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Case Report

Pediatric pulmonary Langerhans cell histiocytosis complicated by recurrent hemopneumothoraces

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ABSTRACT

Langerhans cell histiocytosis is a rare disease of clonal proliferation and deposition of immature dendritic cells in various tissues, including the lungs, causing inflammation and organ destruction. We report a case of a 4-year-old girl with refractory multisystem Langerhans cell histiocytosis complicated by recurrent bilateral hemopneumothoraces in a pediatric tertiary hospital in Cape Town, South Africa. Video-assisted thoracoscopy revealed chronic inflammation of her pleura, with pleural fibrosis seen on histology. Despite pleurodesis, she continued to have recurrent hemopneumothoraces until she was started on a hydroxyurea-containing regimen with a good response.

Keywords: Pneumothorax, Hemopneumothorax, Langerhans cell histiocytosis, Video-assisted thoracoscopic surgery

INTRODUCTION

Pediatric pulmonary Langerhans cell histiocytosis is rare in children and usually occurs as part of a multisystemic disease that may involve the bones, skin, lungs, liver, spleen, brain, or the hematopoietic system.[1,2] Presenting features of pulmonary involvement include cough, dyspnea, wheezing, chest pain, and recurrent pneumothoraces.[2,3] Hemothorax is an unusual presentation of pediatric pulmonary Langerhans cell histiocytosis. We report a case of a 4-year-old girl with refractory multisystem Langerhans cell histiocytosis complicated by recurrent right-sided pneumothoraces, who later developed recurrent spontaneous bilateral hemopneumothoraces in a pediatric tertiary hospital in Cape Town, South Africa.

CASE REPORT

A 4-year-old HIV-negative girl with a history of night sweats, poor weight gain, and recurrent wheezing for two years was referred to our facility on account of a right pneumothorax and multiple lytic rib lesions [Figure 1]. There was no personal or family history of atopy and no family history of asthma. On examination on arrival, she was well perfused, not pale, and afebrile. Her weight for age plotted just below the median. She had a respiratory rate of 30 breaths per minute, and her oxygen saturation was 95% in room air. She had decreased air entry of the right

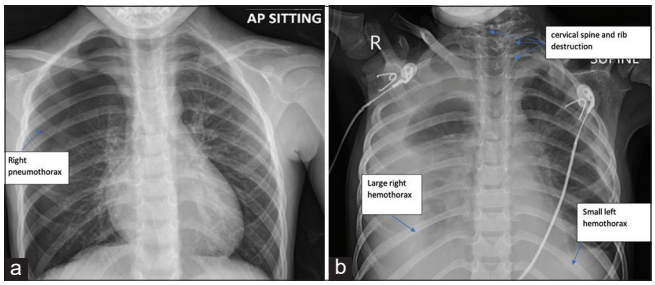

Figure 1: A 4-year-old girl with Langerhans cell histiocytosis. Chest X-rays show (a) right pneumothorax and (b) destruction of ribs and bilateral hemothoraces.

hemithorax, with a right-sided intercostal drain (ICD) *in situ* and bilateral wheezes. The cardiovascular examination was normal. A non-tender hepatomegaly, 2 cm below the costal margin, was noted on abdominal examination. She was alert and interactive.

Her investigations included a bone scan, which revealed multiple lytic skeletal lesions. Her urine catecholamine levels were normal, her tuberculosis workup was negative, and her bone marrow trephine biopsy did not reveal any malignant or granulomatous disease. A diagnosis of Langerhans cell histiocytosis was confirmed on clavicular biopsy. This was further classified as a multisystem disease involving the liver and lungs, confirmed on a positron-emission tomography scan. Her response to the recommended first-line treatment of prednisone and vinblastine was poor. She continued to have recurrent right pneumothoraces on second-line (vincristine and cytarabine) and third-line (cladribine and cytarabine) chemotherapy, requiring multiple ICD insertions. She subsequently developed bilateral hemopneumothoraces requiring fluid resuscitation and bilateral ICD drainage. The effusions were paucicellular, predominantly blood with scanty reactive lymphocytes. No organisms were cultured. Due to her recurrent hemopneumothoraces, the child had a right-sided video-assisted thoracoscopy [Figure 2] and pleurodesis. The thoracoscopy revealed a small bleb on the lower edge of the lower lobe of the right lung and inflammation of the parietal pleura with upper and anterior middle lobes adherent to the chest wall. Her lung biopsy was normal, but her pleural biopsy showed chronic inflammation and fibrosis. She continued to have right hemopneumothoraces despite pleurodesis until she was started on next-line therapy containing hydroxyurea more than a year after the initial presentation, to which she responded well and had no further hemopneumothoraces.

DISCUSSION

Langerhans cell histiocytosis is a rare disease of clonal proliferation and deposition of immature dendritic cells in various organs and tissues, accompanied by an inflammatory infiltrate.[1,4] Most of these pathologic cells have mitogen-activated protein kinase (MAPK) pathway mutations, commonly in the BRAFV600E gene.[1] Langerhans cell histiocytosis may involve a single system or may be multi-systemic. Single-system disease may be unifocal or multifocal.[1,4]

Lung involvement in pediatric Langerhans cell histiocytosis is about 7.4–24%.[2,3] Pulmonary Langerhans cell histiocytosis may present with a dry cough, tachypnea, dyspnea, chest pain, and wheezing. Other presentations are bullae formation and respiratory failure secondary to pneumothoraces. Children may also have constitutional symptoms such as malaise, weight loss, and fever. Pulmonary Langerhans cell histiocytosis is diagnosed based on characteristic radiologic findings in a patient known to have Langerhans cell histiocytosis. Bilateral interstitial infiltrates, mostly symmetrical, with a reticulonodular pattern, with or without cysts, are the most common finding on chest X-ray and computed tomography scans;[2] however, only cysts and nodules are diagnostic.[4] Diagnosis may also be made on cytology and immunohistochemical staining of bronchoalveolar lavage fluid in a non-smoker or lung biopsy. Lung biopsy is useful in a single-system lung disease but unnecessary if other sites are more accessible for biopsy in the setting of multisystem disease. The presence of >5% CD1a+ and CD207+ cells on biopsy supports the diagnosis of pulmonary Langerhans cell histiocytosis.[1,4]

Treatment of pulmonary Langerhans cell histiocytosis includes supportive management such as optimizing nutrition, routine immunizations, influenza vaccination, and smoking cessation. Definitive treatment includes various chemotherapeutic agents, including MAPK therapy, such as trametinib.[5] Complications may be managed with supplemental oxygen, ICDs, careful mechanical ventilation, and pleurodesis as required.[1,3,4,6] Lung transplantation is also another treatment option.[7]

Spontaneous hemothorax is the presence of pleural fluid with a hematocrit, which is more than 50% of that of blood, in the absence of trauma or iatrogenic causes.[8,9] In some cases, with time, dilution may reduce the hematocrit of a spontaneous hemothorax to as low as 25% of that of blood.[9] Any pleural effusion with hematocrit more than 5% looks bloody; therefore, measuring the hematocrit is important to distinguish a hemorrhagic pleural effusion from a hemothorax. Nevertheless, not all institutions routinely check the hematocrit of bloody pleural fluid. We did not measure our patient's pleural fluid hematocrit. Our patient had typical signs of pediatric pulmonary Langerhans cell histiocytosis, including recurrent wheezing and pneumothoraces requiring multiple ICDs. However, her presentation of hemothoraces as a manifestation of Langerhans cell histiocytosis is unique.

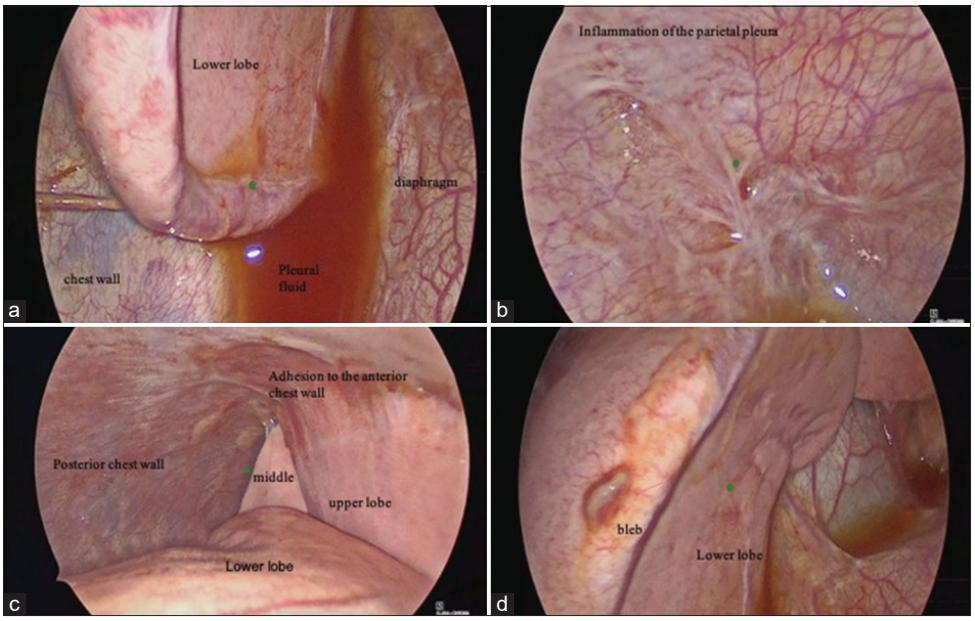

Figure 2: A 4-year-old girl with Langerhans cell histiocytosis and recurrent hemopneumothoraces who underwent right video-assisted thoracoscopic biopsy. Thoracoscopic pictures show (a) hemothorax, (b) inflammation of the parietal pleura, (c) adhesions to the anterior chest wall, and (d) bleb of the lower lobe.

This could have been a result of disrupted adhesions between the parietal and visceral pleura or bleeding from ruptured bullae.[9] This could also have been from the rupture of congenitally abnormal vessels between the parietal pleura and bullae,[8] but there was no evidence of this on biopsy. The disease course is variable among patients, with involvement of the spleen, liver, or hematopoietic system portending a worse prognosis.[4] Therefore, management is individualized. Management of our patient is similar to that in a series by Eckstein *et al*, where chemotherapy, repeated ICDs, and pleurodesis were employed.[6] Pleurodesis is not always successful in preventing the recurrence of pneumothoraces, however, and may need to be repeated.[6] Our patient required ICDs on the same side post-pleurodesis until she was switched to a regimen that included hydroxyurea, a known therapy for myeloid disorders, which has been used to treat recurrent Langerhans cell histiocytosis successfully.[10]

CONCLUSION

Pediatric Langerhans cell histiocytosis can present as a prolonged debilitating disease with recurrent pneumothoraces that are difficult to manage. Hemothorax, a rare complication, can result from inflammation of the pleura. Management involves a multidisciplinary approach and may require an individualized treatment plan. Thoracoscopy may be useful to confirm the site of bleeding and for biopsies and pleurodesis.

Acknowledgment

We thank the patient and her family, as well as the multidisciplinary team that was involved in her management.

Ethical approval

The Institutional Review Board approved the research/study at the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee, number HREC REF 733/2023, dated October 30, 2023.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the

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