Rebound enlargement of an ectopic cervical thymus mimicking relapse of lymphoblastic lymphoma

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A previously healthy 6-year-old boy was referred to our hospital with a tumor in the right upper mediastinum on chest X-ray. Physical examination showed no abnormal respiratory sounds, hepatosplenomegaly, or palpable tumor. On MRI, a right mediastinal tumor, $37 \times 38 \times 25$ mm in size, with low intensity on T1-weighted images and high intensity on T2-weighted images was seen. A left-sided cervical mass, $27 \times 29 \times 10$ mm in size, and several small lesions were seen in the liver and kidneys; all were of intensities similar to those of the mediastinal tumor (Fig. 1a, b). On histopathological examination of the biopsied samples from the mediastinal tumor, diffuse proliferation of medium-sized atypical lymphocytes with scant cytoplasm and fine chromatin was seen (Fig. 2); immunohistochemistry was positive for CD79a, CD10, and CD34, and negative for CD3, CD7, and CD20. Bone marrow aspiration showed a normocellular marrow with 5.4% lymphoblasts, suggesting involvement of lymphoma cells. These findings led to a diagnosis of precursor B-cell lymphoblastic lymphoma (LBL) stage IV.

After the induction phase of chemotherapy (vincristine, cyclophosphamide, daunorubicin, L-asparaginase, and prednisolone), all of the tumors disappeared on MRI (Fig. 1c, d), and lymphoblasts were undetectable in the bone

marrow. The patient subsequently received chemotherapy that included an early intensification phase, a central nervous system prophylaxis phase, a late intensification phase, and a maintenance phase. Follow-up MRI revealed no tumor at the beginning of maintenance chemotherapy, but the cervical mass re-emerged at the ninth month (Fig. 1e, f), at which time the mass was $35 \times 40 \times 11$ mm in size and larger than at the onset of LBL. An ultrasound of the neck detected a lobulated, low-density structure with hyperechoic lines. The patient was asymptomatic.

The reappearance of the enlarged cervical mass was initially suspected to be a relapse of LBL. An open biopsy was performed. On histopathological examination of the mass, normal thymic tissue with no evidence of lymphoma cell involvement was seen (Fig. 3). Flow cytometry confirmed cells positive for CD3, CD4, CD7, and CD8, and negative for CD10, CD19, and CD20. The cervical mass was diagnosed as an ectopic thymus. In accordance with the protocol, chemotherapy was continued for the following 6 months. The patient achieved complete remission, and the ectopic thymus remained unchanged in size 7 months after chemotherapy.

The MRI and ultrasound can be used to diagnose ectopic thymus. MRI is the most accurate diagnostic method, showing slightly higher signal intensity than that of muscle on T1-weighted images and signal intensity close to that of fat on T2-weighted images. Ultrasound is the most convenient and non-invasive diagnostic modality. Ultrasound examination of normal thymic tissue shows multiple echogenic linear structures and foci. In the present patient, the ultrasound characteristics were potentially compatible with those of cervical ectopic thymus. However, it was difficult to differentiate a relapse of LBL from a non-neoplastic lesion as MRI revealed close similarities between the mediastinal LBL and the cervical mass. Therefore, a biopsy was performed to allow histopathological confirmation and surface marker analysis.

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Fig. 1 **a, b** MR T2-weighted images at the onset of LBL. A mediastinal tumor has grown into the spinal canal, compressing the spinal cord. There is a cervical mass with intensities similar to those of the mediastinal tumor (*arrow*). **c, d** Two months after induction

therapy. Both the mediastinal tumor and cervical mass have disappeared. **e, f** Nine months after maintenance therapy. The larger cervical mass has reappeared

Fig. 2 Photomicrograph of the resected specimen from the mediastinal tumor shows diffuse infiltration of lymphoma cells (H&E, $\times 300$)

The thymus gland is known for its variability in size and configuration in both health and disease. The thymus is the most sensitive organ in the body in terms of its atrophic reaction to stressful factors, such as starvation, fever, and chemotherapy. The thymus can also regrow to its original size after atrophy or, at times, rebound to a larger size. Reactive thymic hyperplasia following chemotherapy for malignant tumors may be misdiagnosed as residual tumor or disease relapse, leading to unnecessary chemotherapy. In the present patient, the ectopic thymus disappeared after intensive induction chemotherapy and re-emerged after maintenance chemotherapy was started. The re-enlargement of the thymus may have represented a rebound phenomenon due to decreased treatment intensity.

Fig. 3 Photomicrograph of the resected specimen from the cervical mass shows normal thymic tissue with Hassall's corpuscles (H&E, $\times 200$)

Administration of exogenous glucocorticoids leads to apoptosis of thymocytes and thymic shrinkage, which is useful for differentiation between physiological thymic enlargement and pathological lesions. However, in patients with steroid-responsive lymphoma and leukemia, prednisolone administration may result in misdiagnosis. Recently, FDG-PET has become a widespread tool for the staging of cancers, including lymphoma. However, tumors may be indistinguishable, as FDG uptake is increased in the thymus in both patients after chemotherapy and in normal children. Surgical biopsy is necessary for confirmation of the diagnosis of ectopic thymus, especially when malignancy is possible.