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Case Report

TDT (-), KIT (+), CD34 (+), CD99 (+) precursor T lymphoblastic leukemia/lymphoma

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Abstract: Although the definition of precursor T lymphoblastic lymphoma (T-LBL) is based only on histopathology, most cases cannot be diagnosed only by HE sections. Since 95% of T-LBL expresses TdT and TdT is expressed only in lymphoblasts, immunohistochemical demonstration of TdT is mandatory for the diagnosis of TLBL. However, little is known about the expression of other precursor cell molecules. A 58-year-old woman with myelodysplastic syndrome (RAEB) became overt acute myelogenous leukemia (AML). She was treated twice with allogeneic peripheral blood stem cell transplantation from her son. Nine months later, imaging modalities detected a soft tissue tumor around the left ileal bone. A biopsy was performed. Histologically, the tumor cells were malignant polymorphic lymphoid cells with hyperchromatic nuclei and inconspicuous nucleoli. Immunohistochemically, the tumor cells are positive for CD45, CD45RO, CD34, KIT (CD117), CD99 (MIC-2), p53, CD10, PDGFRA, and Ki67 (labeling=60%). They were negative for pancytokeratin AE1/3, pancytokeratin CAM5.2, TdT, CD3, CD20, CD79α, CD43, CD56, CD57, CD30, bcl-2, κ-chain, λ-chain, cytokeratin (CK) 7, CK20, synaptophysin, chromogranin, smooth muscle actin, p63, MPO, CD68, lysozyme, and ASD esterase. Although TdT was negative, other precursor cell markers (KIT, CD34, and CD99) were positive and the lymphoid cells showed T-cell lineage, the diagnosis was T-LBL. The patient died of lymphoma/leukemia 11 months after the diagnosis. The author stress that TdT, KIT, CD34 and CD99 should be included in panels of precursor T-cell neoplasms. In addition, the author think that KIT, CD34 and CD99 are helpful for the diagnosis of T-LBL in cases negative for TdT. Further, it is unique that this case was not myeloid sarcoma but precursor T-cell neoplasm, and that T-LBL develops during AML.

Keywords: Precursor T-cell neoplasm, TdT, histopathology, immunohistochemistry

Introduction

Precursor T lymphoblastic leukemia (T-ALL)/ T lymphoblastic lymphoma (T-LBL) is a neoplasm of lymphoblasts committed to the T-cell lineage, typically composed of small to medium-sized blast cells with scant cytoplasm, moderately condensed to dispersed chromatin and inconspicuous nucleoli, involving bone marrow and blood (T-ALL) and sometimes presenting with primary involvement of nodal and extranodal sites (T-LBL) [1]. However, the diagnosis of T-LBL was usually not made only by HE sections. Immunohistochemical study was mandatory to diagnose T-LBL. Since 95% of T-LBL is immunoreactive for TdT [2], and TdT expression is seen only in lymphoblastic lymphoma [2], immunohistochemical demonstration of TdT was diagnostic for lymphoblastic lymphomas of both B-cell neoplasm and T-LBL. However, little is known about the expression of other precursor molecules in T -LBL. In the present study, the author report TdT (-), KIT (+), CD34 (+), CD99 (+) T-LBL. This case is also unique in that T-LBL developed in acute myelogenous leukemia.

Case report

A 58-year-old Japanese woman with myelodysplastic syndrome (RAEB) became overt acute myelogenous leukemia (AML). She was treated twice with allogenetic peripheral blood stem cell transplantation from her son. Nine months later, imaging modalities detected a soft tissue tumor around the left ileal bone (**Figure 1**). A biopsy was performed. Histologically, the tumor cells were malignant polymorphic lymphoid cells with hyperchromatic nuclei and inconspicuous

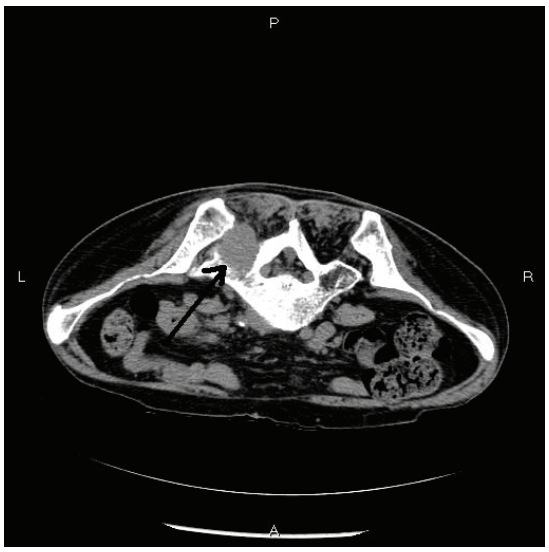

Figure 1. CT examination. A soft tissue tumor (arrow) is seen near the right iliac bone.

nucleoli (**Figures 2A** and **2B**).

An immunohistochemical study was performed with the use of Dako Envision method (Dako, Glostrup, Denmark), as described previously [3, 4]. Immunohistochemically, the tumor cells are positive for CD45 (**Figure 3A**), CD45RO (**Figure 3B**), CD34 (**Figure 3C**), KIT (CD117) (**Figure 3D**), CD99 (MIC-2) (**Figure 3E**), p53 (**Figure 3F**), CD10, PDGFRA, and Ki67 (labeling=60%) (**Figure 3G**). They were negative for pancytokeratin AE1/3, pancytokeratin CAM5.2, TdT (**Figure 3H**), CD3, CD20, CD79α, CD43, CD56, CD57, CD30, bcl-2, κ-chain, λ-chain, cytokeratin (CK) 7, CK20, synaptophysin, chromogranin, smooth muscle actin, p63, MPO, CD68, lysozyme, and ASD esterase. Although TdT was negative, other precursor cell markers (KIT, CD34, and CD99) were positive and the lymphoid cells showed T-cell lineage (CD45RO), the diagnosis was TLBL. Despite therapy, the patient died of lymphoma and leukemia 11 months after the diagnosis. Autopsy was not performed.

Discussion

The current tumor is not myeloid sarcoma, because no myeloid markers (MPO, lysozyme, ASD esterase, CD68 and CD43) were negative. Positive reaction for CD45RO and CD10 also exclude myeloid sarcoma. The present tumor is not blastic NK/T cell lymphoma, because CD56 and CD57 were negative. In general, sarcoma occurring during AML is myeloid sarcoma [5]. However, the present case is T-LBL. It is interesting whether the T-LBL arose from the lymphocytes of patient or lymphocytes of donor (her son). This point should be examined in future.

The present soft tissue tumor showed histologically significant cellular atypia. Immunohistochemical investigation showed that the tumor cells were positive for p53 and showed high (60%) Ki-67 labeling, indicating that the current tumor is malignant. The tumor was positive for

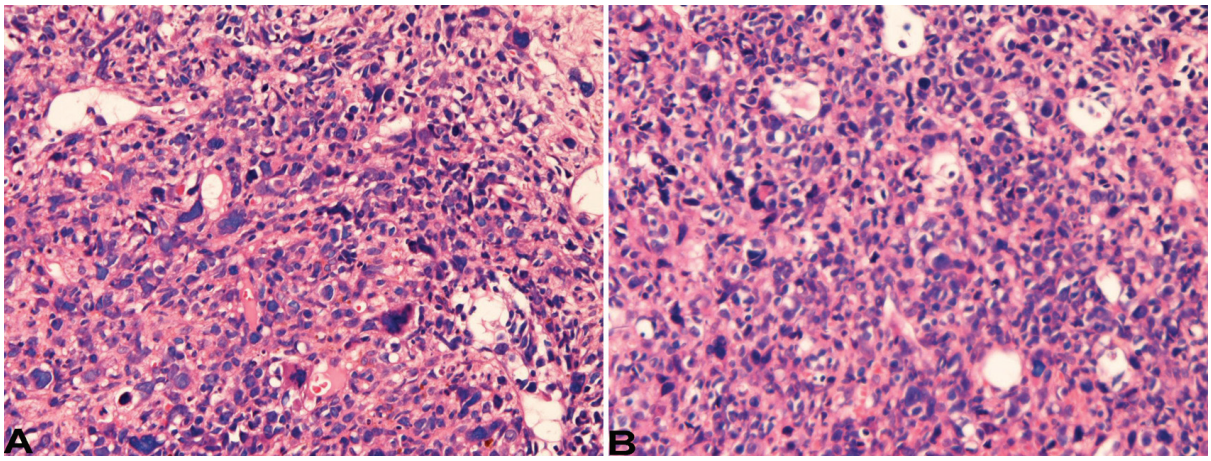

Figure 2. A,B. Microscopic picture. The tumor cells show polymorphism. The tumor cells have hyperchromatic nuclei and inconspicuous nucleoli.

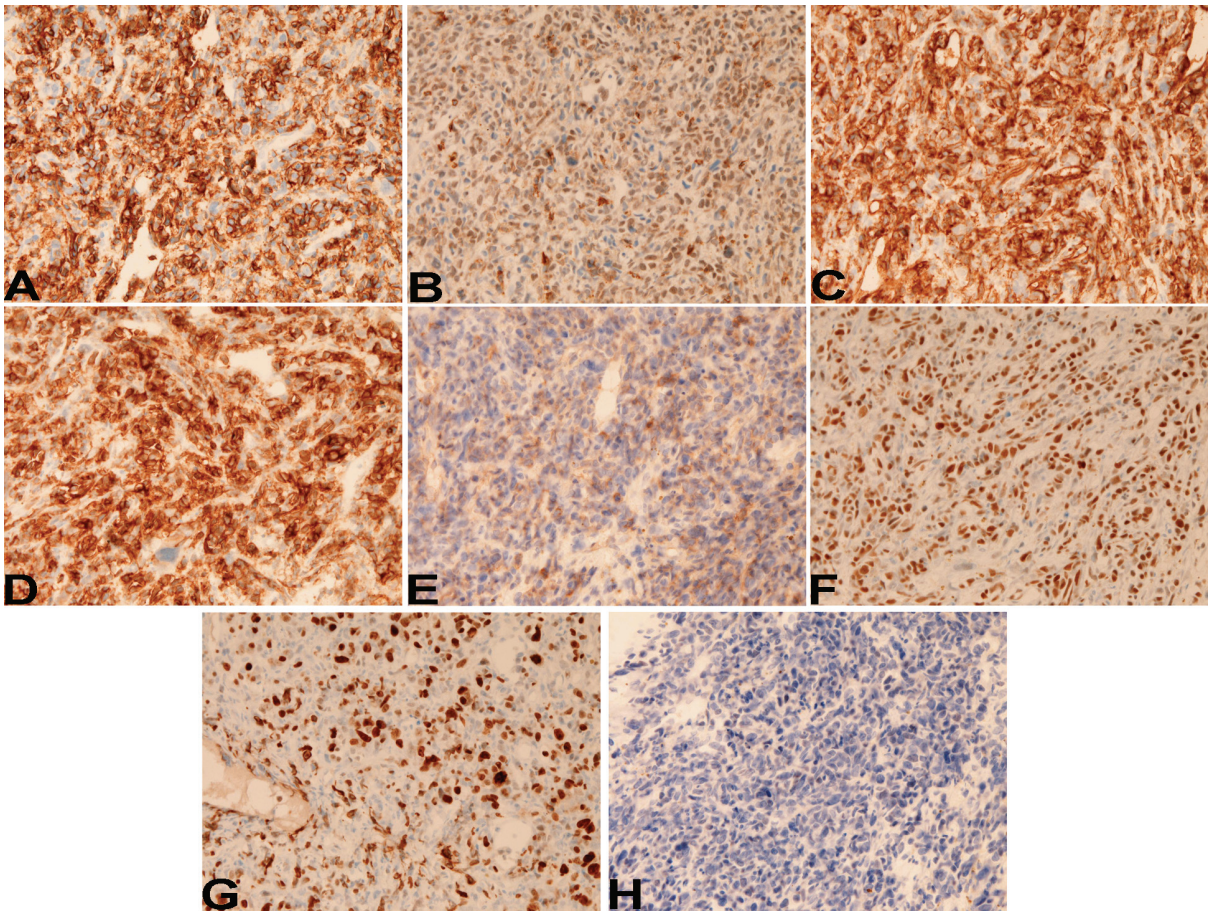

Figure 3. Immunohistochemical findings. The tumor cells are positive for CD45 (A), CD45RO (B), CD34 (C), KIT (D), CD99 (E), p53 (F) and K-i67 (labeling=60%), but negative for TdT (G).

CD45, indicating that the tumor is leukocytic malignancy. The present soft tissue tumor expressed a T-cell lineage marker (CD45RO), but negative for B-cell lineage markers (CD20, CD79α, bcl-2, κ-chain, λ-chain) and NK-cell markers (CD56, CD57). Therefore, the present tumor is malignant T-cell neoplasm. The negative immunoreactions of various CKs, CD30, synaptophysin, chromogranin, smooth muscle actin, and p63 indicate that the present tumor is not carcinoma, anaplastic large cell lymphoma, neuroendocrine tumors, smooth muscle tumors, and epithelioid malignancies.

TdT is expressed in 95% in lymphoblastic lymphoma [2], and positive expression of TdT was widely used to diagnose lymphoblastic lymphoma [1]. However, other precursor markers (KIT, CD34, CD99) have been only infrequently examined. Only several studies have investigated the expression of CD34, KIT and CD99 in lymphoblastic lymphoma [1, 6-10]. TdT was negative in the present case, but the present case expressed KIT, CD34 and CD39. Therefore, the author diagnosed the tumor as TdT (-), KIT (+), CD34 (+), CD99 (+) T-LBL.

Soslow et al [6] examined the expressions of TdT, CD34, CD99 and bcl-2 in lymphoblastic lymphoma and lymphoblastic leukemia. TdT was positive in 17/20 (85%), CD34 in 6/23 (26%), and CD99 in 17/24 (70%). These antigens were negative in all cases of non-lymphoblastic leukemia and lymphoma [6]. Bcl-2 was positive in 92% in lymphoblastic lymphoma, while it was positive in 25% in non-lymphoblastic leukemia [6]. In the present case, bcl-2 was negative. KIT is well known to be expressed primitive leukocytes. KIT expression is associated with CD34 expression, as in the case of gastrointestinal stromal tumor [7, 10]. Co-expression of KIT/CD34 is rare [7, 10]. In the

present case, the coexpression of KIT/CD34 was present. Therefore, the current case is very rare T-LBL. CD99 (MIC-2) is a marker of Ewing sarcoma/PNET, but it is expressed in primitive leukocytes including lymphoblastic lymphoma [9], and its expression correlated with TdT positivity. However, TdT was negative and CD99 was positive in the current case.

The current case expressed PDGFRA, a phenomenon not previously reported. The reason of the PDGFRA expression is unclear. The genes of KIT and PDGFRA are located in near positions [11, 12]. The expression of KIT in T-LBL may be associated with the positive expression of PDGFRA, like gastrointestinal stromal tumor [11, 12]. CD10 was positive in the present tumor. CD10 positivity may be seen in T-LBL [1].

In summary, the author reported a case of T-LBL with TdT (-), KIT (+), CD34 (+), CD99 (+), bcl-2 (-) immunophenotype. The author wants to stress that TdT, KIT, CD34 and CD99 should be included in panels of T-cell neoplasms. In addition, the author thinks that KIT, CD34 and CD99 are helpful for the diagnosis of T-LBL in cases negative for TdT. Furthermore, the present case showed that T-LBL may occur during the course of AML.

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