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*Case Report*

# Unexpected Mediastinal Mass Etiology in B-Acute Lymphoblastic Leukemia

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## ABSTRACT

Leukemic masses are a known complication in patients with hematologic malignancies. Here we present a case regarding a patient with recently diagnosed B-acute lymphoblastic leukemia (B-ALL) who presented with multiple sites of extramedullary involvement including an anterior mediastinal mass. This mass persisted despite multiple rounds of multiagent cytotoxic therapy. In this report, we summarize the literature regarding mediastinal masses in the setting of B-ALL and illustrate that such masses in patients with leukemias may have surprising etiology, separate from the primary disease.

**Keywords:** mediastinal mass, B-acute lymphoblastic leukemia, schwannoma

## INTRODUCTION

Extramedullary manifestations are uncommon in patients with B-acute lymphoblastic leukemia (B-ALL). These manifestations can include central nervous system, renal, hepatic, and dermatologic involvement.[1] T-acute lymphoblastic leukemia is more classically associated with involvement of the mediastinum, usually presenting as an anterior mediastinal mass.[2] This is most likely due to the role of the thymus in T-cell maturation/development; however, it has been noted that B-ALL has also been reported to involve the mediastinum, although this is extremely rare.[3–6]

Herein, we report a patient with recently diagnosed B-ALL who presented with both bone marrow involvement and multiple sites of extramedullary B-ALL. Notably, the patient also harbored a large mediastinal mass that exhibited focal increased uptake on initial positron emission tomography–computed tomography (PET-CT). This case highlights the importance of maintaining a broad differential in diagnosing mediastinal masses for all patients, and that etiologies may be unrelated to the patient's primary disease. Informed written and verbal consent to publish this case was provided by the patient.

## CASE SUMMARY

A 52-year-old man with history of type 2 diabetes mellitus and hypertension initially presented with 2 months of worsening abdominal pain associated with nausea and decreased appetite. The patient was found to have abdominal lymphadenopathy and subsequent excisional biopsy with flow cytometry was consistent with B-ALL. Bone marrow biopsy showed 84% blasts and Philadelphia-negative with *TET2* and *KRAS* mutations. Initial PET-CT showed multiple sites of extramedullary involvement including fluorodeoxyglucose (FDG)-avid mediastinal and abdominal lymphadenopathy with standardized uptake value (SUV) of 10.7 in the former and 11.4 in the latter. Other involved sites included both kidneys with SUV of 19.7. Following formal diagnosis with B-ALL, the patient was started on multiagent cytotoxic chemotherapy consisting of hyper-CVAD (cyclophosphamide, vincristine, doxorubicin and dexamethasone) and rituximab.

After four cycles of hyper-CVAD–based chemotherapy, repeat PET-CT showed interval resolution of all extramedullary sites with the exception of the anterior mediastinal mass that persisted, remaining stable in size (7.6 × 4.9 cm) (Fig. 1). The differential diagnosis included persistent B-ALL tumor mass, infectious etiology including

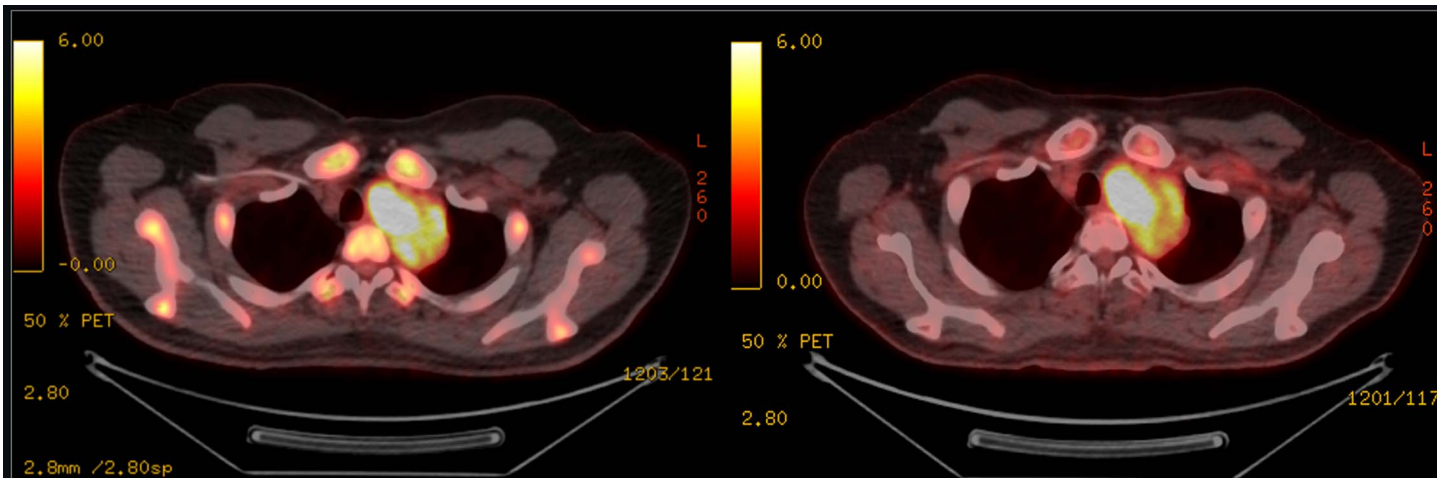


**Figure 1.** Initial PET-CT (left) showing FDG-avid mass in upper mediastinum measuring 7.6 × 5.2 cm with SUV of 10.7. Diffusely increased activity noted in the skeleton and bilateral kidneys with FDG-avid mediastinal and abdominal lymphadenopathy. After four cycles of cytotoxic chemotherapy, restaging scan (right) showed interval resolution in kidneys, skeleton, and abdominal lymph nodes, but mediastinal mass persisted with stable size and increased SUV. FDG: fluorodeoxyglucose; PET-CT, positron emission tomography–computed tomography; SUV: standardized uptake value.

tuberculosis or fungal infection, or other tumors/second malignancies. Sputum analysis was negative on acid-fast and Grocott-Gomori methenamine silver (GMS) staining. Transthoracic biopsy was performed on the mediastinal mass that showed a monotonous cellular spindle cell tumor and variable myxoid to hyalinized stroma (Fig. 2). Immunohistochemistry (IHC) was negative for PAX-5, a marker of B cells. This indicated that the mass was unlikely to be an extension of the patient's B-ALL; however, IHC was significant for diffusely reactive S-100 protein and glial fibrillary acidic protein (GFAP). Based on pathology and IHC, preliminary diagnosis of schwannoma was made and the patient was referred to the cardiothoracic surgery team for consideration of surgical resection. A successful R0 resection of the mass was performed with confirmatory final pathology ultimately demonstrating benign schwannoma without regional lymph node involvement (Fig. 3).

The patient tolerated the procedure well and restarted his B-ALL chemotherapy program after recovering from surgery. The patient is now doing well in maintenance chemotherapy phase, now 24 months post-surgery, and his B-ALL remains in first complete remission, achieving both minimal residual disease (MRD) negativity by conventional flow cytometry and additional MRD negativity by clonoSEQ adaptive next-generation sequencing testing. Chest CT imaging post-surgery reveals complete resolution of the mediastinal mass, and to date there has been no recurrence of this mass, and the patient remains on room air with preserved fit Eastern Cooperative Oncology Group performance status.

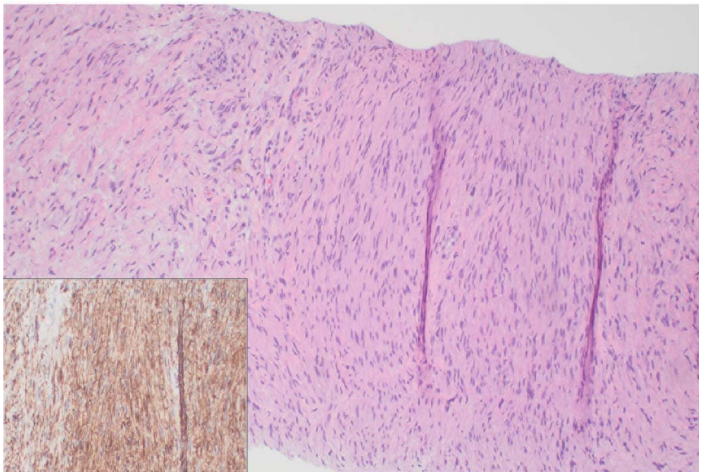

**Figure 2.** Transthoracic biopsy was performed that was negative for B-cell origin (negative PAX-5) but unexpectedly demonstrated schwannoma (S100+, glial fibrillary acidic protein+). Despite the size, the patient reported no symptoms. The hematoxylin-eosin stain shows proliferation of spindly shaped cells that are marked by S100 (inset, ×100) with variable myxoid to hyalinized stroma.

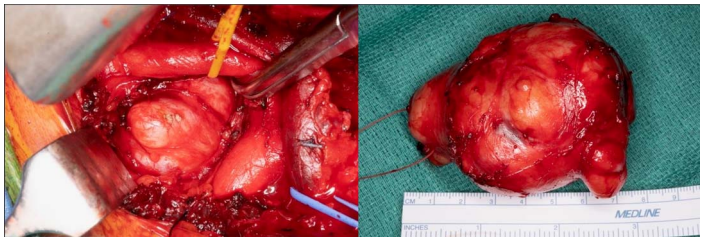

**Figure 3.** Successful R0 transthoracic resection of the mediastinal mass via trapdoor sterno-thoracotomy, demonstrating a well-circumscribed mass between the innominate and left common carotid arteries. Final size was 7.5 × 5.8 × 5.3 cm. Samples sent for pathology revealed encapsulated nodular tumor with no evidence of spread to regional lymph nodes (0/10 left thymic and left internal mammary nodes), consistent with diagnosis of benign mediastinal lymphadenopathy.

## DISCUSSION

This case illustrates the importance of maintaining a large differential diagnosis in the approach to patients with mediastinal masses and hematologic malignancies. Thymic malignancies and lymphomas are the most common causes of anterior mediastinal masses representing 35% and 25% of incidences respectively.[7] Neurogenic tumors are a less frequent cause of mediastinal masses, but when they do occur, schwannomas are found to be the most common type (~50%), although they are classically located in the posterior mediastinum.[8,9] Besides malignancies, other etiologies for anterior mediastinal masses must be evaluated for, including infectious and endocrine/thyroid etiologies.

Schwannomas are benign tumors that are typically associated with the genetic disease *NF2*-related schwannomatosis; however, they also occur sporadically, as in this patient's case. Concern for NF2-related schwannomatosis was low in this patient given negative skin findings for café-au-lait spots, nonsignificant family history, and negative genetics testing. Malignant transformation and occurrence of malignant peripheral nerve sheath tumors in the setting of mediastinal schwannomas have been reported.[10] In addition, some patients with mediastinal schwannomas can present with symptoms of chest pain and shortness of breath secondary to mass effect, including in some cases, presentation with superior vena cava syndrome.

To our knowledge, this is the first written case detailing a patient with coinciding B-ALL and a mediastinal schwannoma. In addition, there are no reported genetic disorders that manifest as, or increase the risk for, both B-ALL and schwannomas. In addition, genetic testing in this patient for NF2 was negative. The clinical picture suggests that the development of these two diseases was coincidental, an unlikely but ostensibly possible event.

## CONCLUSION

In cases of large mediastinal masses in the setting of hematologic malignancies, we recommend casting a broad differential diagnosis for etiologies and convening a multidisciplinary team to plan for obtaining adequate tissue biopsy to aid in confirmation of the diagnosis.

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