Occupational Asthma Caused by Exposure to Alumina

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Alumina, also known as aluminum oxide (Al_2O_3), is a naturally occurring mineral with a high melting point (2072°C) and remarkable hardness. It is known for its versatility, featuring high porosity, the ability to absorb heavy metals and contaminants, and exceptional density, hardness, and wear resistance. This makes it invaluable as an electrical insulator, in the production of ball mills, and in equipment for water and gas purification. It is also used to obtain aluminum. At the respiratory level, exposure to aluminum or its derivatives by welders can cause pneumoconiosis (with or without progression to fibrosis [1]), occupational asthma (OA) due to potassium aluminum tetrafluoride [2], and potroom asthma [3]. Reported mainly in aluminum smelters, potroom asthma is characterized by respiratory symptoms similar to asthma in workers producing aluminum using electrolytic cells. It is unclear whether the cause is direct exposure to aluminum or exposure to fluorides associated with these industrial processes [3,4].

To our knowledge, there are no reports in the literature of asthma secondary to exposure to alumina dust. Here we present the first case of OA due to alumina demonstrated through specific inhalation challenge (SIC).

The patient was a 41-year-old man (smoker [40 packs/year]; body mass index, 37), with no other relevant history. He had worked for 15 years in the construction of outdoor swimming pools and for the last 3 years in a company that manufactured absorbent material for insulation using alumina as raw material. To produce this material, the patient mixed alumina powder with sodium bicarbonate and potassium permanganate for 8 hours a day, 5 days a week. He wore an FFP2 mask at work for respiratory protection. The patient gave his consent for publication.

Two months after starting the job, he developed rhinitis, conjunctivitis, dry cough, and dyspnea. The symptoms began early, approximately 1 hour after arriving at work, improved with inhaled ß-adrenergics, and were clearly work-related, as they abated on weekends and during vacation periods or periods of sick leave.

Respiratory auscultation was normal. A blood test showed an eosinophil level of 300/µL, IgE level of 902 kU/L, and a positive ImmunoCAP Phadiatop result (Phadia AB) (41.60 kU_A/L). Forced spirometry revealed FEV_1 of 3.59 L (75%; z-score, –1.92) and an FEV_1/FVC ratio of 71% (z-score, –1.28). The methacholine test result was positive, with a PC_{20} of 6.6 mg/mL and FeNO of 7 ppm. Chest computed tomography showed nonspecific bronchial thickening.

Given the suspicion of OA due to alumina, an SIC was performed following the recommendations of the European Respiratory Society [5]. Briefly, the patient was exposed on successive days for increasing periods to a mixture of 20 g of alumina powder with 150 g of lactose in a 7-m^3 challenge cabinet and with the mixture being tipped from one tray to another at 30 cm from the face. FEV_1 was measured every day prior to exposure, at 10-minute intervals during the first hour after exposure, and every hour thereafter for a maximum of 12 hours. The day before the exposure, the patient was tested with placebo (powdered lactose). On the first day, after a 10-minute exposure to alumina, FEV_1 had dropped progressively at 7 hours after exposure; this reached a maximum of 19% between 10 and 12 hours after exposure (Figure). The decrease was accompanied by mild bronchospasm that required treatment with inhaled bronchodilators. At 24 hours after exposure, PC20 to methacholine was 4 mg/mL and FeNO 11 ppb.

OA is a disease characterized by variable airway obstruction and/or bronchial hyperresponsiveness due to causes and conditions that can be attributed exclusively to a specific work environment [6]. It is estimated that the average proportion of asthma cases in adults attributable to occupational exposure is between 10% and 15% and that this is currently the most common work-related respiratory disease in developed countries [7]. More than 400 agents have been associated with its pathogenesis. Metals are especially important, with platinum, nickel, chromium, cobalt, zinc, and manganese being the most frequently involved [8]. The present description suggests that aluminum should be added to this list.

The tests confirmed the relationship between alumina and the development of OA but did not enable us to establish the mechanism via which this disease develops. The high IgE levels, the presentation of atopy, and the high eosinophil rate may suggest an IgE-mediated mechanism; however, the late reaction in the SIC suggests that the immunological mechanism involved was independent of IgE. This last option seems to be supported by the observation of neutrophilia and elevated IL-8 in induced sputum recorded by Sikkeland et al [9] in 15 healthy individuals exposed to alumina through an SIC performed to assess its ability to generate inflammation in the airway.

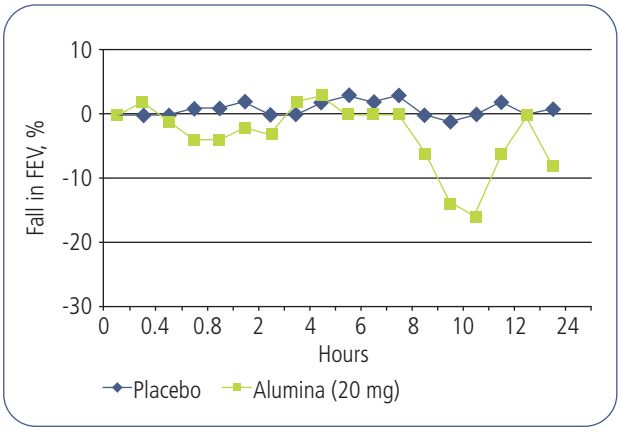

Figure. Result of specific inhalation challenge to alumina powder.

The mechanism involved in the pathogenesis of OA when the agent is a metal is not well defined. Among the possibilities proposed are exposure to platinum, in which the basic mechanism involved in the development of asthma is IgE-dependent, or exposure to other agents, such as chromium or nickel, in which the mechanism can be IgE-dependent or not [6].

The differential diagnosis of OA due to aluminum should include potroom asthma and OA due to other derivatives of aluminum or other metals. It is essential to conclusively determine the source of exposure and the type of industrial process involved in order to identify the agent. While potroom asthma has been related to exposure to agents released during the smelting process [3], other activities, such as aluminum welding, have been related to the development of OA, as demonstrated by exposure to potassium aluminum tetrafluoride [2].

In conclusion, given the increase in the use of aluminum, and especially alumina in multiple industrial processes, exposure to these elements should be acknowledged as a possible cause of respiratory disease (especially OA). This would make it possible to provide a rapid response to potentially affected patients and to implement primary prevention measures designed to avoid future exposures.

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Conflicts of Interest

Xavier Muñoz reports a relationship with Sanofi that includes grant funding and speaking and lecture fees. Xavier Munoz reports a relationship with GlaxoSmithKline that includes grant funding, speaking and lecture fees, and reimbursement for travel. Xavier Munoz reports a relationship with Novartis Pharmaceuticals Corporation that includes grant funding and travel reimbursement. Xavier Munoz reports a relationship with Boehringer Ingelheim Pharmaceuticals Inc that includes speaking and lecture fees. Xavier Munoz reports a relationship with Laboratorios Gebro Pharma SA that includes speaking and lecture fees. Xavier Munoz reports a relationship with Menarini Laboratories that includes travel reimbursement. Xavier Munoz reports a relationship with Faes Farma that includes travel reimbursement. Xavier Munoz reports a relationship with Chiesi Pharmaceuticals Inc that includes speaking and lecture fees. Xavier Munoz reports a relationship with AstraZeneca that includes grant funding, speaking and lecture fees, and travel reimbursement. María Florencia Pilia is a researcher supported by the Contratos Predoctorales de Formación en Investigación en Salud (PFis) program from

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