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A Lung Lavage Technique in an Infant with Pulmonary Alveolar Proteinosis[☆]



Técnica de lavado pulmonar en lactante con proteinosis alveolar

To the Editor:

The treatment of choice for alveolar proteinosis in children is whole-lung lavage, by which proteinaceous material deposited in the alveoli is removed by instilling saline solution directly into the lung.¹ This procedure, which is rarely performed in the pediatric setting and for which no specific equipment has been developed, is a true technical challenge.²

We report the case of a female infant who was healthy until the age of 7 months, when she was diagnosed with acute myeloblastic leukemia type M5. She received a haploidentical stem cell transplant (SCT) from her father at the age of 13 months in her first full remission. She developed a post-SCT complication of generalized host-versus-graft disease, requiring intensive immunosuppressive treatment. Two months after the SCT, a chest computed tomography (CT) performed for persistent fever was normal.

She developed respiratory disease at the age of 20 months (7 months post-SCT), following *Klebsiella pneumoniae* sepsis, with progressive breathing difficulties and hypoxemia.

As her respiratory symptoms failed to improve despite antibiotic therapy, a chest CT was performed that showed a bilateral “crazy-paving” appearance. The patient was anesthetized and a simultaneous bronchoalveolar lavage (cytology showed abundant, dense granular material, PAS staining positive; *Pseudomonas aeruginosa* was grown on culture) and lung biopsy via mini-thoracotomy were performed. This allowed us to rule out infection and interstitial lung disease due to surfactant deficit, and to confirm the diagnosis of alveolar proteinosis.

Given these findings, we decided to perform therapeutic lung lavage. A total of 2700 ml of warm saline solution was delivered to the right lung in 12 aliquots of 27 ml/kg. Two weeks later, the procedure was repeated in the left lung, using around 2500 ml.

Given the unavailability of double-lumen tubes for children under 8 years old, we decided to introduce 2 endotracheal tubes using direct laryngoscopy:

- One, 3.5 mm in diameter, was placed in the trachea to maintain ventilation.
- The other, 3 mm in diameter, with a balloon, was placed in one of the main bronchi, and telescoped until it reached the correct length and caliber; this one was used for the instillation of serum (Fig. 1A).

The correct placement of both tubes was confirmed with flexible bronchoscopy and fluoroscopy.

Fluid was introduced and removed from the bronchus by gravity; the tubes were alternately clamped to allow entry or exit of fluid (Fig. 1B).

After each procedure, the patient was admitted to the intensive care unit for 12 h. She received corticosteroids to prevent laryngeal edema and was extubated after a few hours without complications.

Clinical response after lavage of both lungs was very good, and her hypoxemia resolved rapidly. Two weeks after the procedure, a high-resolution, low-radiation CT of the chest was performed, revealing persistent ground-glass lung lesions, but to a lesser extent than before.

The presence of autoantibodies against granulocyte monocyte-colony stimulating factor (GM-CSF) in blood was ruled out, and GATA2 mutation testing was also normal.

Five months after the procedure, lung lavage was repeated due to reappearance of hypoxemia, and the patient again showed clinical improvement.

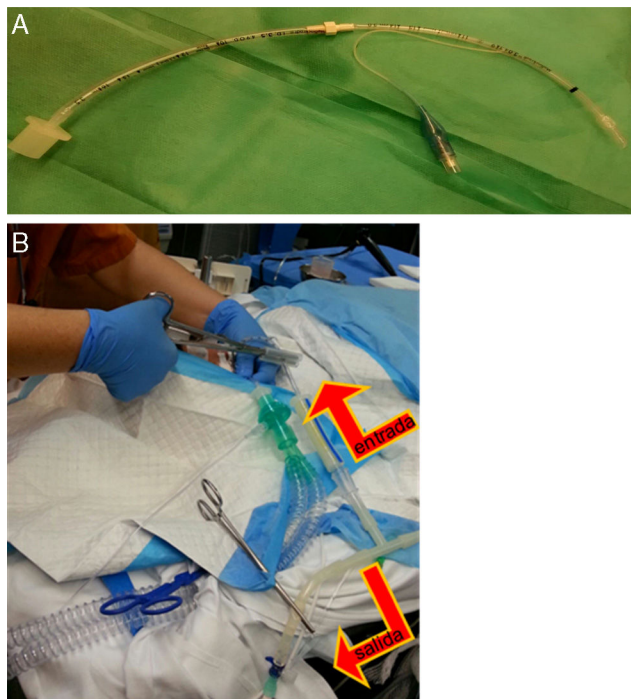


Fig. 1. (A) Endotracheal tube, 3 mm with balloon, extended by connecting it with another 3.5 mm tube, through which the warm saline solution was instilled and collected after it was placed in the main bronchus. (B) Image showing the tube located in the trachea, used to ventilate the patient, and the tube placed in the main bronchus, used to instill the saline solution with an alternating clamping system (the outflow was clamped at the time of instillation and the inflow was clamped at the time of emptying the lung fluid), indicated by the arrows.

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We use this case to describe the procedure and equipment used for whole-lung lavage in an infant, with practical suggestions for performing the technique, including the simultaneous use of 2 endotracheal tubes, one of which was lengthened to allow selective intubation. This system was selected because partial lavage with instillation of smaller aliquots of saline solution via the bronchoscope to the different lung segments is more laborious, although this could be an option in patients with severe respiratory failure who may not tolerate whole-lung lavage.³

The trigger in our patient was thought to be a transient dysfunction of alveolar macrophages (responsible, along with type II pneumocytes, for surfactant catabolism) due to immunosuppression, causing occupation of the alveolar space.⁴ Another factor associated with this disease in the literature is infection, and in our case, the microorganisms in blood and in bronchoalveolar lavage may have played an important role in determining the course of the patient's respiratory disease.⁵

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Management Difficulties in a Patient With EGFR-Mutation Positive Lung Adenocarcinoma and Cerebral Metastases[☆]



Difícil manejo en paciente con adenocarcinoma de pulmón con mutación de EGFR y enfermedad cerebral

To the Editor:

We report the case of a 49-year-old man, who was an occasional smoker. In 2007, a chest radiograph was obtained during an episode of acute bronchitis, which showed a solitary pulmonary nodule, subsequently confirmed on computed tomography (CT). Fiberoptic bronchoscopy did not yield any histological material, so a fine needle aspiration biopsy was performed, which revealed the presence of lung adenocarcinoma. After the case was discussed by the tumor committee, surgical intervention was performed. The pathology study reported adenocarcinoma requiring adjuvant chemotherapy. One year later, contralateral pulmonary and hepatic relapse was revealed on CT. Given the early tumor relapse, the likelihood of the tumor being resistant to chemotherapy, and the clinical characteristics of the patient, the tumor was biopsied again and the sample was sent for molecular analysis, including determination of epidermal growth factor receptor (EGFR) status. This test was positive, reporting an exon 19 deletion, so treatment began with erlotinib. Six months later, the CT showed complete response, subsequently confirmed on PET/CT. The patient continued on the same treatment, with regular assessments, for another 5 years. At that time, as the various radiological tests performed during the previous 5

years showed no evidence of disease, we decided to discontinue treatment under close monitoring. Two months later, the patient presented with headache, vomiting and instability. A head CT was performed, revealing a cerebellar lesion measuring 3×4 cm, with intense perilesional edema. After the possibility of systemic relapse was ruled out by CT and PET/CT, oligometastasis was confirmed and it was decided that the best treatment was local resection of the lesion, in accordance with the various clinical guidelines that advocate local treatment as the best approach in oligometastatic disease, if feasible. Histological analysis confirmed that the lesion was metastasis from the previous lung adenocarcinoma. Development of a T790M resistance mutation was suspected, so the EGFR analysis was repeated. This ruled out secondary resistance and confirmed the presence of the exon 19 deletion. Despite the absence of systemic disease, the high risk of relapse led us to reinstate anti-EGFR treatment, and the patient currently remains free of both systemic and cerebral disease.

Our case illustrates the difficulties encountered in managing patients with EGFR mutations and predicting their clinical progress. EGFR belongs to the ErbB family of membrane receptors with tyrosine kinase activity. Between 5% and 10% of non-small cell lung cancers have EGFR mutations; they occur more commonly in women and are associated with little or no consumption of tobacco.¹ The finding of a mutation of this type predicts a better response to targeted drug treatment than to cytotoxic chemotherapy. However, not all mutations are the same: exon 19 deletion is the most common and predicts a better treatment response, followed by exon 21 insertion (L858R); finally, exon 20 alterations are associated with drug resistance.^{2,3} It should be emphasized here that the typical evolution of this tumor is marked by an initially good response to the inhibitor, followed by the development of secondary resistance, the most common mechanism being the appearance of the T790M mutation.⁴

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