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CASE REPORT

B-ALL with CD34 Negative and Surface Immunoglobulin Light Chain Restricted Expression

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SUMMARY

Background: **The morphologic features of acute lymphoblastic leukemia (ALL) overlap greatly with other blastoid-HGBL or some mature B-cell lymphomas. Blastoid morphology is currently a diagnostic challenge.**
Methods and Results: **Our case presents a B-ALL with surface IgD and immunoglobulin light chain Kappa restricted expression, CD13 and CD33 were partial expressed and negative for CD34. The patient achieved morphologic remission after one cycle of treatment.**
Conclusions: **In this case, the expression of immunophenotypic features does not clearly distinguish whether the B cells are in a mature or immature stage. In some situations, these lymphoblasts cells are hardly distinguishable from mature cells.**
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KEYWORDS

lymphoblastic leukemia, high grade B-cell lymphoma, blastoid morphology, blastoid B-cell neoplasms

CASE REPORT

In February 2024, a 64-year-old female presented with thrombocytopenia for about one week. WBC was 4.13 x 10^9/L, HB was 111 g/L, PLT was 27 x 10^9/L.
The PET/CT scan showed high fluorodeoxyglucose (FDG) uptake throughout the body and splenomegaly. This can be consistent with diffuse bone infiltration and splenic infiltration changes in lymphoma. The bone marrow (BM) aspirate smear revealed 10% abnormal cells, most tumor cells were medium-sized to big, the cytoplasm was basophilic and contained multiple vacuoles. The nuclei were round, with finely or clumped chromatin and clear large nucleoli (Figure 1). BM immunohistochemical staining: MPO- (myeloperoxidase negative), PAX5+, TdT (partial dim positive), CD34-, CD117-, CD20-, CD3-, CD5-. BM flow cytometry analysis: the FSC of tumor cells were big, and positive for cTDT, CD10, CD22, CD38, HLA-DR, sKappa,

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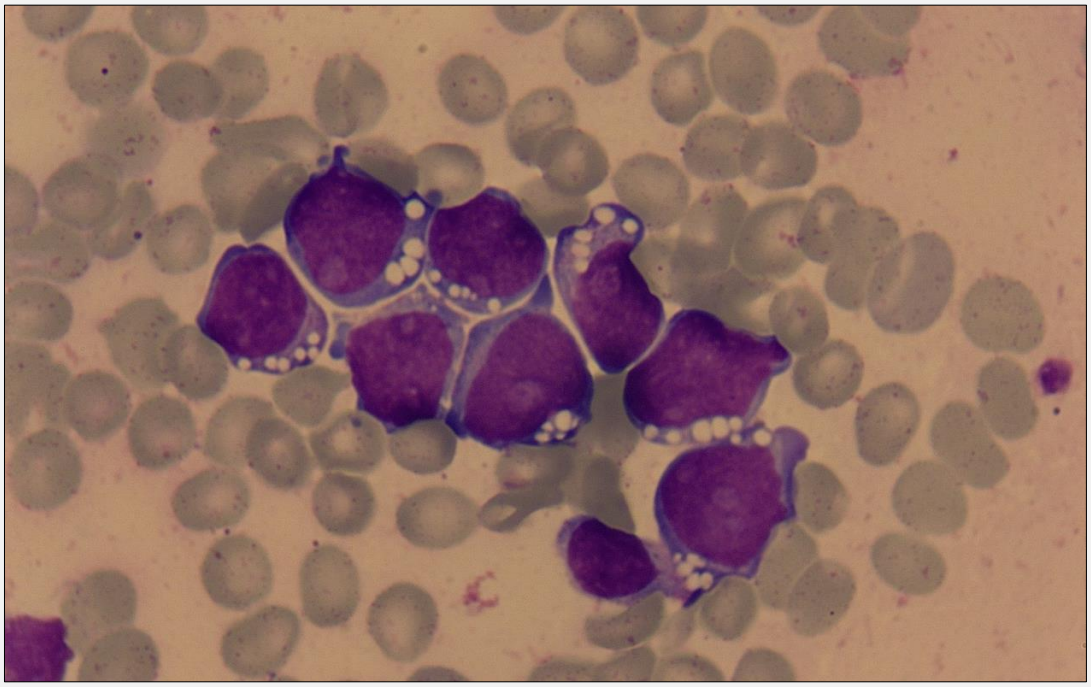

Figure 1. Wright-Giemsa staining of tumor cells.

sIgD, CD19 (dim), CD45 (dim), CD45RA (dim), CD33 (part), CD13 (part), negative for cMPO, cCD3, cCD79a, CD34, CD117, CD5, CD20, CD200, FMC7, CD23, CD 30, CD45RO, CD103, sIgM, sLambda, CD11b, CD14, CD15, CD16, CD64, CD36, CD2, CD7, CD4, CD8, CD56, and CD57. The tumor cells were confirmed B cell lineage, but the tumor cells were positive for surface IgD, immunoglobulin light chain Kappa restricted expressed, and negative for CD34. Myeloid-associated antigens, such as CD13 and CD33 were partial expressed. Cytogenetic analysis revealed a normal karyotype (46,XY [20]). Fluorescence in situ hybridization (FISH) results were negative for *BCR::ABL*, *TCF3::PB X1*, *TEL::AML1*, *IGH::C-MYC*, *IGH::BCL2*, *MLL*, *MYC*, *P53/CEP17*, *BCL2* , *BCL6*, and positive for *IGH*. Gene mutation analysis including 22 somatic mutations and insertions/deletions was performed using DNA extracted from BM aspirate specimens, and mutations of IKZF1, ERG, KMT2D-PAD were not detected. A final diagnosis of B-cell acute lymphoblastic leukemia (B-ALL) was made. She received one cycle treatment of VDCLP (Vincristine + Daunorubicin + Cyclophosphamide + Pegaspargase + Prednisone). After treatment, the BM biopsy revealed a normal karyotype (46,XX [11]) with morphologic remission.

DISCUSSION

Blastoid morphology and the overlapping immunophenotypic features between blastoid HGBL and B-ALL make the diagnosis challenging. A mature B-cell immunophenotype has also been occasionally identified in rare cases of B-ALL [1,2]. In a subset of B-ALL cases, the tumor cells show an aberrant immunophenotype such as dim or negative CD20, negative CD34, dim CD 45, TdT expression, and the expression of surface light chains, as shown in this study, that can mimic blastoid-HGB. B cells are generated in the bone marrow, emerging as antigen-naïve B cells that express membrane IgM as a B cell receptor. Mature naive IgM + IgD + B cells, which are mediated through differential splicing of the primary heavy chain transcripts, circulate through the follicles of secondary lymphoid tissues until they encounter antigen. Immature B-cells exhibit at least partial surface expression of IgM while in mature B-cells IgM is only present on the cell surface membrane [3,4]. B-ALL is an immature B-cell neoplasm that usually expresses TdT, CD34, CD10 bright, CD19, CD22, but is negative for CD20 and surface immunoglobulin light chain. Myeloid- associated antigens, such as CD13 and CD33, may also be aberrantly expressed. Terminal deoxynucleotidyl transferase (TdT) is strongly expressed in lymphoid precursor cells (both T- and B-cells). TdT

is useful in distinguishing immature B-cells from mature B-cells [5]. A small subset of HGBL cases includes lymphoma cells showing blastoid morphology and the differential diagnosis is challenging. In 2021, Mahsa Khanlari, et al. [6] used six features to develop a scoring system that is significantly different between blastoid-HGBL and B-ALL. Their results showed that the presence of surface light chain restriction, TP53 mutation, BCL6 expression, and the absence of expression of myeloid antigen (CD13 and/or CD33) and KRAS and NRAS mutation all support a diagnosis of blastoid-HGBL, whereas the converse and presence of B-ALL associated translocations support a diagnosis of B-ALL. In the CD34 negative B-ALL case with a score of 3, KMT2A (MLL) rearrangement, KRAS mutation, and CD33 expression were detected which supported a diagnosis of B-ALL. Lianqun Qiu, et al. [7] previously developed six-point flow cytometry-focused and three-point immunohistochemistry-focused scoring systems to distinguish blastoid HGBL from B-ALL. In 2023, they used both scoring systems together to improve the accuracy of classification of blastoid B-cell neoplasms. The six-point scoring system which was developed in bone marrow specimens based on flow cytometric analysis of five markers (CD45, CD10, CD20, CD38, and TdT) together with MYC expression by immunohistochemistry and/or MYC-rearrangement by FISH. This scoring system had a 100% sensitivity and 94% specificity in the differential diagnosis of blastoid B-cell neoplasms. The three-point immunohistochemistry (IHC)-based scoring system included three markers detected by immunohistochemistry, BCL6, TdT, and MYC; MYC also could be detected by FISH for rearrangement. They found that blastoid-HGBL more frequently expresses brighter CD45, CD20, CD38, BCL6, and MYC and less frequently expresses bright CD10 and TdT. Blastoid-HGBL more frequently has MYC rearrangement, a complex karyotype, and TP53 aberrancies. Accurate diagnosis is crucial for the successful clinical management of ALL. The use of morphological characterization of lymphoblast cells is not always easy. In some situations, these lymphoblasts cells are hardly distinguishable from mature cells.

Ethical Approval:
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Declaration of Interest:
None of the authors have a conflict of interest to disclose.

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