Bilateral Pneumothorax Secondary to Air Leak Syndrome 22 Years After Allogeneic Bone Marrow Transplantation☆

Neumotórax bilateral secundario a un síndrome de fuga aérea 22 años después de un trasplante alogénico de médula ósea

To the Editor,

Air leak syndrome (ALS) is a rare, severe, non-infectious complication of allogeneic bone marrow transplantation (ABMT) that generally affects patients with constrictive bronchiolitis (CB) in the context of graft-versus-host disease (GVHD). Prognosis is very poor.[1–3] Diagnosis of ALS is usually radiological and it may present in the form of pneumothorax, pneumomediastinum, and interstitial and/or subcutaneous emphysema.[4,5] We report a case of ALS 22 years after ABMT in a patient with a history of acute lymphoblastic leukemia.

Our patient was a 32-year-old man who presented in our hospital with dyspnea on minimal exertion and chest pain. Significant history included acute lymphoblastic leukemia diagnosed at the age of 6 years, treated with chemotherapy and prophylactic cranial radiation therapy. Four years later, at the age of 10, he presented testicular relapse of the leukemia, and underwent ABMT after conditioning with chemotherapy and total body irradiation. The patient developed several non-infectious complications associated with his treatment regimen: primary hypogonadism, bilateral cataracts, growth hormone deficiency, syndrome of inappropriate antidiuretic hormone secretion, etc. At the age of 28 years (18 years after ABMT), the patient was diagnosed with CB in the context of grade I GVHD, in addition to skin and intestinal manifestations. He was treated with low-dose corticosteroids in an attempt to minimize the development of opportunistic infections, and because non-severe forms of GVHD have a "graft-versus-tumor" effect that reduces the likelihood of tumor relapse. However, the patient's lung function tests continued to deteriorate progressively despite escalation of the dose of corticosteroids. The patient also presented a first episode of left pneumothorax (4 months before admission to our hospital), which was treated with a chest tube in another center. At the time of admission to our hospital, he had a forced vital capacity of 1230 ml (27.2% predicted) and a forced expiratory volume of 1060 ml (27.7% predicted). Chest radiography revealed a loss of volume in both lungs and a new left pneumothorax (Fig. 1A). A chest computed tomography (CT) showed signs of CB with areas of air trapping (Fig. 1B) and bilateral pneumothorax (Fig. 1C), and a diagnosis of ALS was given. Despite placement of a left chest tube, the patient died 5 weeks later due to respiratory failure.

ALS is a severe non-infectious complication of ABMT, consisting of extra-alveolar air in the chest in the form of pneumothorax, interstitial emphysema, pneumomediastinum and/or subcutaneous emphysema.[1] This is a very rare complication, and practically all cases of ALS are associated with advanced CB in the context of chronic GVHD.[2] However, in contrast to the generally slow clinical progress of CB (progressive dyspnea, tachypnea, cough), ALS can present in an acute form with chest pain and sudden onset of dyspnea. A diagnosis of ALS carries a very poor long-term prognosis for survival, so radiological detection has important therapeutic and prognostic implications.[3] Most cases of ALS are diagnosed within a period of a few months to 6–7 years after ABMT, and the clinical suspicion of this process is generally confirmed on imaging tests (particularly chest CT). Although chest CT has become a very useful diagnostic tool in the diagnosis and follow-up of complications associated with ABMT, very few references in the literature describe radiological findings in ALS.[4] Our case is interesting because we found no reports in the literature of such late onset of ALS after ABMT, and because only 3 previous cases of ALS with bilateral pneumothorax have been reported.[5] We also believe that in patients who have undergone ABMT with a diagnosis (or clinical suspicion) of CB who present acute chest symptoms (chest pain and/or sudden dyspnea), a CT should be performed to rule out the various radiological manifestations of ALS.

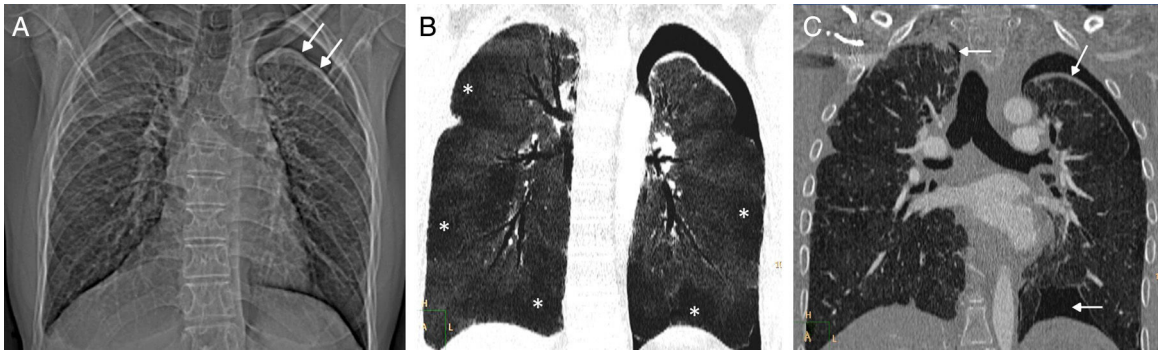

Fig. 1. (A) Chest radiograph showing a loss of volume in both lungs and left pneumothorax (arrows). (B) Minimum intensity projection (minIP) coronal reconstruction of chest CT (pulmonary parenchyma window), showing geographical areas of low attenuation in both lungs (asterisks) associated with areas of air trapping. (C) Coronal image of chest CT (pulmonary parenchyma window) revealing bilateral pneumothorax (arrows).

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Prevalence of Asthma in Children and Adolescents in a Rural Area☆

Prevalencia de asma en la infancia y adolescencia en una zona geográfica de características rurales

Dear Editor,

Asthma, understood as cough, dyspnea and wheezing, is the most common disease in childhood,[1] with around 300 million individuals estimated to be affected world-wide.[2] It generates enormous healthcare costs, causes loss of work productivity among adults, and deeply impacts lives of families with an asthmatic child.[3]

Asthma is an underdiagnosed and undertreated disease, so standardized questionnaires that evaluate symptoms consistent with asthma as disease markers have become the tool of choice for the identification of asthma in descriptive studies.[4,5] The ISAAC questionnaire has been used to determine the prevalence of asthma in all such studies and has contributed valuable data. The prevalence of asthma is known from these studies to be as high as 11.7% in children and 14.1% in adolescents.[5]

In Navarre, a study conducted in 2015[6] found a prevalence of asthma of 10.1% among children and 10.6% among adolescents. However, children had a higher prevalence of "wheezing at any time" than adolescents (22.7% vs 12.9%, respectively). This study was performed in a metropolitan area of Pamplona, an urban district with towns of at least 10 000 inhabitants. No studies have been previously conducted in childhood asthma in Navarre. In Galicia, a study performed in 2010 in a rural population of children and adolescents[7] showed that the prevalence of asthma in children and adolescents was 6.3% and 15.3%, respectively.

In the 6- to 7-year age group, 38% had had wheezing at any time, and 13.2% had recent wheezing. Recent cough at night was detected in 21.9%, and recent wheezing during exercise in 6.3%. In the 13- to 14-year age group, 20.1% had had wheezing at any time, and 11% had recent wheezing. Taking these data into account, the aim of our study was to determine the prevalence of symptoms consistent with asthma in rural areas of Navarre, and to contribute new data to the ISAAC study.

The validated version of the ISAAC study questionnaire in Basque and Spanish was used in the study, depending on the linguistic model of the school in which it was administered (Annex I). Seven Basic Health Areas (BHA) in central Navarre were selected because they contained 2 towns of approximately 10 000 inhabitants (Tafalla and Estella) and were close to the workplaces of the investigators (the 15 towns are widely dispersed and each school had to be visited on several occasions). Schoolchildren aged between 6 and 7 years and 13 and 14 years attending the schools in these areas were selected.

Firstly, towns within the BHA that had schools were identified. In total, 19 schools located in 15 towns participated in the study, although these schools catered for children from a total of 45 different localities. This is because some villages have as few as 34 inhabitants.

In Spain, school attendance is obligatory between the ages of 6 and 16 years, so these schools gave us access to 100% of the study population.

To administer the questionnaires to the 2 age groups, an email containing a description of the study and requesting a meeting with the principal was sent to each school. In this way, each school decided voluntarily to participate in the study. The school principal obtained the approval of the school board and the parent-teacher association to participate in the study. Mothers and fathers also signed a form authorizing the questionnaire to be administered to their children.

Field work was carried out between September 2014 and February 2015.

Each questionnaire was scanned and the data were entered in the SPSS® statistical program to determine the prevalence of asthma symptoms by age group and sex, using the following statistical methods: 95% confidence interval (CI), Chi-squared test, adjusted analyses, odds ratio (OR), and unconditional logistic regression.

A total of 969 questionnaires were distributed: 607 (62.6%) to the 6- to7-year age group and 362 (37.4%) to the 13- to 14-year age group. In the 6- to 7-year group, 449 of the 607 questionnaires for parents were completed (74%). In the 13- to 14-year age group, 348 of the 362 questionnaires distributed were completed (96.1%). The final study population consisted of 797 schoolchildren. Distribution by age groups was: 449 (56.3%) in the 6- to 7-year group and 348 (43.7%) in the 13- to 14-year group; and by sex: 414 (52%) boys and 383 (48%) girls.

Descriptive data on the prevalence of symptoms of asthma by age group and sex are shown in Table 1.

In this study, data on the prevalence of symptoms consistent with asthma in rural areas of Navarre were determined for the first time. The number of studies in other rural areas in Spain is small. The percentage of schoolchildren who had had wheezing at any time is significantly higher among children aged 6–7 years (18.3% in boys and 16.2% in girls), than in the 13- to 14-year group (6.7% in boys and 7.3% in girls). The frequency of recent wheezing was 14.1% in primary schoolchildren and 10% in secondary schoolchildren. However, 13.4% of schoolchildren aged 13–14 years had had asthma at some time, compared to 11.7% of children in the 6- to 7-year group. As we can see, the prevalence of asthma is higher

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