International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Okafor LC et al. Int J Reprod Contracept Obstet Gynecol. 2025 Jun;14(6):1961-1964
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20251590

Case Report

Abnormal uterine bleeding as first symptom of acute promyelocytic leukaemia: a case report and literature review

Love Chimezirim Okafor[1]*, Ebelechukwu Adaobi Obi[1], Chinenye Ukoha[1], Aminyene Essien Meraiyebu[2], Kingsley Iyoko Iseko[2], Uchechi Nzerem Olua[3]

[1]Department of Obstetrics and Gynaecology, The Limi Hospitals, Abuja, Nigeria
[2]Department of Radiology, The Limi Hospitals, Abuja, Nigeria
[3]Department of Family Medicine, The Limi Hospitals, Abuja, Nigeria

Received: 24 January 2025
Revised: 15 March 2025
Accepted: 03 May 2025

***Correspondence:**
Dr. Love Chimezirim Okafor,
E-mail: okaforlove@yahoo.com

ABSTRACT

Abnormal uterine bleeding is common within gynaecology practice. It affects up to one-third of women during their lifetime. Hematological cancer is a rare form of coagulopathy leading to abnormal uterine bleeding. Uterine bleeding caused by coagulopathy as a complication of acute promyelocytic leukaemia can be fatal. The aim was to document a rare case of acute severe abnormal uterine bleeding as first symptom of haematological cancer (Acute Promyelocytic Leukaemia). She was a 45-year-old Para 2 woman who presented at the emergency room with chief complaint of uterine bleeding of six days duration. She also developed a throbbing headache that suddenly intensified, initially on the left side of her head, radiating to the periorbital area. Assessment of Acute promyelocytic Leukaemia complicated by Subarachnoid haemorrhage was made. She was referred to National Hospital Abuja for further management. Uterine bleeding caused by coagulopathy as a complication of acute promyelocytic leukaemia can be life threatening, hence early diagnosis and treatment is imperative.

Keywords: Uterine bleeding, Haematological cancer, Acute promyelocytic leukemia, Subarachnoid haemorrhage

INTRODUCTION

Abnormal uterine bleeding is defined as menstrual bleeding of abnormal length, quantity or timing unrelated to pregnancy.[1] It is the direct cause of a significant healthcare burden for women, with affectation of their mental and physical health not excluding their families and the society.[2,3] Abnormal uterine bleeding is common within gynaecology practice. It affects up to one-third of women during their lifetime.[1-4] About 5-10% of reproductive age women will seek medical care for menorrhagia.[5] Abnormal uterine bleeding has a variety of causes as per FIGO (International Federation of Obstetrics and Gynaecology) classification.[6,7] The acronym PALM-COEIN aids in classification of abnormal uterine bleeding, with PALM for structural aetiologies (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia) and COEIN for non-structural aetiologies (coagulopathies, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified).[4,6] Hematological cancer is a rare form of coagulopathy leading to abnormal uterine bleeding.[1,5] Uterine bleeding caused by coagulopathy as a complication of acute promyelocytic leukaemia can be life threatening, hence early diagnosis and treatment is imperative.[5] The evaluation of abnormal uterine bleeding involves detailed history, abdominopelvic examination, laboratory testing that includes pregnancy test and complete blood count, and in suspected malignancy peripheral blood film. Ultrasound scan is the first-line tool for assessing structural abnormalities causing uterine bleeding.[4-6] There are a few documented current literatures of abnormal uterine bleeding leading to diagnosis of

haematological cancer.[1,5,8-10] Hence we report a rare case of acute severe abnormal uterine bleeding as first symptom of haematological cancer (APL).

CASE REPORT

A 45-year-old para 2 woman presented at the emergency room with chief complaint of uterine bleeding of six days duration. The bleeding involved large clots, necessitating frequent changing of vulva pad every 1-2 hours, and was so profuse that she used about four adult diapers daily. There was associated dizziness and lethargy necessitating her presentation. This marked the first occurrence of such heavy menstrual bleeding for her. Prior to presentation, she had regular 23/24-day cycle, menstruating for four days, without a history of dysmenorrhea, menorrhagia, or post-coital bleeding.

There was no history of abdominal swelling, thyroid disease, or polycystic ovary syndrome. There was no history of chronic medical conditions. Her two previous deliveries were via spontaneous vaginal delivery at full term, with both children alive. While on admission she developed a throbbing headache that suddenly intensified, initially on the left side of her head, radiating to the periorbital area.

Upon presentation, she appeared pale, fatigued, and had difficulty walking unaided. Her blood pressure was 80/50 mmHg, with a pulse rate of 120/min, characteristically low in volume. Gynecological examination revealed excessive uterine bleeding, yet normal findings for the cervix, uterus, and ovaries. Pelvic ultrasonography displayed normal ovaries, a bulky uterus with an intra-uterine collection measuring 64mls, and a thin endometrial thickness of 2 mm. pregnancy test yielded negative result.

Complete blood count revealed pancytopenia: white blood cell count (0.43×109/l), severe anemia (haemoglobin: 5.4 g/dl, haematocrit 15.6%, MCV: 84.4 fl), and thrombocytopenia (19×109/l). The clotting profile indicated reduced Activated partial thrombin time (APTT) at 18.1 seconds, with normal prothrombin time. A cranial CT scan revealed an irregular hyperdense area within the sulcus of the right frontal lobe, indicating a 6.9×1.2 cm acute subarachnoid hemorrhage.

Treatment for acute severe uterine bleeding included intravenous tranexamic acid and mefenamic acid. Given signs of hemodynamic instability, intensive fluid replacement via intravenous crystalloid, colloid solutions, and four packs of fresh whole blood were administered. Concurrently, a peripheral blood smear was performed to investigate the underlying cause of hemorrhage and thrombocytopenia.

Examination revealed 70% abnormal myeloblasts, featuring characteristic immature, bilobed “apple-core” nuclei and heavily granulated cytoplasm, indicative of acute promyelocytic leukemia (APL). Upon diagnosis of leukemia complicated by subarachnoid hemorrhage, she was transferred to the National Hospital Abuja’s Haematology and Oncology Department for further evaluation and management on financial reason.

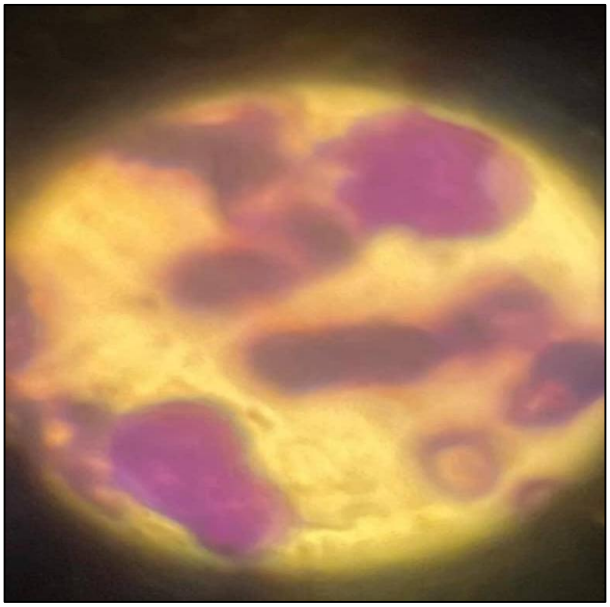

Figure 1: Gynecological examination.

DISCUSSION

Abnormal uterine bleeding is a common gynaecological problem that can occur at any age. The causes can be structural and non-structural as per FIGO.[5,6] Abnormal uterine bleeding as first presentation of haematological cancer is rare. A study estimated the incidence of abnormal uterine bleeding as the chief presenting symptom as 3.6 cases per 1000 women with haematological cancer.[1]

The interaction of numerous coagulation and fibrinolysis factors and inhibitors, hormonal factors and platelets are needed for haemostasis. Menorrhagia may be the first clinical manifestation of a bleeding disorder as any flaw in these interactions can result in bleeding. Our patient presented with acute severe uterine bleeding. Similar presentation has been reported in other literatures in reproductive age women.[1,5,9,10] Hematological cancer has also been reported to present as uterine mass, leukemia relapse in the cervix of the uterus, postmenopausal bleeding, and uterine mass.[8,11]

Acute promyelocytic leukemia (APL), a subtype of acute myeloid leukemia (AML) is relatively rare in adults, accounting for only 10-15% of AML each year.[5,13] Most of these patients are in their reproductive age. Our patient was 45 years old.[1,5,8-10]

Clinically, patients suffering from APL almost always present with haematological manifestations such as petechiae, ecchymosis, hematuria, epistaxis and menometrorrhagia.[10] Heavy bleeding can be the first sign

in at least 80% of cases of APL especially in the early phase of the disease.[5] The haemorrhagic diathesis often precedes the diagnosis of leukemia by two to eight weeks.[10] In our patient, acute severe uterine bleeding was the first presenting complaint and because of the acute onset, its severity and the haematological picture we suspected and made diagnosis of APL within 3 days. Studies have been documented of similar diagnosis of APL while other studies reported a diagnosis of acute lymphocytic leukemia.[1,5,9,10,11]

Hematological test may show anaemia, thrombocytopenia and characteristic blood film picture and these aid to diagnose and determine the specific subtypes of acute myeloid leukemia.[14] The haemorrhage of APL has been characterised as a form of disseminated intravascular coagulation (DIC) and thrombocytopenia, with prolongation of prothrombin and thrombin, elevation of serum fibrinogen degradation products and decreased levels of factor V and fibrinogen.[5,10] Reduction of platelet level is attributed to bone marrow failure, and DIC seen in over 90% of patients attributed to fibrinolysis shown to result from the expression of Annexin II, a receptor for fibrinolytic protein on the surface of the leukemia cells (malignant promyelocytes).[5,15]

These promyelocytes release plasminogen and elastase that activate the coagulation cascade, generate thrombin and drain fibrinogen, clotting factors, and platelets.[5] Leukemia does not usually form tumors so imaging is not usually useful in making the diagnosis. Assessing the bone marrow for leukemic cells is essential in diagnosis of leukemia.[14] Our patient had pancytopenia and peripheral blood film diagnostic of APL. Studies with similar haematological picture have been reported.[1,5,10]

Upon suspicion of the possible diagnosis based on clinical findings and peripheral blood film picture even without waiting for a bone marrow examination, treatment should be commenced immediately as very prompt supportive measures are lifesaving in the first few days of treatment in APL than those with other subtypes of AML.[5] Treatment with platelet transfusion to maintain platelet count above 50×109/l, fresh frozen plasma to replace clotting factors and red cell transfusion for correction of anaemia are necessary.[5,10] The main method of management of APL coagulopathy is early commencement of All-trans retinoic acid (ATRA) which results in rapid resolution of bleeding tendency and quick normalization of coagulation tests and fibrinogen.

Chemotherapy (anthracycline-based) combined with ATRA gives cure rate of up to 80%.[5,10,16,17] ATRA and Arsenic trioxide incorporation for induction/maintenance has also been found to improve survival. Our patient received fluid resuscitation, intravenous tranexamic acid and whole blood transfusion before she was referred to National Hospital Abuja's hematology and oncology department following diagnosis of APL and subarachnoid haemorrhage.

Haemorrhagic death, most commonly the result of intracranial hemorrhage is the leading cause of treatment failure in acute promyelocytic leukemia.[19,20] Our patient had developed subarachnoid hemorrhage before she was referred.

CONCLUSION

This case underscores the significance of considering and investigating uncommon origins of AUB. Women of reproductive age group with anaemia, thrombocytopenia or pancytopenia should be investigated for possibility of hematologic cancer. Timely diagnosis and treatment of leukemia presenting as abnormal uterine bleeding can be lifesaving.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Nebgen DR, Rhodes HE, Hartman C, Munsell MF, Lu KH. Abnormal uterine Bleeding as the presenting symptom of Hematologic Cancer. Obstet Gynecol. 2016;128(2):257-362.
2. Singh S, Best C, Dunn S, Leyland N, Wolfman WL. Abnormal uterine bleeding in premenopausal women. J Obstet Gynecol Can. 2013;35(5):473-5.
3. Matteson KA, Raker CA, Clark MA, Frick KD. Abnormal uterine bleeding, health status, and usual source of medical care: analyses using the Medical Expenditures Panel Survey. Journal of women's health (Larchmt). 2013;22(11):959-65.
4. Wouk N, Helton M. Abnormal Uterine Bleeding in premenopausal women. Am Fam Phys. 2019;99(7):435-43.
5. Bodur S, Ayaz Y, Topallar F, Erdem G, Gun İ. Severe uterine haemorrhage as first manifestation of acute leukemia. Eastern J Med. 2011;62-5.
6. Munro MG, Critchley HO, Broder MS, Fraser IS. FIGO classification system (PALM COEIN) for causes of abnormal uterine bleeding in non-gravid women of reproductive age. International J Obst Gynecol. 2011;113:3-13.
7. Okafor LC, Ogoke NC, Taiwo WO, Adagadzu SJ, Iseko KI, Meraiyebu AE. Abnormal Uterine Bleeding due to Retention of Fetal bones after Abortion: A case report. Open J Obst Gynaecol. 2023;13:1881-5.
8. Mishra K, Muralidaran C, Jandial A, Mittal BR, Varma S. Uterine mass and menorrhagia: a rare presentation of acute myeloid leukemia with arduous clinical course. Balkan Med J. 2018;35(3):282-4.
9. Blaicher W, Jager U. Abnormal vaginal bleeding as first symptom of acute leukemia. Arch Gynecol Obst. 2001;265(1):55-6.
10. Prabhu TRB. Promyelocytic Leukemia presenting as acute haemorrhage. South Asian Fed Obst and Gynecol. 2010;2(3):220-1.

11. Tsagkas N, Troussa A, Vorgias G, Tzaida O, Zagorianakou N, Gonidi M. Extramedullary Leukemia Presenting at the Cervix of the Uterus. Case Reports in Obstetrics and Gynecology. Case Rep Obstet Gynecol. 2020;2020:8492036.
12. Henes M, Nauth A, Staebler A, Becker S, Henes JC. Postmenopausal bleeding as first manifestation of an acute myelogenous Leukemia: A case report and review of literature. Med Oncol. 2010;27(3):815-9.
13. Tallman MS, Nabhan C, Feusner JH, Rowe JM. Acute promyelocytic leukemia: evolving therapeutic strategies. Blood. 2002;99:759-67.
14. Test for acute myeloid leukemia (AML). American Cancer Society. Avaialble at: https://www.cancer.org/cancer. Assessed on 30 January 2024.
15. Hajjar KA, Acharya SS. Annexin II and regulation of cell surface fibrinolysis. Ann N Y Acad Sci 2000;902:265-71.
16. Tallman MS, Andersen JW, Schiffer CA. All-trans retinoic acid in acute promyelocytic leukemia: long-term outcome and prognostic factor analysis from the North American Intergroup Protocol. Blood 2002;100:4298-302.
17. Sanz MA, Lo-Coco F. Modern approaches to treating acute myelocytic leukemia. J Clin Oncol. 2011;29(5):1067.
18. Gill H, Raghupathy R, Lee CY. Acute Promyelocytic leukemia: population-based study of epidemiology and outcome with ATRA and oral-ATO from 1991 to 2021. BMC Cancer. 2023;141:2885-93.
19. Naymagon L, Mascarenhas J. Hemorrhage in acute promyelocytic leukemia: Can it be predicted and prevented. Leu Res. 2020;94:106356.
20. Abedin S, Altman JK. Acute promyelocytic leukemia: preventing early complications and late toxicities. Hematology Am Soc Hematol Educ Program. 2016(1):10-5.

Cite this article as: Okafor LC, Obi EA, Ukoha C, Meraiyebu AE, Iseko KI, Olua UN. Abnormal uterine bleeding as first symptom of acute promyelocytic leukaemia: a case report and literature review. Int J Reprod Contracept Obstet Gynecol 2025;14:1961-4.