Acute promyelocytic leukemia with an unusual presentation of secondary postpartum hemorrhage

TO THE EDITOR: Acute leukemia during pregnancy is rare [1-8]. The exact incidence of acute promyelocytic leukemia (APL) in pregnant women is unknown; however, approximately 50 such cases have been reported in the literature [1-4, 7, 8]. APL is a unique type of acute myeloid leukemia (AML) characterized by proliferation of neoplastic promyelocytes bearing a specific chromosomal translocation t(15;17). We report a case of APL with an unusual presentation of secondary postpartum hemorrhage (PPH).

CASE
A 30-year-old woman (gravida 2, para 2, abortus 0) delivered a 2.1 kg baby girl through normal vaginal delivery but was otherwise healthy. She received 2 units of whole blood transfusion during labor and was discharged 3 days later. However, she was re-admitted 6 days following discharge with complaints of excessive bleeding per vaginum and bleeding gums. On examination, she was pale and afebrile with a pulse rate of 72 beats/min and blood pressure of 110/70 mmHg. There was no icterus, pedal edema, or lymphadenopathy, and no complaint of fever or bruising. Ultrasound revealed clots within the uterus possibly due to retained products of conception. There was hepatomegaly but no splenomegaly. Hematological investigations revealed the followings: hemoglobin level, 8.8 g/dL; total leukocyte count, 6.5×10^6/L; platelet count, 44×10^9/L; hematocrit, 24.4%; red blood cell count, 2.62×10^9/L; differential leukocyte count: blasts, 2%; promyelocytes, 65%; neutrophils, 4%; and lymphocytes, 29%. The abnormal promyelocytes were 2–4 times the size of small mature lymphocytes and had a moderate amount of cytoplasm with granules and Auer rods. The nuclei contained fine chromatin and 1–3 prominent nucleoli, and hallmark faggot cells were also observed (Fig. 1). The promyelocytes were strongly positive for myeloperoxidase. She was diagnosed with AML, suggestive of APL. Bone marrow aspiration was advised along with immunophenotyping and cytogenetic studies. The coagulation profile revealed the followings: prothrombin time, 15 sec (control, 13 sec); activated partial thromboplastin time, 31 sec (control, 30 sec); serum fibrinogen level, 110 mg/dL; D-Dimer level, 16–32 μg/mL fibrinogen equivalent units (reference range, <0.5 μg/mL fibrinogen equivalent units). Other biochemical tests were within normal limits. However, the patient died of hypovolemic shock following excessive blood loss. Therefore, further investigations could not be performed. During the antenatal period, the patient had a hemoglobin range of 9–9.5 g/dL, a total leukocyte count of 6–8×10^6/L, and a platelet count of 160–190×10^9/L. A peripheral blood smear revealed microcytic hypochromic red cells; however, no abnormal cells or blasts were seen on any smears during the antenatal period. Moreover, she had a normal coagulation profile.

Acute leukemia during pregnancy is very rare with an estimated frequency of 1 in 75,000–100,000 [3, 6, 7]. AML accounts for approximately two-thirds of leukemia cases seen during pregnancy and the diagnosis is generally made during the second and third trimesters [3, 5]. PPH is occasionally due to an underlying coagulation or hematologic disorder, but PPH as a presentation of APL is extremely rare [8]. APL is commonly complicated by disseminated intravascular coagulation (DIC), seen in >90% of patients, and a life-threatening hemorrhage can occur in the brain, gut, or less frequently, the uterus. In such cases, it is very important to diagnose the underlying disorder as APL and it is curable with a good prognosis. The treatment of choice for APL is all-trans retinoic acid followed by conventional chemotherapy [1-3]. This case report is important as it highlights the fact that APL can be a rare cause of PPH. A peripheral blood smear should be performed in all cases of unexplained DIC.

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Fig. 1. Peripheral blood smear showing abnormal promyelocytes. Inset shows a faggot cell (Wright’s stain, ×1,000).
Lymphoplasmacytic non-Hodgkin lymphoma/Waldenström’s macroglobulinemia with CD5+, CD23+, and CD10-

TO THE EDITOR: In lymphoplasmacytic lymphoma/Waldenström’s macroglobulinemia (LPL/WM), the immunophenotype of the neoplastic population generally does not show positivity for CD5, CD23, or CD10 monoclonal antibodies, with only 5–20% showing positivity. However, this immunophenotypic particularity does not exclude a diagnosis of Waldenström’s macroglobulinemia; moreover, CD5 and/or CD23 monoclonal antibody positivity can characterize a subset of patients with high IgM values; these patients are at risk for hyperviscosity-related complications.

WM was first described by Jan Waldenström in 1944 [1] and is classified as an indolent B-cell lymphoplasmacytic lymphoma (LPL) or LPL/WM [2]. It is a lymphoproliferative neoplasm characterized by the presence of a serum IgM monoclonal component associated with bone marrow lymphocytic infiltration. According to the Workshop on WM held in Athens in 2002 [2], the diagnosis (Table 1) is principally based on the following two essential findings: 1) the quantitative presence of any serum IgM monoclonal component and 2) bone marrow infiltration by lymphoid cells with a lymphoplasmacytic aspect.

In WM patients, the serum IgM monoclonal component concentration varies widely. However, while finding a monoclonal IgM component is a prerequisite for the LPL/WM diagnosis, it is not a specific feature of WM. In fact, an IgM monoclonal component can be found in other lymphoproliferative disorders, such as chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL), splenic marginal zone lymphoma (SMZL), diffuse large cell lymphoma (DLCL), mantle cell lymphoma (MCL), myeloma and IgM monoclonal gammapathy of undetermined significance (IgM-MGUS)(Table 1).

The lymphomatous nature of bone marrow infiltration must be confirmed using flow cytometry and immunohistochemistry to define the immunophenotype. Bone marrow infiltration, usually intertrabecular, is represented by small lymphocytes with evidence of clonal plasmacytoid differentiation. Mast cells are often present, supporting growth of the lymphoplasmacytic population [3]. WM does not show cytogenetic chromosome marker alterations, with most patients displaying a normal karyotype. However, various numerical and structural abnormalities have been described, of which the most frequent is deletion of the long arm of chromosome 6q [4]. Recently, a MYD88 L265P mutation has been observed in more than 90% of WM patients. This has an important diagnostic impact and will improve understanding of the WM pathophysiological mechanism and is likely to improve therapeutic outcomes [5].

We report the case of a 74-year-old male who had a

Table 1. Diagnostic criteria for Waldenström’s macroglobulinemia and IgM monoclonal gammapathy of undetermined significance.

| Waldenström’s macroglobulinemia | IgM monoclonal gammapathy of any entity |
|---------------------------------|----------------------------------------|
| a) Serum IgM monoclonal component | < 3 g/dL |
| b) No morphological evidence of bone marrow lymphoplasmacytic infiltration (even in the presence of evident immunophenotypic or molecular clonality) |
| c) Neither symptoms or signs due to the serum IgM monoclonal component |

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