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Case report

# Unilateral Pleural Effusion in a Pediatric Patient: A Case of T-Cell Acute Lymphoblastic Leukemia Complicated with COVID-19

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## ABSTRACT

**Background:** Exudative pleural effusion in children is mainly caused by bacterial infections. Here, we present a 2.5-years-old boy with acute fever, unilateral pleural effusion, and poor response to the insertion of chest tube.

**Case description:** The patient was admitted to the Taleghani Hospital of Gorgan (northeast of Iran) with complaint of fever starting from a week ago. The patient was treated with intravenous (IV) antibiotics and a chest tube was inserted. Considering the poor response to this treatment and leukocytosis, further assessments were made. Microbial examination of pleural fluid and SARS-CoV-2 test of nasopharyngeal swab were negative. Pleural biopsy and bone marrow aspiration analysis by flow cytometry revealed T-cell-acute lymphoid/lymphoblastic leukemia (ALL). The patient was referred to the oncology ward and chemotherapy was performed. After four weeks, he started to develop symptoms of respiratory distress, fever, and melena. The next SARS-CoV-2 test on throat swab was suspicious. Chest CT scan showed centrilobular ground glass opacity and peribronchial wall thickening in both lungs in favor of COVID-19. Treatment started with hydroxychloroquine, cotrimaxazole, meropenem, vancomycin, and pantoprazole. The patient was transferred to the PICU because of respiratory distress and decreased $O_2$ saturation. Four days later, repeated test on nasopharyngeal swab was positive for COVID-19. Unfortunately, the patient did not respond to treatment and passed away a few days later.

**Conclusion:** T-cell ALL is an aggressive type of leukemia with poor response to treatment, and plural effusion is a rare presentation of malignancy in children. Our patient's condition was unfortunately complicated with COVID-19 involvement and he passed away before we see the effect of treatment on ALL.

**Keywords:** Pleural effusion; Pediatric; Bone marrow aspiration; Acute lymphoid/lymphoblastic leukemia; COVID-19

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## Introduction

Pleural effusion is defined as accumulation of fluid in the pleural space. The condition can have various causes and may be a life-threatening (1). The type of the effusion is classified into transudate and exudate based on the amount of protein, lactate dehydrogenase (LDH), and some other factors in the fluid. Increased vascular permeability of the lungs can cause an exudative effusion. A complete evaluation for the possible cause in exudative effusion is essential. The main causes of an exudative fluid are infections (parapneumonic, tuberculosis pleurisy, fungal, and viral infections), malignancies, autoimmune inflammatory diseases, pulmonary embolism, pancreatitis, and some drugs (2). However, the main cause of exudative pleural effusion and empyema in children is bacterial infection (3, 4), mostly caused by Streptococcus pneumonia (5, 6). Malignancy is a rare cause of pleural effusion in children. Lymphoma is the most common malignancy associated with pleural effusion. About 5% of patients with Hodgkin's or non-Hodgkin's lymphoma will develop a pleural effusion. In addition, T-cell lymphoblastic leukemia can also cause a malignant pleural effusion. Common symptoms of pleural effusion are dyspnea, cough, and chest pain that are more severe in effusions with greater volumes. Respiratory distress is an important symptom that needs urgent management (2). Here, we present a 2.5-years-old boy with acute fever, one-sided pleural effusion, and poor response to the insertion of chest tube.

## CASE PRESENTATION

A 2.5-year-old boy was admitted to the pediatric infectious ward in Taleghani Hospital of Gorgan, northeast of Iran, with a history of fever starting from a week ago. He was the third child, with a normal development, and no history of previous admission. There was no history of suspected contact and recent travel. He had no history for allergic reactions or hyperreactive airway disease. In physical examination, he had multiple bilateral, enlarged lymph nodes less than 0.5 cm in diameter in his neck. Right shift of heart and mediastinum, alveolar opacity in the left side, and fading of diaphragmatic border was reported in an upright chest X-ray and a possibility of left side pleural effusion was raised. SARS-CoV-2 test (RT-PCR) of nasopharyngeal swab was negative. In pleural sonography, massive accumulation of fluid was reported in the left pleural space with floating particles, and heart and mediastinum had been shifted to the right. Intravenous (IV) ceftriaxone and vancomycin as well as IV fluid treatment was started. The temperature was charted and fever was controlled with acetaminophen. A left sided chest tube was inserted by a pediatric surgeon on the third day of admission, and the aspirated fluid sample was sent to laboratory for tuberculosis and other possible bacterial infections, which were reported as negative. Characteristics of an exudate effusion were confirmed. Analysis of the pleural fluid is shown in (table 1).

**Table 1. Analysis of the pleural fluid the patient**

| Variable | Amount | | Normal range |
|---|---|---|---|
| Glucose (mg/dl) | 20 | | The same as that of plasma |
| Protein (g/dl) | 3.8 | | 1.5 |
| WBC (cells/mm$^3$) | 2300 | PMN:35% | <1700 consisting of 75% macrophage ,23% lymph and 2% mesothelial |
| | | Lymphocyte:65% | |
| RBC (cells/mm) | 180000 | | 0 |
| LDH (U/l) | 1910 | | <200 |

WBC: White blood cell, RBC: Red blood cell, LDH: Lactate dehydrogenase, PMN: polymorphonuclear leukocytes

(Table 2) shows the blood biochemical parameters that were normal during the hospitalization.

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**Table 2. The analysis of blood biochemical parameters**

| Parameter | Day 1 | Day 3 | Day 5 | Day 8 | Day 12 | Normal range |
|---|---|---|---|---|---|---|
| WBC (mm) | 20000 | 33600 | 22300 | 36700 | 38900 | 4000-10000 |
| Neutrophil | 15600 | 20832 | 11819 | 14680 | 15560 | 60% |
| Lymphocyte | 4400 | 11088 | 8920 | 22020 | 21395 | 40% |
| Hemoglobin (g/dl) | 10.3 | 10 | 9.9 | 9.9 | 10 | 12-14 |
| Hematocrit (%) | 32 | 30.5 | 29.7 | 29.7 | 31.4 | 26-32 |
| Platelet (per µl) | 596000 | 356000 | 384000 | 245000 | 222000 | 150000-450000 |
| ESR (mm/hour) | 45 | 52 | 42 | 20 | 18 | <20 |
| CRP | | Negative | | Negative | | Negative |
| LDH (U/L) | | | 2040 | 1582 | | 500-700 |

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, LDH: Lactate dehydrogenase

After the insertion of chest tube, fever and the amount of pleural fluid reduced and resolved completely after a few days. Three days later, fever relapsed and the amount of the pleural fluid increased. The second RT-PCR test was negative for SARS-CoV-2. Second chest tube was inserted and pleural tissue samples were sent for histopathologic analysis. Analysis of the pleural fluid was in favor of empyema and suspected for superimposed infections. Fibrinolytic was prescribed at three consecutive doses through chest tube and fever ended.

A spiral CT-scan without contrast was done after the insertion of the chest tube, and a bilateral mosaic attenuation, left sided pleural effusion about 100 cc, and subcutaneous emphysema in the left hemithorax and cervical region were detected (Figure 1).

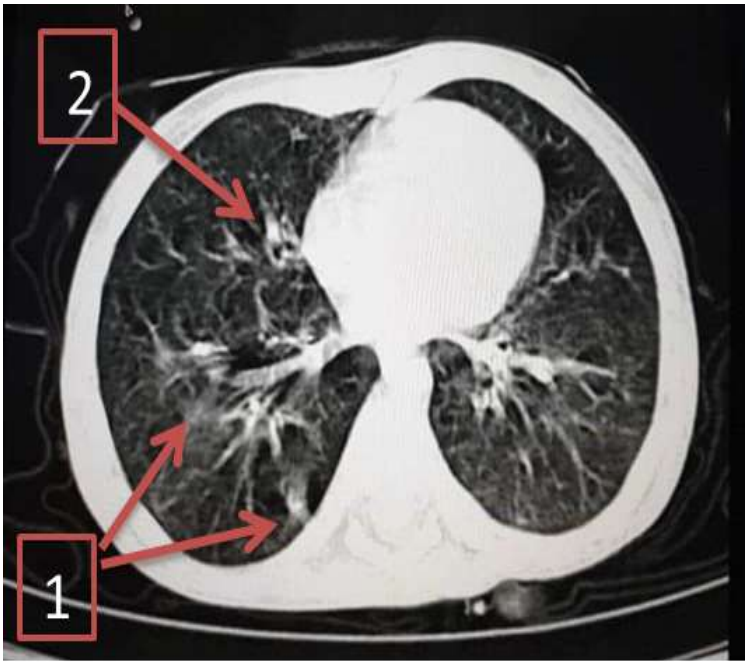


**Figure 1. The spiral CT of the patient showing centrilobular ground glass opacity (1) and peribronchial wall thickening (2) in both lungs**

Considering that the WBC and LDH level did not reduce after the insertion of the second chest tube, work-up was performed for immunodeficiency, collagen-vascular diseases, and malignancies. The level of IgM, IgG, IgE, and IgA were in normal range, and the nitroblue tetrazolium (NBT) test was reported to be 93%. The pleural tissue analysis revealed infiltration of lymphocytic series cells, both in tissue and fluid, which suggested lymphoproliferative disorders. Consultation with a pediatric oncologist was requested, and a bone marrow aspiration was performed. The results of bone marrow flow cytometry were compatible with T-cell acute

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lymphoid/lymphoblastic leukemia (ALL) with 75% blast cells. After confirming the diagnosis of ALL, the treatment was planned accordingly and chemotherapy was performed for three weeks.

At the 4th week of hospitalization, the patient started to show symptoms of respiratory distress, fever, and melena. Result of the SARS-CoV-2 test of nasopharyngeal swab was suspicious. Chest CT showed centrilobular ground glass opacity and peribronchial wall thickening in both lungs in favor of COVID-19. Treatment was initiated with hydroxychloroquine, cotrimaxazole, meropenem, vancomycin, and pantoprazole. Four days later, repeated PCR test on throat swab for COVID-19 was positive. Before receiving the RT-PCR result, patient was transferred to the PICU because of respiratory distress and decreased $O_2$ saturation. Unfortunately, the patient did not respond to treatment and passed away a few days later.

## DISCUSSION

The presented case was first admitted with complaint of fever. The patient had one-sided pleural effusion in the imaging modalities. Poor response to fluid drainage raised suspicion on non-infectious reasons for pleural effusion. Based on the pleural biopsy and bone marrow aspiration results, our patient was diagnosed with T-cell ALL. Non-Hodgkin's lymphoma is the most common cause of malignant pleural effusion in children (7). Pleural effusion is an uncommon presentation of ALL (9). Leukemia is the most important malignancy in children that accounts for about 25% of new malignancies in the USA. Pre-B cell ALL is more common, while T-cell ALL is more aggressive, usually accompanied with central nervous system (CNS) involvement, and with a poorer prognosis (10-12). Common manifestations include hyperleukocytosis and involvement of lymph nodes, CNS, spleen, and mediastinal masses (11).

Malignant pleural effusion in ALL and acute myeloid leukemia (AML) is rare (13). Agarwal et al. reported a 22-years old man with AML (M2) and leukemic pleural infiltration. The mentioned case had low-grade fever and dyspnea for three months and normal hemoglobin level with no other signs and symptoms (14).

Our patient had no history of disease and significant weight loss or bleeding before admission. Pleural effusion was the first manifestation of ALL, in contrast with some cases that had reported malignant pleural effusion in patients with a history of AML and ALL (8, 14). However, in one study, a 20-years old man was presented with mediastinal mass and pleural effusion secondary to lymphoma (15).

Malignant pleural effusions have an estimated rate of 13.7% (16). It seems that an accurate evaluation of the pleural effusions in children is crucial while considering the possibility of malignancies. Although T-cell ALL is still considered as a poor prognosis condition with a high mortality rate, in recent years, the treatment course and outcomes of these patients have been improved (17). Thus, timely initiation of the treatment can improve outcome. Moreover, complete vaccination of the patients against influenza virus, coronavirus disease 2019 (COVID-19), chicken pox, and bacteria such as pneumococcus and Haemophilus infulanza, etc. along with chemotherapy is very effective in improving the treatment outcome. Our patient's condition was unfortunately complicated with COVID-19 involvement and he passed away before we see the effect of treatment on ALL.

## CONCLUSION

T-cell ALL is an aggressive type of leukemia with poor response to treatment, and plural effusion is a rare presentation of malignancy in children. Our patient's condition was unfortunately complicated with COVID-19 involvement and passed away before we see the effect of treatment on ALL.

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### Ethics approvals and consent to participate

Consent was obtained from the patient's parents for publication after ensuring confidentiality of personal information. This case report has been approved by the ethics committee of Golestan University of Medical Sciences (IR.GOUMS.REC.1399.084).

### Conflict of interest

The authors declare that there is no conflict of interest regarding publication of this article

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