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Case Report

A Rare Case of Pulmonary Adenocarcinoma in an 8-Year-Old Patient with Persistent Respiratory Manifestation: A Case Report Study

Lobat Shahkar[a] Noora Bigdeli[a] Mahdi Mazandarani[b]
Narges Lashkarbolouk[b]

[a]Taleghani Pediatric Center, Golestan University of Medical Sciences, Gorgan, Iran; [b]Endocrinology and metabolism research center, Tehran University of medical sciences, Tehran, Iran

Keywords
Adenocarcinoma · Bronchoalveolar carcinoma · Lung cancer · Pediatrics · Pediatric oncology

Abstract
Pulmonary adenocarcinoma is an extremely infrequent cancer in children. This cancer usually presents with unspecific manifestations that lead to delays in diagnosis. The treatment protocol for adenocarcinoma in children remains challenging due to its rarity. We presented an 8 years old with a chief complaint of a non-purulent cough, dyspnea, hemoptysis, and weight loss. Decreased lung sounds and wheezing in the left lung were heard during auscultation. The radiographic evaluation showed a mediastinal mass in the left middle upper. A biopsy was performed, and adenocarcinoma was reported. Based on being at stage 1, a lobectomy was the proper treatment for her. Although adenocarcinoma is rare in pediatrics, we suggested that physicians consider taking chest X-rays in patients with persistent respiratory manifestations, especially those with critical symptoms. Early detection leads to diagnosing patients in lower stages, which results in a good prognosis and better treatment outcomes.

Introduction

Adenocarcinoma is the primary and extremely rare lung cancer in children. The incidence of this cancer is estimated to be 1 in 2 million, or 0.2% of all childhood malignancies. Adenocarcinoma is the most common pulmonary cancer in women and nonsmokers, and the mean age of patients is 45 years. The prevalence of this disease in boys and girls is equal but

Correspondence to:
Narges Lashkarbolouk, nargeslashkarbolouk@gmail.com

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has contrasted in adults. The progression of atypical adenomatous hyperplasia to bronchoalveolar carcinoma turns into invasive adenocarcinoma [1, 2].

According to studies, most patients have metastatic adenocarcinoma at the time of diagnosis. This poor prognosis outcome is due to delays between presentation and the ultimate diagnosis of childhood lung cancer. This delay is associated with nonspecific clinical presentation, the rarity of disease incidence in children, and the median survival of this cancer is 6–9 months. A study by Balzer et al. [3] declared that stage IV children with adenocarcinoma are present in up to 50% of the cases at cancer diagnosis [3, 4].

In adults, there is an association between risk factors (active or passive smoking, underlying infections, pulmonary cysts, air pollution, genetic mutation) and adenocarcinoma. However, in children, usually, these risk factors are not founded. The molecular mutations in nonsmokers children are more predominant and can be detected, which include EGFR, KRAS, BRAF, ALK receptor tyrosine kinase (ALK), or ROS-1 [3–6].

Clinical presentations include persistent cough, recurrent pulmonary infections, chest pain, wheezing, hemoptysis, metastatic disease symptoms, or asymptomatic in some cases. Recurrent pneumonia and failure of medical treatment should be suspected of pulmonary malignancy [7, 8].

Chest radiographs can lead to a diagnosis of this cancer. Chest X-ray findings are similar to pneumonia consolidation of the lung, atelectasis, bronchial obstruction, and well-circumscribed solitary round or ovoid mass [9–12].

For diagnosing and staging, biopsy tissue and immunohistochemistry should be done. The oncogene driver mutations are also tested for histologic subtype and deciding the systemic therapy. The treatment of this cancer is based on its stages; usually consist of surgery, chemotherapy, radiotherapy, or a combination of these methods. However, there are no pediatric-specific protocols for adenocarcinoma chemotherapy because of its rarity, and it is unlikely that evidence-based guidelines will ever be generated in the pediatric population. The surgery for children can be lobectomy or pneumonectomy with the removal of involved lymphatics. Different etiologist should be considered in patients based on their clinical history (family history of cancer), clinical features (very young age, no evidence of genetic syndrome), and response to chemotherapy. Patients usually receive several cycles of different agents targeting the immune system to control tumor growth and metastasis. Genomic sequencing technologies applied to tissue specimens can detect targetable driver mutations, and using these analytical approaches to non-tumoral samples could identify germline mutations [3–7, 9, 12].

In this case report, we present an 8-year-old adenocarcinoma patient who presented with persistent respiratory symptoms and hemoptysis. Her respiratory symptoms did not resolve with outpatient treatments; therefore, she was referred to our center. There was a mass in her radiographic evaluation that was biopsied, which led to the diagnosis of adenocarcinoma for her. Based on her being on stage 1 of adenocarcinoma, the proper treatment with lobectomy was performed for her.

Case Presentation

An 8-year-old female was admitted to our hospital with a chief complaint of hemoptysis. She had respiratory symptoms such as a non-purulent cough and dyspnea since 3 months ago that have been treated with outpatient medication. The symptoms improved, but they never resolved completely. Another exacerbation of her respiratory manifestation started about 2 weeks ago then hemoptysis occurred 3 days before admission. The volume of hemoptysis was about 110cc per day and was in the form of blood clots. She also had a history of weight

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loss (5 kg) over 2 weeks. There was no history of fever, nocturnal sweating, nausea, or vomiting. She had close contact with a person suffering from respiratory tuberculosis in her medical history. In the maternal history, there were no complications during pregnancy and delivery, and no congenital abnormality was reported in her siblings. There was no family history of genetic predisposition or carcinogenic genetic disease. Polluted air environments were not reported in her living area.

During the physical examination at the admission, her pulse rate was 110/min, and her O_2 saturation was 96% without oxygen supplement. The decreased lung sound and wheezing in the upper left lung were heard in auscultation. In our initial evaluation, in her chest X-ray, perihilar infiltration and a soft tissue shadow in the hilar of the left lung were observed (Fig. 1).

Based on her chest X-ray findings, a chest computed tomography (CT) scan with intravenous contrast was ordered. A 32 × 25 mm mediastinal mass was seen in the left middle upper mediastinal area with homogeneous intensity and a compressive effect on the left bronchus. A consolidation containing a cavity and air trapping in the left lung parenchyma due to the compressive effect of the mediastinal mass was also reported. There was no pleural effusion in radiographic findings (Fig. 2a–c).

We did fiberoptic bronchoscopy to further evaluate the mass lesion in the CT scan. A mass lesion with complete left bronchus obstruction was seen, and bronchoalveolar lavage specimen was obtained, which was negative for bacteria, fungus, mycobacteria, and malignancy.

In her laboratory result, she had anemia, leukocytosis, and an erythrocyte sedimentation rate of 115 mm/h. Blood culture and urine culture were negative. Due to COVID-19 global pandemic, polymerase chain reaction (PCR) for COVID-19 was taken negatively. Moreover, because of the high prevalence of tuberculosis infection in the area and a history of close contact with tuberculosis patients, purified protein derivative (PPD), three sputum samples analysis, and tuberculosis PCR tests were performed, resulting in negative, as well.

Based on her clinical findings and laboratory and radiological evaluation results, we also considered vasculitis for the patient, but her antinuclear antibodies, peripheral antineutrophil cytoplasmic antibodies, antineutrophil cytoplasmic antibodies, and double-stranded deoxyribonucleic acid levels were negative.

Then we scheduled pediatric surgery consultation, and the surgeon recommended a mass biopsy. A mass sample was taken, and adenocarcinoma of the lung was reported after that lobectomy was done for the patient. According to the pathology result of lobectomy, a 3 × 3 × 2 cm well-differentiated adenocarcinoma with invasion to the main bronchus was seen. There was no lymphadenopathy invasion. No metastases were founded; therefore, a lobectomy was performed for our case. We referred her to the pediatric oncologist for treatment and advised her family to do a genetic evaluation test. In our follow-up, she was investigated for metastasis with MRI and PET scan, which were fortunately negative. Because of her stage 1 (T1N0M0) condition, treatment with lobectomy without a chemotherapy regime was the best choice for her. She is still on routine medical follow-up (Fig. 3).

Discussion

In our case report, an 8-year-old female was admitted with a chief complaint of a non-purulent cough, dyspnea, and hemoptysis in the past 3 months. She had a history of significant weight loss (5 kg) over 2 weeks. Decreased lung sound was heard in the upper left lung, along with wheezing in the left lung during auscultation. Her radiography showed a mediastinal mass in the left middle upper mediastinal area with homogeneous intensity and a compressive effect on the left bronchus. Then pediatric surgeon did a mass biopsy, and stage 1 of the lung adenocarcinoma was reported. Therefore, just a lobectomy is performed without any chemotherapy.

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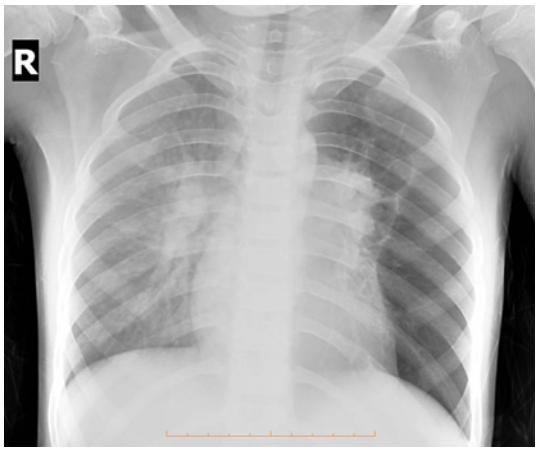

Fig. 1. Initial CXR showed a perihilar infiltration and a soft tissue shadow in the hilar of the left lung.

The mean age of presentation of adenocarcinoma is not apparent due to its rarity. However, a study by Balzer et al. [3], reported that the average onset of symptoms in 62 cases was 14 years. In our study, the patient's symptoms were presented at the age of 8 years, which occurred earlier than in other studies, indicating our case's rarity and this rarity can affect children of any age [3, 11].

The most common features of the disease at the time of diagnosis were usually respiratory symptoms such as cough, chest pain, shortness of breath, and hemoptysis. In some cases, the diagnosis was made after the failure of an antibiotic trial for a suspected respiratory infection. Nonspecific clinical presentation leads to a delayed diagnosis and a higher prevalence of the metastatic disease. In line with studies, the common symptoms in our patient were a non-purulent cough, dyspnea, and hemoptysis. Furthermore, our patient also received a few outpatient antibiotic medication before she was admitted to our hospital. Due to the patient's prevalent respiratory symptoms, the patient was diagnosed early and, fortunately, had no metastases at the time of diagnosis. In most cases, the median delay time for diagnosis is about 6–9 months, but in our case, it was about 3 months since the symptoms started [2, 4].

There are no specific radiographic findings for adenocarcinoma to help the diagnosis. The existence of a radiographic abnormality despite adequate treatment of inflammatory processes should be further evaluated. Radiographic findings of adenocarcinoma can be similar to infectious diseases or congenital pulmonary lesions. Our case has a left lobe mass in her radiographically, which was diagnosed as adenocarcinoma [1, 5, 7].

Once the diagnosis and staging have been established, the next step is the optimal treatment for children, and there are no evidence-based guidelines and protocols inferred from treatment. As mentioned, treatment can be surgery, chemotherapy, or both. Most studies report that young children with adenocarcinoma are more likely to undergo surgery, even if it is metastatic. This is probably due to the better performance status of younger children, clinical biases, and clinical interpretation of guidelines for resecting high-stage primary cancers. National Comprehensive Cancer Network mentioned that surgery is an independent favorable prognostic factor for survival and should be considered an option when possible. The recommendations for surgery are based on disease stage, patient performance status, and limited metastatic disease. Similar to our study, our patient was diagnosed with stage 1 adenocarcinoma, which was only treated with lobectomy [2–4, 6].

According to pediatric guidelines, systemic chemotherapy should be done for disseminated metastatic disease. Due to the rarity of adenocarcinoma, there is no specific pediatric chemotherapy regimen, and different regimens have been used for patients. In a study conducted by Scarpino et al. [11] , patients received various chemotherapy treatments, and no patient treated with systemic therapy survived longer than 19 months [10].

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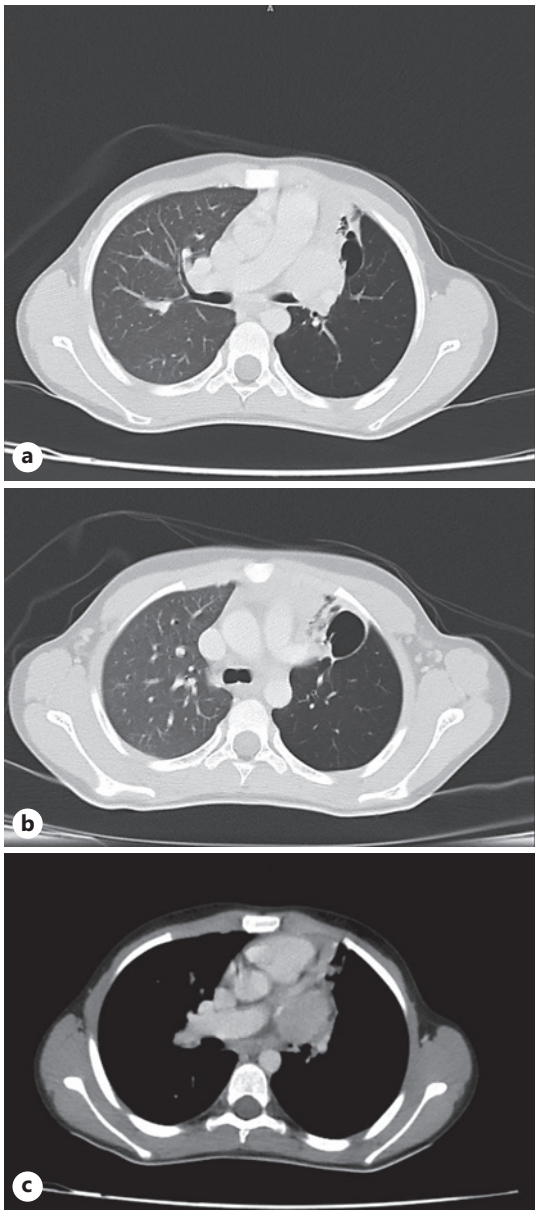

Fig. 2. a Chest computed tomography (CT) showed a 32 × 25 mm mediastinal mass in the left middle upper mediastinal area with homogeneous intensity and a compressive effect on the left bronchus. A consolidation containing a cavity and air trapping in the left lung parenchyma due to the compressive effect of the mediastinal mass was also observed. **b** Chest computed tomography (CT) showed a consolidation containing a cavity, and air trapping in the left lung parenchyma due to the compressive effect of the mediastinal mass was also observed. **c** Mediastinal view of chest computed tomography (CT) showed a 32 × 25 mm mediastinal mass in the left middle upper mediastinal area with homogeneous intensity and a compressive effect on the left bronchus.

Primary adenocarcinoma in children usually has an aggressive growth pattern and a high mortality rate (90%), with a median survival rate of 7 months after diagnosis. The study by Rojas et al. [12] declared a 5-year survival rate of 26% in their study series. Case studies have reported a mortality rate of over 51%, and mortality rates are already high despite early diagnosing and new treatment regimens options. Our patient responded to appropriate treatment during the 3-month follow-up, and no signs of cancer recurrence or metastases were observed [10–12].

One of the treatment challenges is that children differ from adults in many aspects of drug therapy, including drug administration, medicine-related toxicity, and taste preferences. New regulatory requirements and collaborative research between pediatric oncologists and adult specialists must be strengthened and supported to develop targeted therapies for children [3, 8, 10, 11].

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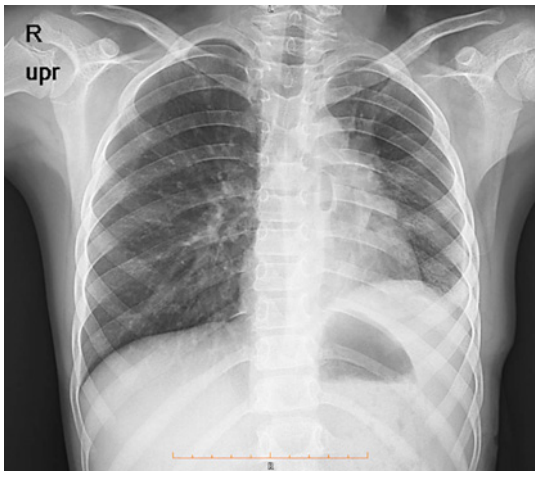

Fig. 3. Follow-up chest X-ray after lobectomy treatment.

The following are the strengths of our study. We presented an 8-year-old patient with adenocarcinoma, which is younger than the median age for diagnosis. Also, the time interval of diagnosis in our study was 3 months, less than the average of 6–9 months. We faced limitations during our evaluation; due to the restriction in our hospital, we had to refer the patient to a facilitated center for further evaluation and treatment.

Conclusion

Because of the rarity of adenocarcinoma, treating this disease could be challenging for physicians. Therefore, we suggested that physicians order chest X-rays in patients with persistent or recurring respiratory manifestations, especially those who have crucial symptoms such as hemoptysis and weight loss in their medical history. Early detection is an important factor of good prognosis and satisfactory treatment outcome in patient. Diagnosing patient in lower stage also can improve patients' quality of life and reduces the burden of treatment costs.

Patient Perspective

The patient's legal guardian was open to the idea of presenting and sharing his child's rare condition with all doctors around the world. Due to timely diagnosis, the patient was treated at a low stage with lobectomy. She did not need extensive chemotherapy or surgery treatments. All of the mentioned factors led to patient and family satisfaction with the process of diagnosis and treatment of the patient.

CARE Checklist

The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531986).

Statement of Ethics

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. The purpose of this case report was completely

explained to the patient's legal guardian and they were assured that her information would be kept confidential by the researchers. This case report was performed in line with principles of the Declaration of Helsinki. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

L.Sh. advised the case report study. M.M. and N.L. gathered patient's medical and health records. N.B. did the biopsy and lobectomy. N.L. wrote the first draft of the manuscript, and all authors commented on previous versions. All authors read and approved the final manuscript.

Data Availability Statement

The datasets used during the current study are available from the corresponding author on reasonable request. All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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