Case Report

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Tuberculosis Pleurisy in a Case of Burkitt Lymphoma Secondary to Rituksimab Treatment

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Abstract

Non-Hodgkin's lymphoma (NHL) accounts for 60% of childhood lymphomas and is the fourth most common childhood malignancy. Burkitt's lymphoma (BL) accounts for 40% of NHLs. Burkitt's lymphoma is mostly of abdominal origin and has the highest cell count doubling rate. Tuberculosis (TB) is one of the chronic diseases caused by the *Mycobacterium tuberculosis* bacillus, which has high morbidity and mortality and occurs most frequently in the lung. In this case report, we present a patient with a previous diagnosis of BL who developed pleural effusion while under rituximab-ifosfamide carboplatin etoposide treatment, and TB polymerase chain reaction (PCR) was revealed to be positive in the TB PCR screening test of the pleural fluid. To our knowledge, there is no previous study of the coexistence of BL and TB pleurisy in the literature. When pleural effusion develops in patients with BL under chemotherapy treatment, it should be kept in mind that TB may be present, and anti-TB treatment should be started as soon as the diagnosis is made. There is limited information in the literature about the frequency of tuberculous pleurisy in patients with BL.

Keywords: Burkitt's lymphoma, tuberculosis, pleural effusion, tuberculous pleurisy, rituksimab

Introduction

Non-Hodgkin's lymphoma (NHL) are mostly fast-growing, high-stage tumors. It is more common in boys (1). NHL is divided into approximately 60 subtypes based on morphological, immunophenotypic, genetic, and clinical features. Some deoxyribonucleic asid (DNA) and ribonucleic acid (RNA) viruses play a role in disease development. Epstein-Barr virus (EBV) is the most common virus among them. It has been observed that 90% of Burkitt's lymphoma (BL) cases are associated with EBV infection (2).

Burkitt's lymphoma accounts for 40% of NHLs. Burkitt's lymphoma is mostly of abdominal origin and has the highest cell count doubling rate (3). Burkitt's lymphoma, which is the fastest-growing human tumor with a doubling time of approximately 12-24 hours, is an aggressive B-cell neoplasia. It usually occurs as an extranodal disease and is epidemiologically divided into three types: endemic, non-endemic, and associated with immune deficiency. Endemic type; jaw (most common), liver, adrenal glands, stomach, intestine, pancreas, salivary glands, thyroid, testis, and heart; non-endemic type: abdomen (most common), and 15-20% of the chin; and the type associated with immunodeficiency often involves the lymph nodes (4).

Tuberculosis (TB) is one of the oldest known chronic diseases in human history. It is caused by the *Mycobacterium tuberculosis* bacillus, develops slowly and insidiously, has high morbidity and mortality, and occurs most frequently in the lung (5). While the TB point prevalence rate in Turkey was 25 per hundred thousand in 2009, it was 63 per hundred thousand in the World Health Organization European Region and 201 per hundred thousand worldwide (6). The rate of new cases in 17,402 patients was 91.6% (n=15,943), and 62.7% (n=10,906) of the patients diagnosed with TB showed lung involvement (7).

Case Report

In this case report, we present a patient who was previously diagnosed with BL, who developed pleural effusion while under rituximab-ifosfamide carboplatin

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etoposide (R-ICE) treatment, and who had a positive TB PCR for the test from the pleural fluid. To our knowledge, there is no previous study of the coexistence of BL and TB pleurisy in the literature.

A 9-year-old male patient applied to an external center because she had abdominal pain and occasional vomiting for 2 months. A heterogeneous solid mass lesion with a size of 137x130x80 mm, starting from the upper paraumbilical area and covering the pre-subumbilical area, was observed in the entire abdominal ultrasound radiography of the patient. As a result, the patient was admitted to the emergency department of University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital, and to the pediatric surgery service after the first evaluation. In the follow-up of the patient, whose CA-125 was 46.5 in the first blood examination, a tru-cut incisional biopsy performed from the solid mass lesion was CD20 positive, CD3 negative, PanCK negative, NSE negative, synaptophysin negative, chromogranin negative, S100 negative, and Ki-67 proliferation index negative. In the applied immunohistochemical study, CD10-positive cells were detected in the neoplastic cells. Our patient was diagnosed with BL stage 3 according to the anamnesis, examination, and biopsy results. The patient was started on the NHL chemotherapy protocol with the 1st A4 course, followed by the 1st B4 course, the 2nd A4 course, the 2nd B4 course, and the 1st Cc course. However, in the interim evaluation made before the 2nd CC, it was decided to start R-ICE treatment due to the rapid growth of the patient's mass and the positive CD20 in positron emission tomography. It was planned to take the R-ICE2 course after the R-ICE1 cycle.

However, due to dyspnea and a decrease in right lung breath sounds on auscultation, X-ray screening of the lung was performed, and widespread opacity consistent with pleural effusion was observed in the right lung (Figure 1). A contrast-enhanced thorax computed tomography report taken on the same date was interpreted as a diffuse effusion with an anterior-posterior diameter of 7 cm on the right (Figure 2). Diagnostic and excretory thoracentesis were performed by the pediatric surgeon. 350-400 cc of serohemorrhagic fluid were drained. TB-DNA PCR and pleural fluid culture were performed on the drained pleural fluid. On the thorax ultrasound X-ray taken on December 24, 2020, a pleural effusion with a thickness of 1.5 cm in the thickest part of the right hemithorax was observed. In the lung X-ray screening, the opacity in the right lung was resolved, and the sinuses were opened (Figure 3).

In the follow-ups, 8 mm thick pleural fluid was observed in the right hemithorax on thorax ultrasound radiography. The TB-DNA PCR screening test of the pleural fluid was positive. The culture of pleural fluid was negative for microbiological tests. The patient's medical history revealed no close contact with TB. It was thought that there might be TB activation after rituximab treatment. The patient consulted the pediatric infection unit, and anti-TB treatment was initiated according to recommendations with isoniazid, rifampicin, ethambutol, and pyrazinamide. Because rituximab could activate TB, instead of R-ICE, ICE treatment was preferred.

Discussion

Burkitt's lymphoma is the most aggressive form of NHL. The high proliferation rate is approximately 100% due to the doubling time in cells at 24 h and the presence of the celluler-MYC proto-oncogene, especially from cytogenetic-specific changes (8). Obstructive jaundice has been reported in some BL cases with pancreatic and hepatic lymph node involvement.

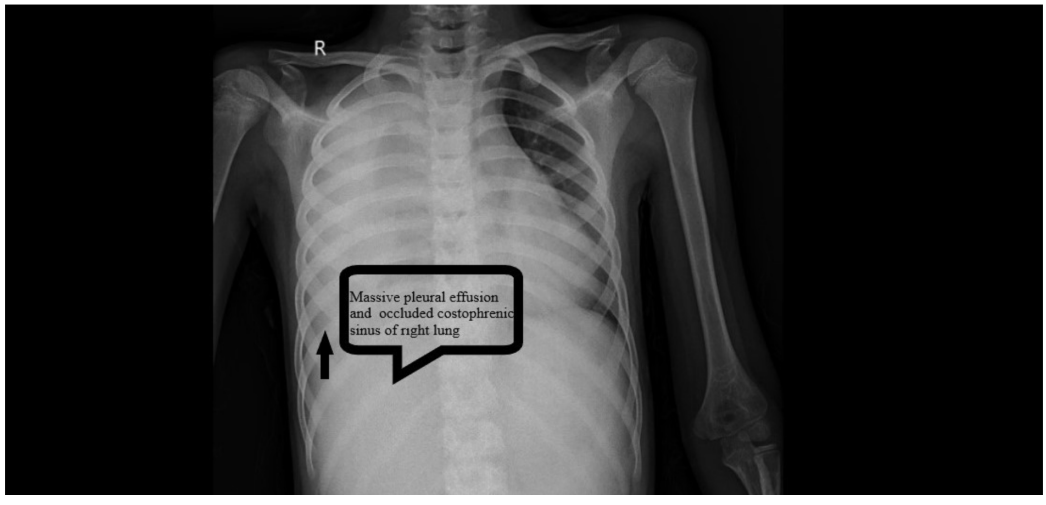

Figure 1. Widespread opacity consistent with pleural effusion was observed in the right lung. The right lung sinus is closed

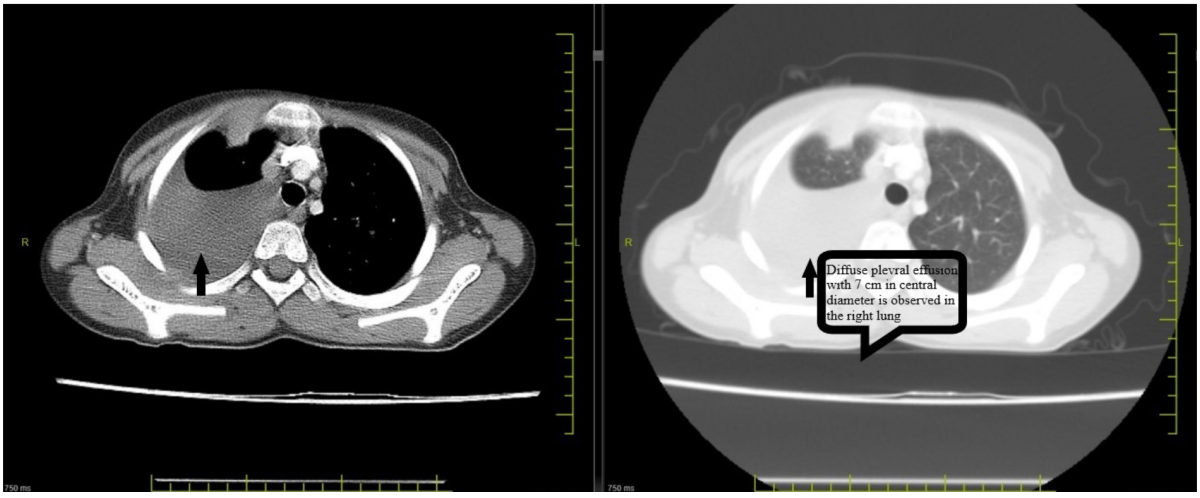

Figure 2. Computerized tomography image of the thorax with contrast. A diffuse pleural effusion with a central diameter of 7 cm is observed in the right lung

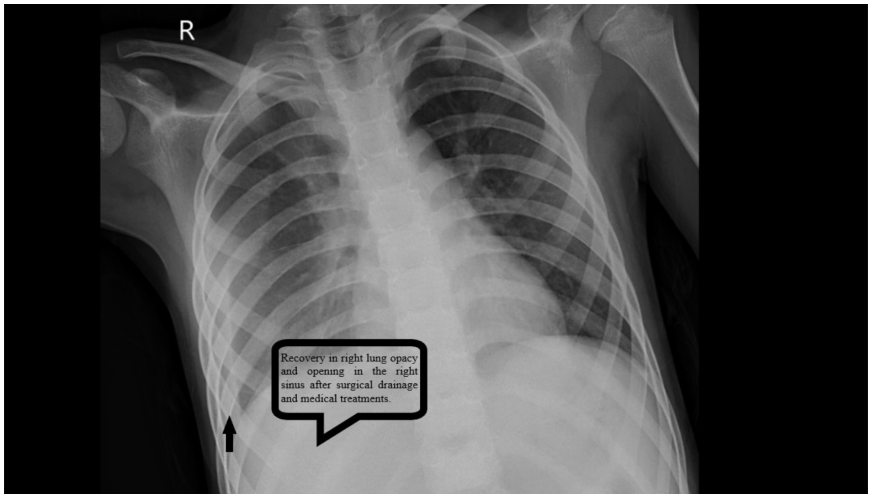

Figure 3. Recovery in right lung opacities and an opening in the right sinus are observed in X-ray screening of the lung after surgical drainage and medical treatments

Burkitt's lymphoma is classified as endemic (e.g., childhood type in Africa), sporadic (with AIDS), and subendemic. Endemic BL is a rapidly growing malignancy. The most common site of the disease is the face (primarily the mandible and often other facial bones), and 55-75% of patients have facial involvement. Involvement in the form of "bulky disease" is often seen in the abdomen.

Rituximab has shown efficacy in adults with B-cell cancers, including diffuse large B-cell lymphoma and BL, and is considered to be the standard of care in addition to chemotherapy in most patients with high-grade B-cell NHL.

Tuberculosis can affect pulmonary and extrapulmonary foci, and treatment and prognosis may vary according to the affected organ. Although TB pleurisy can generally be considered a form of extrapulmonary TB, it is common with pulmonary TB. The disease results from the opening of the subpleural caseous focus in the lung or the foci in the adjacent lymph node and bone to the pleura 6-12 weeks after the primary infection. It can be seen as a complication of primary pulmonary TB, with a rate of 2-38% (9).

Birlutiu et al. (10) reported a case of HIV-TB and BL with central nervous system involvement. This report is similar to our case; immunodeficiency conditions promote infections like TB.

In the Hu et al. (11) study, a 20-year-old female after kidney transplantation presented abdominal pain and multiple nodules throughout the body diagnosed on lung histopathology, and lung histopathology specimens tested positive for the *TB* gene. Additionally,

BL was diagnosed as metastatic after the completion of a liver and bone marrow biopsy. After diagnosis of TB, the patient received intensification of anti-tubercular therapy, and for BL, rituximab, cardioprotection, hepatoprotection, and alkalinization of urine were added. These data show us that, as in our case, TB can be provocative in BL patients, and immunomodulatory drugs can worsen it (11).

Gulleroglu et al. (12) retrospectively evaluated 78 pediatric renal transplant recipients for the occurrence of infectious disease. Eighteen transplant patients received rituximab therapy for various causes. The study revealed that rituximab treatment may be associated with a high risk of infectious disease (12). However, there is no other unique report in the literature of pediatric BL with TB pleurisy that is provoked by rituximab treatment of BL.

Conclusion

When pleural effusion develops in patients with BL under chemotherapy treatment, particularly rituksimab treatment, it should be kept in mind that TB may be present, and anti-TB treatment should be started as soon as the diagnosis is made. Drug interactions should also be considered while preparing the treatment protocol.

Ethics

Informed Consent: Consent for publication have been taken from the patients' parents.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: H.A.S., S.A., D.O.Y., O.T., A.A., Design: H.A.S., S.A., D.O.Y., O.T., A.A., Data Collection or Processing: H.A.S., S.A., D.O.Y., O.T., A.A., Analysis or Interpretation: H.A.S., S.A., D.O.Y., O.T., A.A., Literature Search: H.A.S., S.A., D.O.Y., O.T., A.A., Writing: H.A.S., S.A., D.O.Y., O.T., A.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

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