (TSK, Japan). The pathology study showed spindle cell proliferation, with no characteristic pattern, swirling cellularity, moderate pleomorphism, occasional karyomegaly, and few mitotic figures, as well as more hypocellular areas with less compact stroma.

Immunohistochemistry results were as follows: S100-positive, vimentin-positive, and Sox-10 positive, consistent with schwannoma with focal degenerative changes (Fig. 1).

The majority (approximately 95%) of pleural tumors are malignant, and mostly metastatic,⁴ while benign pleural tumors are unusual. Among the benign tumors, schwannomas usually occur in the posterior mediastinum, especially in a paravertebral site. Schwannomas located in the lateral chest wall are uncommon, and account for less than 5% of these tumors.⁵ Pathological findings are characteristic and consist of a proliferation of tumor cells growing eccentric to the nerve with a spindle-like appearance; there are densely cellular areas (Antoni A) in which the nuclei are may occasionally palisade to form Verocay bodies, and less compact areas (Antoni B).⁶ They are almost always positive for S100.

From a clinical point of view, schwannomas may be asymptomatic or cause cough, chest pain, or dyspnea.² Malignancy is exceptional and has been described primarily in patients who have received RT.⁷

Chest ultrasound usually shows anechoic tumors and can generally discriminate well between benign and malignant tumors.⁸ However, in our case, the image lacked well-defined borders, and given that the existence of pleural metastasis could have therapeutic implications, we decided to perform an ultrasound-guided biopsy of the lesion.

Other imaging techniques should clarify the differential diagnosis between solitary pleural lesions, such as lipomas, single metastatic lesions, mesotheliomas, fibrous tumors, and other neurogenic tumors. In schwannoma, CT with contrast can distinguish heterogeneous lesions with different cellularity demarcating the Antoni type A or B areas, with enhancement of the former suggesting areas of cystic degeneration.⁹ On MRI, schwannomas usually display an isointense image in T1, similar to muscle, sometimes called the “split fat sign” that appears as a peripheral margin of displaced fat in the neurovascular bundle,¹⁰ with hyperintense signal in T2, although the cystic regions may have a low signal intensity. MRI is also useful for visualizing vascular involvement. Positron emission tomography/computed tomography (PET/CT), however, is of limited utility, given that often shows high uptake,¹¹ even in benign tumors, preventing the differential diagnosis with metastases of tumors from another source.

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