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Transformation of a previously diagnosed diffuse large B-cell lymphoma to plasmablastic lymphoma

To the Editor: A 55-year-old previously healthy woman presented with extensive deep venous thrombosis of ileal, femoral, and popliteal right veins and B symptoms of 1-month evolution. Complete blood counts were within normal limits, and there was no renal or hepatic dysfunction. Computerized tomography (CT) revealed a large pelvic mass of 12 cm of transverse diameter compressing the right iliac vessels, and several abdominal and mediastinal enlarged nodes, some of them with central necrosis. Fine-needle aspiration biopsy of the pelvic mass showed a diffuse large B-cell lymphoma (DLBCL) with Ki67 >90%. The malignant cells were CD20+, CD10+, CD45+, BCL6+, and focal BCL2+. MUM1 and MYC were not tested at this time. A bone marrow biopsy showed no lymphomatous involvement. The disease was classified as stage III-B, bulky disease, IPI low/intermediate, with LDH 720 U/L (Normal: <250 U/L).

We started treatment with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone). The patient completed two cycles, with an improvement on her performance status, but we observed de novo ipsilateral thigh skin infiltration, which on CT showed extension to limb's subcutaneous tissue and femoral acetabulum (Fig. 1A,B, upper panel). There was rapid clinical deterioration with thigh enlargement (thigh perimeter 60 cm). A skin biopsy was performed, and the patient was admitted to start chemotherapy. Fluorescence In Situ Hybridization analysis showed t(8;14) with MYC and Immunoglobulin heavy locus rearrangement, and trisomy 8. The patient received Burkimab (rituximab, methotrexate, vincristine, ifosfamide, dexamethasone, etoposide, and cytarabine). The skin biopsy showed that the malignant cells were CD20−, CD45−, PAX5+, CD38+, CD138+, MUM1+, and Epstein-Barr Virus (EBV) LMP1−, consistent with plasmablastic lymphoma (Fig. 1, lower panel). HIV ELISA was non reactive. Response to Burkimab was short, as patient clinically deteriorated with emaciation, expansion of the thigh perimeter (64 cm), and a papular-vesicular erythematosus rash over thigh skin infiltration. We then changed strategy to ESHAP (etoposide, cisplatin, methylprednisolone, and cytarabine) in preparation for autologous hematopoietic stem cell transplant. Even though there was improvement of renal function within the first few days of ESHAP, as well as reduction of the thigh perimeter (49 cm), patient's performance status progressively worsened. Right after the second cycle, there was recrudescence and intralesional hemorrhage, reaching the thigh a maximal perimeter of 79 cm (Fig. 1C, upper panel). Along with progression of the thigh/pelvic mass and skin infiltration, there was also rapid progression of cachexia and intolerance to oral feeding with intractable vomiting needing high dose of antiemetics and placement of a nasopharyngeal tube. Given resistance to treatment, we stopped all curative measures, and all efforts were focused on palliative care. Patient died 3.5 months after diagnosis of plasmablastic transformation.

Plasmablastic lymphoma (PBL) is a high-grade neoplasm that arises from terminally differentiated B-cells undergoing further differentiation into plasma cells. The pathogenesis of this disorder is incompletely understood. However, MYC rearrangements and EBV infection have emerged as possible contributors for the development of PBL. MYC rearrangements would prevent physiological apoptotic cell death while EBV infection would favor plasmablastic transformation of mature B-cells but blocking further plasmacytic differentiation [1].

We performed a systematic literature review looking for transformed PBL cases. Few cases of PBL transformed from another hematological disease have been described, most of these arising from chronic lymphocytic leukemia (CLL) and follicular lymphoma [2], as well as at least two cases described from previous plasmacytomas [3,4]. There are, however, no cases describing transformation from DLBCL. With the current case, it was not possible to define whether there was clonal evolution of the previously diagnosed DLBCL into PBL, or there was presence of synchronous DLBCL and PBL at diagnosis. However, given the possible same precursor cell (a B-cell), it is hypothesized that this was a case of DLBCL transformed to PBL. We cannot as well ignore the possibility that there could have been therapeutic pressure mediated by anti-CD20 therapy, similar to what has been seen in CLL and anti-CD19 therapy [5], which could have selected a plasmablastic clone.

PBL is an aggressive disease with a dismal prognosis with median survival times shorter than 1 year [1]. There is no standard of care for these patients, but when treatment has a curative purpose, regimens should include intensive chemotherapy followed by autologous hematopoietic stem cell transplantation in first remission, which we projected on our patient, however her clinical conditions did not permit such treatment option. More recently, the addition of the proteasome inhibitor bortezomib to combination chemotherapy have suggested improved response rates and survival [6].

We present a case of DLBCL transforming to PBL in an HIV-negative individual. Based on our systematic review, no similar case had been previously described. This clinical case was not only a truly diagnostic challenge, given its rarity, but also a major therapeutic challenge, with a rapidly progressing disease with minor and transient response to treatment and a fatal outcome. The spectrum of transformed PBL continues evolving.

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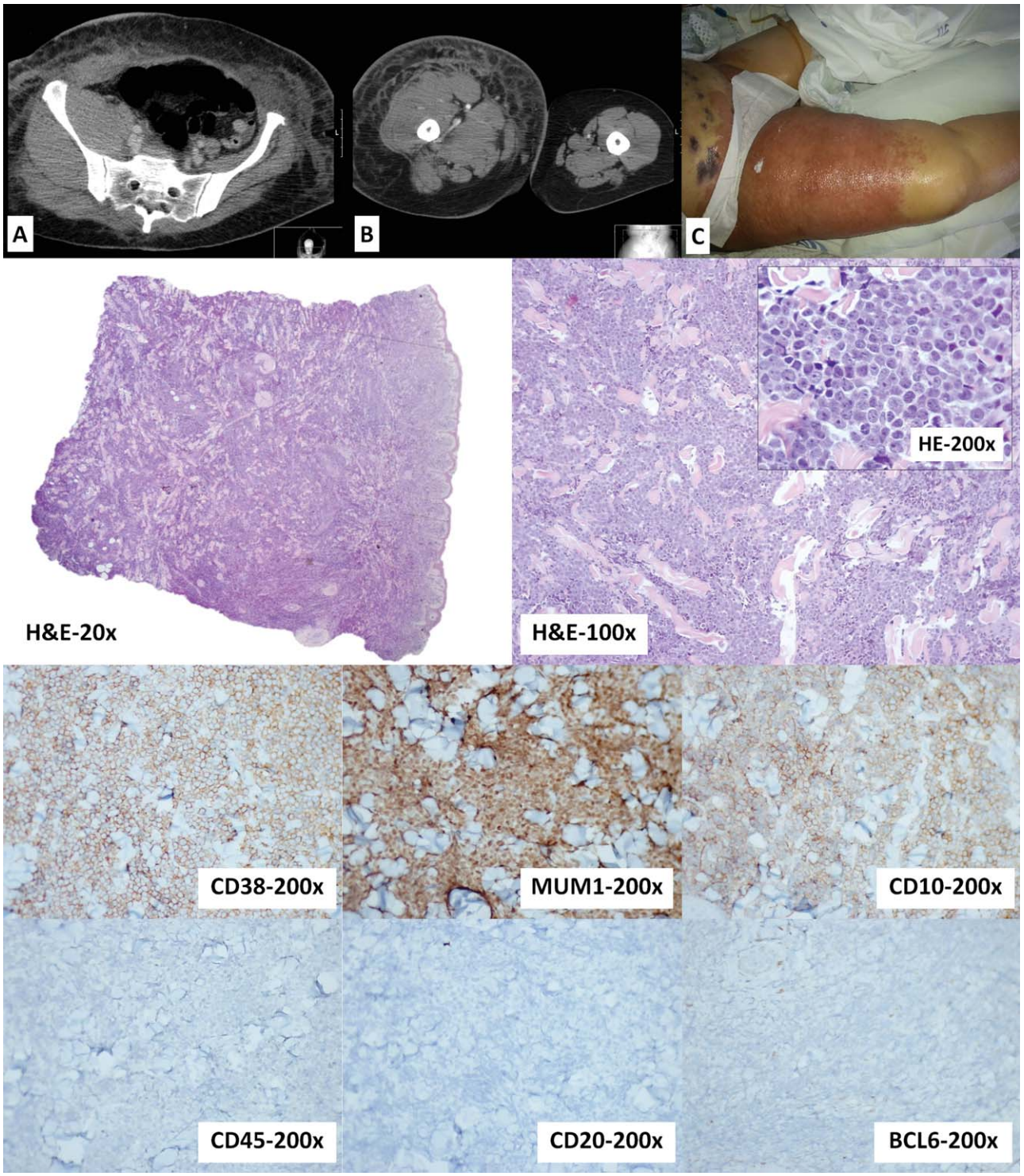

Figure 1. Upper panel: CT scan of the lower abdomen (A) and lower extremities (B), and picture of the patient's lower extremities few days before death (C). Lower panel: Skin biopsy from the abdominal region, showing diffuse infiltration by a medium to large cell population of cells with apparent cytoplasm, ovoid nuclei with prominent nucleoli, and frequent mitosis. These cells were positive for plasma cell marker CD38 and MUM1, and focally for CD10, in the absence of immunoreactivity for CD45, CD20, and BCL-6.

Myelodysplastic syndrome associated with acquired beta thalassemia: "BTMDS"

To the Editor: Most patients with myelodysplastic syndromes (MDS) have macrocytic or normocytic anemia as a result of ineffective erythropoiesis due to clonal hematopoiesis. Occasional patients with MDS have microcytic red blood cell (RBC) indices in the absence of iron deficiency, however, and a high proportion of such patients have decreased alpha globin expression associated with somatic mutations in the chromatin remodeling factor ATRX; an established alternative mechanism for acquired alpha thalassemia in myeloid neoplasia is clonal deletion of the alpha globin cluster on chromosome 16p. This clinicopathological phenomenon has been called "acquired alpha thalassemia–myelodysplastic syndrome" (ATMDS). Here we describe a patient with new-onset microcytic anemia associated with acquired deletion of the beta globin cluster on chromosome 11, resulting in a beta thalassemia-MDS (BTMDS) phenotype. Phenotype-genotype correlation studies may reveal associations of specific mutation patterns with other recurrent MDS-associated hematological findings.

The most common human disorders of hemoglobin synthesis are the inherited alpha and beta thalassemias endemic to tropical and subtropical global regions, and which