CASE REPORT

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Is There Any Relationship between Bilateral Pleural Effusion and Blast Crisis in Chronic Myeloid Leukemia?

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ABSTRACT

Pleural effusion in chronic myeloid leukemia (CML) has been rarely reported in medical practice. Additionally, the correlation of pleural effusion with blast crisis is unknown. This study reported a 66-year-old male patient who was diagnosed with bilateral pleural effusion three months before the blast transformation. Bilateral pleural effusion spontaneously resolved before the blast transformation. The cause of pleural effusion was unknown. Bilateral pleural effusion caused by unknown or known factors, except for that induced by drugs, is a poor prognostic marker for CML and is an unusual indicator of blast crisis. The presentation of the study case indicates that bilateral pleural effusion is an atypical and discernible early indicator of blast crisis onset in patients with CML.

Keywords: Pleural effusion; chronic myeloid leukemia; blastic transformation

INTRODUCTION

Pleural or peritoneal involvement is rare in leukemias. In contrast, pleural or peritoneal involvement is frequently observed in solid hematological cancers and lymphomas. Pleural effusion may occur in patients with chronic myeloid leukemia (CML).[1,2] The etiological factors for pleural effusion in patients with CML include infections, hypoproteinemia, blast involvement, extramedullary (spleen, lymph nodes, skin, meninges, and bone) hematopoiesis, pleural capillary obstruction, and drugs.[3] Here, we report a case with unusual pleural effusion that manifested three months before the blast crisis of CML. This case report aimed to demonstrate the potential prognostic value of bilateral pleural effusion preceding blast crisis and improve our understanding of this clinical manifestation in CML.

CASE REPORT

The patient was a 66-year-old male who was initially diagnosed with CML in 1999. An accidental blood test revealed a high leukocyte count when the patient was aged 49 years. Fluorescent *in situ* hybridization (FISH) analysis revealed that the patient tested positive for BCR-ABL mutation. The patient was initially treated with interferon-alpha. After 3 years, the interferon dosage was reduced to 3 million units due to elevated liver enzymes. Interferon treatment was continued until 2007 because of the complete cytogenetic response. The patient was determined to be in complete cytogenetic remission owing to negative FISH results since the beginning of interferon-alpha therapy. The treatment was changed to imatinib mesylate (400 mg per day) in 2008 owing to the upregulation of liver enzymes and blood lipids. The patient tested negative in FISH tests up to 2016 and was in complete cytogenetic remission.

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In June 2016, the patient was admitted to the hospital with the complaint of left-side pain and the following presentations: fever: 36.5 °C; heart rate: 75/min; blood pressure: 123/70 mmHg. The complete blood count revealed the following findings: hemoglobin: 14.4 g/dL; platelet count: 117,000 platelets/mm^3; leukocyte count: 6,650 leukocytes/mm^3. The peripheral blood smear examination was unremarkable. The erythrocyte sedimentation rate was 75 mm/hour. The patient exhibited physiological biochemical parameters. Antibiotic treatment initiated at the hospital did not alleviate the complaints of the patient. Analysis of tuberculosis-causing agents and other bacterial and viral infectious agents did not yield positive results. In the thorax computed tomography scan, pleural effusion was detected on both hemithoraces (9 mm on the right and 30 mm on the left).

No evidence of heart failure was noted. Pleural effusion examination [protein, lactate dehydrogenase (LDH), cell count, differential, and cytology] did not reveal leukemic involvement or other causes. The patient was discharged in August as the complaints improved and the pleural effusion disappeared although weakness persisted (Figure 1).

In October 2016, the patient was hospitalized again with complaints of high fever and fatigue. The blood count revealed pancytopenia (leukocyte count: 2,200 leukocytes/mm^3; platelet count: 18×10^3 platelets/mm^3; hemoglobin: 10 g/dL). Bone marrow biopsy revealed the infiltration of myeloid blast cells.

Morphological and immunohistochemical findings were consistent with the transformation of CML into acute myeloid leukemia (Figure 2). After 1 week, the patient died due to tumor lysis syndrome and acute renal insufficiency (creatinine: 9.1 mg/dL; LDH: 22.970 IU; potassium: 5.5 mmol/L; urea: 389 mg/dL; uric acid: 13.8; Ca^{2+}: 8 mg/dL) without leukemia treatment. Informed consent was obtained by the daughter of the patient to publish this case report.

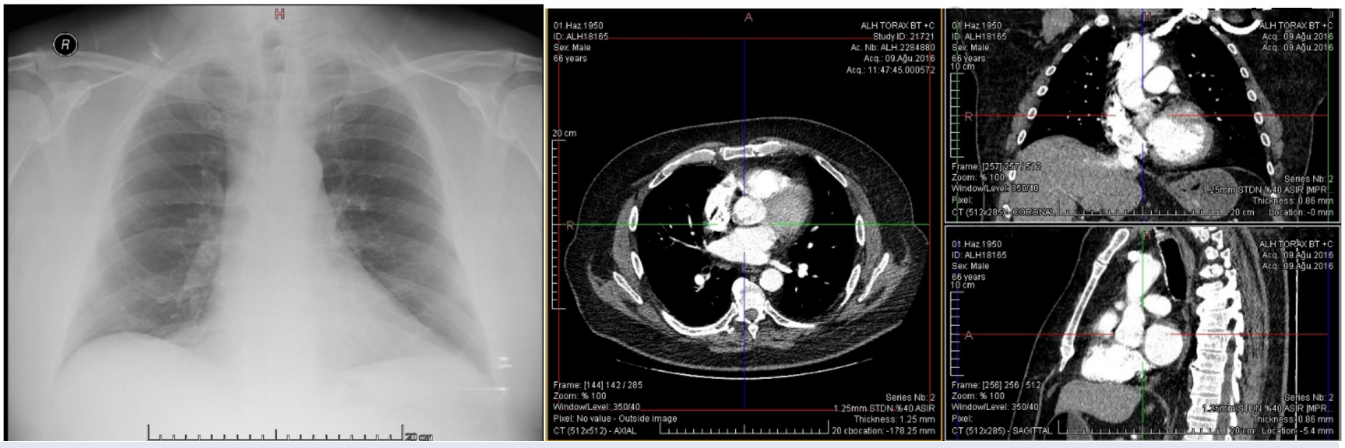

FIGURE 1: Computed tomography scan of the thorax revealed that pleural effusion spontaneously resolved after three months.

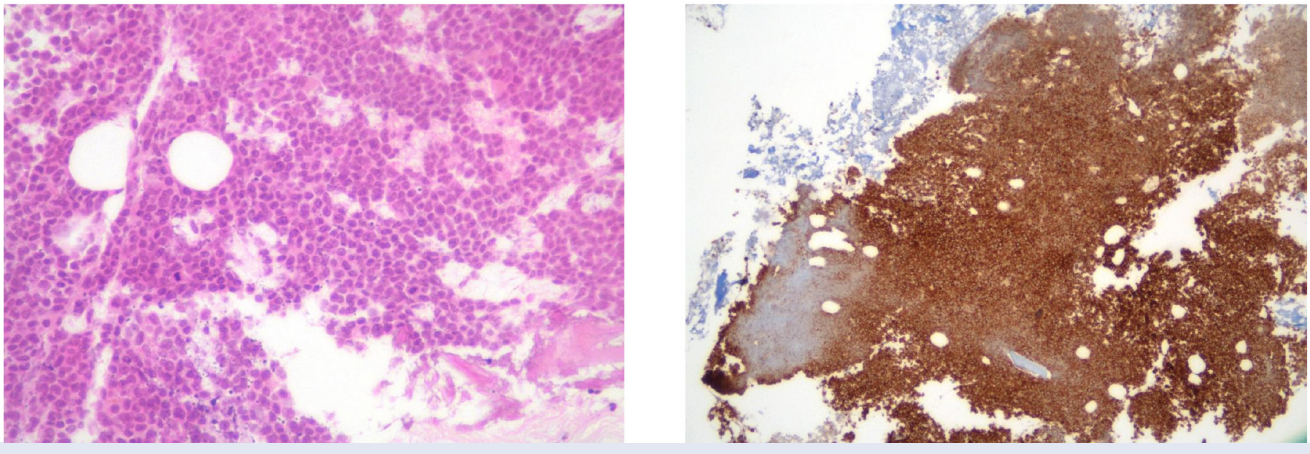

FIGURE 2: Diffuse myeloid blast cell infiltration in the bone marrow (H&E, ×100). IHC analysis of CD34$^+$ blast cells (magnification: ×100).

IHC: Immunohistochemistry, H&E: Hematoxylin and eosin

DISCUSSION

Pleural effusion is a rare finding in both the chronic phase and the acute blast phase of CML. The etiological factors of pleural effusion include leukemic infiltration, extramedullary hematopoiesis, infection, hypoproteinemia, pleural capillary obstruction, leukemic infiltration of the interstitial tissue, and drugs.

The infiltration of leukemia into the pleura typically occurs at the same time as or shortly before the blast crisis phase of bone marrow development.[4] The most common infiltration sites are the brain, testis, skin, breast, soft tissue, synovium, lymph nodes, bones, and the nervous system. However, leukemic infiltration has also been reported in the gastrointestinal tract, ovaries, kidneys, and pleura. Pleural involvement is rare. Isolated pleural blast crises without medullary change are extremely uncommon.[5] In the study patient, pleural blast infiltration was not observed in the chronic and blast phases.

Extramedullary hematopoiesis is also a potential cause of pleural effusion in CML. In contrast to pleural leukemic infiltration, extramedullary hematopoiesis involves hematopoietic cells of the erythroid, myeloid, and megakaryocytic types. The study case did not exhibit extramedullary hematopoiesis.

Infection and hypoproteinemia are proposed as non-cancerous causes of effusion.[2] The study case did not exhibit hypoproteinemia or any other infection.

Cytokine production-induced uncontrolled leukocytosis and enhanced capillary permeability may cause pleural capillary blockage or leukemic cell invasion into the interstitial tissue, leading to the development of pleural effusions in patients with CML.[4] In patients with myeloproliferative disease, the upregulated levels of interleukin (IL)-8, IL-2R, IL-12, IL-15, and IP-10 were independent predictors of poor survival.[6] Similar cytokine profiles have been reported during chimeric antigen receptor T-cell therapy and the infusion of hypercellular leukapheresis products.[7] Leukostasis and platelet dysfunction are predisposing factors for hemorrhagic effusion in CML. The study patient did not exhibit leukocytosis during pleural effusion.

Drugs can also induce pleural effusion in CML. Dasatinib and imatinib, which are tyrosine kinase inhibitors (TKIs), are used to treat CML. TKIs can induce pleural effusion.[8] The pathophysiology of dasatinib-induced pleural effusion has not been elucidated, although TKIs were reported to exert off-target effects on the immune system.[9] The study patient underwent imatinib treatment, but the pleural effusion resolved spontaneously despite the non-cessation of imatinib.

CONCLUSION

Thus, pleural effusion in the study case, which started in June, was resolved in August. One potential reason for pleural effusion is an unknown infectious agent. Unknown causes and cytokines released before blast transformation can also cause pleural effusion. Bilateral pleural effusion caused by known or unknown factors, except that caused by drugs, is a poor prognostic marker in patients with CML and an unusual indicator of blast crisis.

Ethics

Informed Consent: Informed consent was obtained by the daughter of the patient to publish this case report.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.E., F.A., Concept: E.E., F.A., Design: E.E., F.A., Data Collection or Processing: E.E., M.B.A., M.S., Analysis or Interpretation: E.E., F.A., Literature Search: E.E., F.A., Writing: E.E., M.S., F.A.

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