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1579-2129/

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Persistent Atelectasis in a Patient With Cystic Fibrosis: Are Antibiotics Always Needed?*



Atelectasia persistente en paciente con fibrosis quística: ¿debemos tratarla siempre con antibioterapia?

To the Editor,

Plastic bronchitis (PB) is a rare, underdiagnosed entity,^{1–7} characterized by the formation of obstructive bronchial plugs or cylinders of thick, tenacious mucus that cause the collapse of one or more lobes or even a whole lung.^{1,4–7} These casts are often expectorated, but they might be discovered on bronchoscopy or appear in the bronchial tree during autopsy.^{4,7} PB is also called fibrinous bronchitis, pseudomembranous bronchitis, or Hoffman's bronchitis.^{4,6} It has been described in asthma, cystic fibrosis (CF), cyanotic congenital heart diseases, respiratory infections, bronchiectasis, allergic bronchopulmonary aspergillosis (ABPA), acute chest pain in sickle cell disease, alpha thalassemia, etc.^{1,4–7} The pathogenesis of PB is not well understood.^{1,4} There are probably 2 mechanisms involved in its development: (1) bronchial injury or changes in bronchial epithelial function due to inflammation or infection, as occurs, for example, in asthma, bronchiectasis, CF, sickle cell anemia, and (2) deterioration of pulmonary lymphatic drainage, as occurs in congenital heart disease.^{4,6,8} We report a case of PB in a patient with CF, a situation rarely documented in the literature.

Our patient was a 15-year-old boy with a history of CF, chronically colonized with oxacillin-sensitive *Staphylococcus aureus*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa*, who was admitted for fever of 39 °C, asthenia, anorexia, and chest pain in the left hemithorax. Posteroanterior and lateral chest X-ray showed left upper lobe atelectasis. He was admitted for the administration of intravenous antibiotic therapy with piperacillin–tazobactam and tobramycin. The study to rule out other possible causes of atelectasis associated with CF was significant for a total IgE level of 2500 IU/ml and *Aspergillus fumigatus* (AF)-specific IgE of 38.80 IU/ml, IgG, precipitins and skin prick positive for AF, so prednisone 60 mg every 24 h and voriconazole 200 mg every 12 h were added to the treatment. After 15 days of treatment, clinical but not radiological improvement was observed, so a lung CT was performed that revealed complete atelectasis of the left upper lobe and the presence of a hyperdense cast in the bronchial tree (Fig. 1A). Given these findings, a fiberoptic bronchoscopy (FB) was performed, which revealed an obstruction in the entrance to the bronchus of the left upper lobe, caused by a large mucous plug. Using 4.6 mm fiberoptic bronchoscopy with sustained aspiration, a

bronchial cast measuring 7×1 cm (Fig. 1B) could be extracted, that was diagnosed as PB. One month after extraction of the bronchial cast, clinical and radiological improvement was confirmed, and the tapering and gradual withdrawal of corticosteroids began.

In CF, atelectasis occurs as a result of mucus plugs and severe parenchymal disease.³ It is typically treated with IV antibiotics and intensification of respiratory physiotherapy.³ If clinical and radiological improvement is not achieved, as occurred in our patient, complications such as PB must be considered. Several classifications of PB have been proposed: some are based on the histology of the cast,^{1,4,9} distinguishing inflammatory PB from non-inflammatory PB, and others on the associated etiology,¹ which defines PB as caused by a specific disease, or as idiopathic, if the disease is unknown.¹ Madsen et al. recommended a classification based on the associated disease and the histology of the cast, if the etiology of the PB is unclear.^{1,8} Basic treatment of PB is symptomatic, i.e., improvement of alveolar ventilation and mucociliary clearance, and reduction of inflammation and the bacterial or fungal load^{1,4,6} in the case of PB caused by bronchial infection or ABPA. Topical treatment of the bronchial cast is not well defined, and no particular mucolytic agent is considered superior to others¹; the cast may be difficult to remove with bronchial instillation of physiological saline or bronchoscopic suction.¹ Bronchodilators and mucolytics may disintegrate the secretions.^{1,5} Recombinant human DNase (rhDNase) has been used to reduce the viscoelasticity of sputum in patients with CF.³ In our case, rhDNase was instilled under direct vision bronchoscopy to treat the PB. The use of tissue plasminogen activator (0.7–1 mg/kg every 4 h) has been described in PB that develops after the Fontan procedure in children.^{1,4,5,7,10} It has also been reported that inhaled heparin can be effective,^{7,11} since its anti-inflammatory properties can help reduce mucin secretion, prevent activation of the fibrin tissue factor pathway, and reduce vascular filtration. Inhaled anticholinergics can reduce the formation of casts, and low-dose macrolides can decrease mucin production by inhibiting kinase 1 and 2 activation and reducing the severity of PB.^{7,12,13} In patients with lymphatic abnormalities, the most effective therapy for PB is selective lymphatic embolization with magnetic resonance-guided lymphography.^{6,7} The role

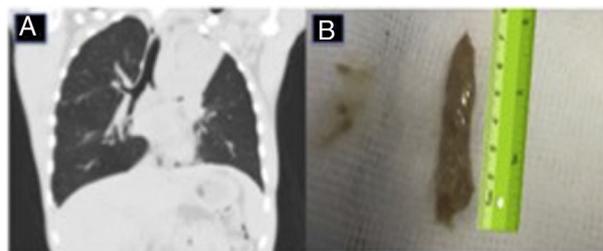


Fig. 1. (A) Complete atelectasis of left upper lobe, containing a hyperdense cast of the bronchial tree. (B) Bronchial cast extracted by fiberoptic bronchoscopy measuring 7×1 cm.

* Please cite this article as: Delgado Pecellín I, Moreno Ortega M, Carrasco Hernández L, Marín Barrera L, Muñoz Zara P, Moreno Valera MJ, et al. Atelectasia persistente en paciente con fibrosis quística: ¿debemos tratarla siempre con antibioterapia? *Arch Bronconeumol*. 2019;55:54–55.

of FB might be questionable in our patient, but we decided to use this technique, given the failure of conservative medical treatment with IV antibiotics, corticosteroids, and antifungal agents. By using FB, we were able not only to diagnose the PB and instill rhDNase in situ, but we could also extract the bronchial casts, thus improving pulmonary ventilation and mucociliary clearance.

In summary, we hope this report of PB in a patient with CF and ABPA will raise awareness in the community of this diagnostic possibility in patients with CF and persistent atelectasis who fail to improve with standard treatments, such as antibiotics, antifungals, and corticosteroids. Risk factors, such as decreased mucociliary clearance, respiratory tract inflammation or infection, hypereosinophilia, and aspergillosis, must be identified and treated. We defend the early use of FB in patients with CF and persistent atelectasis, to assist in the etiological diagnosis, instillation of mucolytics, and extraction of possible bronchial casts.

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1579-2129/

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Aspirin-Exacerbated Respiratory Disease in a Pediatric Patient Treated with Mepolizumab[☆]



Enfermedad respiratoria relacionada con aspirina tratada con mepolizumab en un paciente pediátrico

To the Editor:

Respiratory disease exacerbated by aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) is characterized by asthma, chronic rhinosinusitis, and nasal polyps aggravated by the administration of cyclooxygenase enzyme (COX)-1 inhibitors.

The prevalence among adult asthma patients is estimated at 7%–20%, and is even higher in patients with severe asthma. Symptoms usually begin in the third or fourth decade of life, more frequently in women.¹ It is much more uncommon in children,² and few cases have been reported in the literature to date.^{3–5}

Children with this phenotype tend to have moderate-severe asthma, even when the administration of NSAIDs is avoided. When compared with other asthma phenotypes, patients with aspirin-exacerbated respiratory disease have more frequent exacerbations, need higher doses of inhaled (or in many cases systemic) corticosteroids for asthma control, and show greater spirometric involvement.⁶ Significant rhinosinusal involvement is another aggravating factor.

The underlying pathogenic mechanisms are dysregulation of arachidonic acid metabolism and greater activation of eosinophils, platelets, and mast cells, with increased proinflammatory prostaglandins caused by the administration of COX-1 inhibitors.⁷

Challenge with oral, inhaled or nasal acetylsalicylic acid (ASA) is recommended for diagnostic purposes. Even if the clinical history is consistent, only 30% of patients have a positive response, while in children from a recent Spanish series, the response rate was 4%–10%.⁸ The placebo-controlled oral challenge test is considered the gold standard: increasing doses of ASA are administered, until the standard dose is reached. Approximate sensitivity of the test is 90%.¹ FEV₁ is recorded before each dose and 30 min after, and the test is completed when FEV₁ drops 20% or more from baseline.

The therapeutic approach involves the absolute avoidance of ASA/NSAIDs and drug treatment depending on the severity of the bronchial and nasal symptoms. Avoidance of COX-1 inhibitors is recommended; tolerance of selective COX-2 inhibitors is generally good, although some patients with poorly controlled asthma can also develop reactions.⁹

With regard to pharmacological management, these patients generally have moderate-severe symptoms and need to be treated in accordance with GEMA steps 4–5, with medium or high doses of inhaled corticosteroids with long-acting bronchodilators, combined in most cases with oral anti-leukotriene, which acts on the bronchial and nasal involvement.

When symptoms are refractory to these treatments, other alternatives can be evaluated, such as aspirin desensitization or biologics. Biologics include monoclonal anti-IgE (omalizumab is

[☆] Please cite this article as: Méndez Sánchez A, Gutiérrez Martínez JR, Coca Pelaz A, Vázquez Piñera MA. Enfermedad respiratoria relacionada con aspirina tratada con mepolizumab en un paciente pediátrico. *Arch Bronconeumol*. 2019;55:55–57.