Occupational Allergic Respiratory Disease and Eosinophilic Esophagitis by Wheat Flour in a Baker

Enfermedad respiratoria alérgica ocupacional y esofagitis eosinófila por harina de trigo en un panadero

Dear Editor,

Wheat can cause both immediate and delayed reactions. Immediate, IgE-mediated reactions may be triggered, after eating foods that contain this cereal, or by inhalation of wheat flour (WF), as in baker's asthma (BA).[1,2] The delayed reactions are not IgE-mediated, cause digestive symptoms, as it happens in eosinophilic esophagitis (EoE).[3–6]

We describe a 49-year-old man who worked as a baker for 30 years. He was referred to the allergology clinic by nasoocular itching, watery eyes, sneezing, runny nose, nasal obstruction, dry cough and dyspnea. His symptoms began after handling WF in his workplace, improving during weekends or holidays. He was treated with antihistamines and inhaled budesonide (400 μg/day), with good control for 10 years. In the last 5 years he worsened, needing to increase the dose of inhaled corticosteroids and adding salbutamol as rescue medication.

Simultaneously, he began with symptoms of esophageal dysfunction (SED) (dysphagia, chocking and heartburn). He was treated with omeprazole, 40 daily/20 years, with improvement and resolution of his symptoms but was never studied by a gastroenterologist.

Allergy study, skin prick tests (SPT) and specific IgE (sIgE) were negative (mean SPT wheal <3 × 3 mm and sIg E <0.35 kU/L) to pollens (grass, *Olea europaea* and *Salsola kali*), mites (*D. pteronyssinus*, *D. farinae* and *L. detructor*), molds (*A. alternata*, *Cladosporum* and *Aspergyllus*) and animal dander (cat, dog). SPTs were positive with WF commercial extract (ALK-Abelló, Madrid) and in prick by prick test. Total serum IgE: 135 kU/L. and specific IgE to WF 2.5 kU/L. Specific IgE to gluten, r-ω-5-gliadin, α-amylase and Tri a 14 were all negative (ImmunoCAP, ThermoFisher, Uppsala, Sweden).

The basal spirometry was normal. The methacholine bronchial test with an abbreviated method[7] was positive (PD20: 0.20 mg cumulative dose) while he was working, but, after 3 months of sick leave, it was negative. Chest X-ray was normal.

A specific bronchial test was carried out with WF, tipping it from one tray into another for 15 min. Spirometries were performed at baseline and at 2, 5, 10, 15, 20, 30, 45 and 60 min after the exposure to WF. Peak expiratory flow was measured at baseline and over a period of 24 h (respecting sleeping patterns). A 23% fall in FEV1 was observed 15 min after exposure to WF. The patient did not have any late reaction. A bronchial control test with saline carried out on the previous day was negative.

A sodium dodecyl sulphate polyacrylamide gel electrophoresis immunoblot analysis with WF extract was performed using the Laemmle method.[8] A specific binding was detected between 37 and 70 kDa. Glutenins in within the range of these molecular weights.

Endoscopy (E)1: without taking omeprazole, during a working period and ingesting WF. E2: working, ingesting WF and omeprazole; E3: without ingesting neither WF nor omeprazole and without exposure (sick leave); E4: without omeprazole, without exposure but with ingestion of WF; E5: without omeprazole, working, and without ingesting WF. E6: without omeprazole, without exposure and ingesting a gluten-free diet (Table 1). The diagnosis was made according to the updated international consensus diagnostic criteria for EoE: AGREE conference.[3] Remission is confirmed <15 eos/cga (total and partial remission: <5 and 5–14 eos/hpf, respectively).

In E1, >15 eosinophils/hpf were detected in the esophagus and <3 eosinophils/hpf in the stomach and duodenum. Table 1 shows the patient's responses to omeprazole, to a wheat-free diet, and to the environmental exposure to WF. The avoidance of WF, both by the digestive and the bronchial route, were capable to solve the EoE.

Table 1
Esophagoscopies and number of eosinophils in esophageal biopsies.

Omeprazole	Exposure to inhaled wheat flour at work	Wheat flour-intake	Eos/hpf in the 3 sections of the esophagus
No	Yes	Yes	>15
Yes	Yes	Yes	<3
No	No	No	<5
No	No	Yes	>15
No	Yes	No	>15
No	No	Gluten-free diet-intake Yes	<5

The patient was diagnosed with occupational allergic respiratory disease (OARD)[9] and occupational EoE[5,6] caused by WF. The evolution of the patient has been very good; after being retired from his job and on a wheat-free diet, he is asymptomatic.

EoE and OARD are frequently found as comorbidities along with other atopic manifestations. These two conditions have similar T helper type 2 responses-driven pathophysiology and share common management strategies[10]; this case is a clear example of the multiorganic clinical manifestations of atopy.

EoE experts have so far questioned whether this disease could be caused by the inhalation of allergens. The case described suggests that the answer would be affirmative.[5,6] The small number of reported cases caused by aeroallergens could be justified because, until now, some doctors who treat atopic patients have little experience in the diagnosis and management of EoE.

In Spanish bakers, sensitization to grass pollen and to rTria 14 is frequent, however, our patient is only sensitized to WF. The positive methacholine test, confirms that patient has bronchial asthma and the positive specific bronchial challenge test indicates that it is an OARD by WF.[6]

OARD to wheat proteins is very frequent and its prevalence does not seem to be declining. The researchers on BA point out the strong limitations of its diagnosis and treatment; they think that the isolation and characterization of cereal allergens associated with BA, particularly from WF would allow us to better define major and minor allergens, what would help to provide an adequate diagnostic panel of molecular markers.[2]

The EoE responded to omeprazole[3] but the patient had to follow a gluten-free cereal exclusion diet and to avoid WF inhalation simultaneously to achieve remission. Neither diet nor being off-work separately were sufficient for the resolution of the EoE.

In patients with SED, it is important to study if they have EoE or gastroesophageal reflux disease or both, because can worsen asthma.

We present an unusual case in which WF triggers EoE and an occupational OARD in the same patient, in which the inhalation of WF triggered the two diseases and EoE is caused by the oral and inhalation routes. When we diagnose an OARD, we should ask the patient for SED, since an early diagnosis and treatment will improve the prognosis and the quality of life of these patients.

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Idiopathic Constrictive Pericarditis After Single Lung Transplantation

Pericarditis constrictiva idiopática después del trasplante de pulmón unilateral

Dear Editor:

Constrictive pericarditis (CP) is a rare complication after lung transplantation (LTx), described in small case series after double lung transplantation.[1,2] Its cause is unknown and many theories are proposed. In our cohort, we observed four cases of this rare condition one of them after single lung procedure, which is the first case described in the literature. Our aim is to describe these cases as well discuss about its etiology and diagnosis.

The first case was a 41-year-old male who underwent bilateral LTx for bronchiectasis due to IgA deficiency in October 2008. He was diagnosed with atypical mycobacterial infection one year later. After one year, he presented rapid onset of dyspnea and signs of congestive heart failure. Echocardiogram showed pericardial effusion with signs of cardiac tamponade. Pericardial drainage was performed but he developed refractory cardiogenic shock and subsequently died 48 h after surgery. Autopsy showed an important pericardial thickening and attributed CP as the cause of death.

The second case was a 59 years-old male patient with sequential bilateral lung transplantation due to idiopathic pulmonary fibrosis in February 2013. His postoperative was uneventful but 5 months after he was diagnosed with rectal adenocarcinoma, stage I, treated exclusively with radiotherapy. He was also submitted some months after to a Nissen's fundoplication due to gastric esophageal reflux. He also presented dengue fever. Two years after the LTx, the patient presented with symptoms of right heart failure and the echocardiogram showed pericardial thickening and small pericardial effusion. The cardiac magnetic resonance imaging (MRI) showed signs of constrictive pericarditis. He was submitted to pericardiectomy and epicardiectomy with waffle procedure technique. He recovered his normal function and he is in follow up without symptoms.

The third case was a 44-year-old male who underwent bilateral LTx for bronchiectasis due to tuberculosis sequelae in November 2014. The postoperative was uneventful but nine months after he presented with deterioration in respiratory function. Echocardiogram showed a large pericardial effusion and cardiac MRI showed no signs of pericardial thickening. Pericardial drainage was performed with 800 ml of hemorrhagic fluid and prompt resolution of symptoms. Six months later he developed the same symptoms and without pericardial effusion on echocardiogram. MRI showed a thickened pericardium up to 4 mm thick. Pericardiectomy was performed, the patient recovered his previous status and remains asymptomatic.

The last case was a 59 years-old male with idiopathic pulmonary fibrosis received a single left lung transplantation in December 2014. The procedure was performed by left postero-lateral thoracotomy without CPB and the anastomosis technique was conventional with pericardial window around pulmonary veins and ischemic time of 240 min. The postoperative period was uneventful, with one episode of asymptomatic rejection and Nissen's fundoplication after one year due to gastric esophageal reflux. Two years after the transplant the patient showed acute but progressive dyspnea and signs of right heart failure. No signs of rejection or infection were detected. There were minimal pericardial effusion and pericardial thickening on chest computed tomography scan (CT-scan) and the echocardiogram showed left ventricular ejection fraction (LVEF) of 63%, atypical movement of ventricular septa, minimal pericardial effusion with pericardial thickening without signs of restriction. Cardiac MRI identified restriction on right ventricular filling and a circumferential thickened pericardium of 5 mm. Cardiac catheterization showed equalization of pressures in all cardiac chambers confirming the hypothesis of CP. The patient underwent a median sternotomy and a phrenic-to-phrenic pericardiectomy with epicardiectomy without cardiopulmonary bypass. He was discharged after 17 days and in his follow up there is no complication 15 months after surgery. The specimen confirmed the diagnosis of CP, with pericardial fibrous thickening with areas of fibrin deposition on the surface and some blood extravasation. The postoperative was uneventful with improvement of dyspnea and the patient recovered his regular activities for two years. The echocardiograms performed in this period showed normal LVEF and no signs of constriction. Then, he was diagnosed with pulmonary embolism and major depression with severe impairment of pulmonary function. He was sent to palliative care treatment and died one month after.

Constrictive pericarditis is a fibrous thickening of the pericardium compressing the heart and interfering in its filling. It is related to cardiac surgery, radiotherapy, rheumatological disturbances and tuberculosis. However, half of all cases are idiopathic or after viral infection. Its incidence after cardiac procedures ranges between 0.2 and 2.4%.[3] The incidence in our cohort after lung transplantation is 1.1% which is little higher than the only incidence reported in the literature of 0.4%.[4]

We performed an extensive literature search about this topic. Billings et al. were the first to describe this complication after LTx.[5] After them, few reports and case series were published. There are only 15 cases reported worldwide. Table 1 resumes the main