

# Management of abnormal uterine bleeding caused by leiomyoma in a patient with acute leukemia: a case report

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## Abstract

A 19 years old woman was hospitalized with chief complaint of vaginal bleeding since 1 month before. Physical examination revealed a palpable mass in her abdomen. The patient also experienced gum and nose bleeding with no history of any drug, hormones, or contraceptive use. Sonographical studies of the abdomen and pelvic were suggestive of leiomyoma. Laboratory findings showed leukocytosis ( $15,800/\text{mm}^3$ ) with peripheral blood smear revealing a normochromic normocytic anemia state. Bone puncture performed by the hematology division of internal medicine was positive for acute lymphoblastic leukemia. Blood transfusion was performed to treat anemia. Leuprolide acetate (3.75 mg) was injected for three cycles, with an interval of 28 days, to treat leiomyoma. Last follow-up showed that the patient was transferred to the hematology division of internal medicine after complaints of vaginal bleeding resolved on administration of gonadotropin-releasing hormone analog.

**KEY WORDS:** Abnormal uterine bleeding, leiomyoma, leukemia, leuprolide acetate

## Introduction

Incidence rates of abnormal uterine bleeding in adolescent women have increased in recent years. The etiology varies widely from anovulation, use of certain drugs, to underlying systemic diseases. In addition, although structural abnormalities or neoplasms are more common in older women, incidence rates are also increased in young adolescents.

## Case Report

A 19 years old woman was hospitalized with chief complaint of vaginal bleeding since 1 month before. Physical examination revealed a palpable mass in her abdomen.

The patient also experienced gum and nose bleeding. There was no history of any drug, hormones, or contraceptive use. Personal and family history were not contributory. Abdominal examination showed a pelvic abdominal mass, clinically suspected to be a uterine leiomyoma.


The patient was investigated for routine hematological and sonographical findings. Sonographical studies of the abdomen and pelvic showed uterine enlargement measuring  $12.05 \times 5.90 \times 7.07$  cm with a predominantly solid lesion in uterine measuring  $7.14 \times 3.56$  cm. Other organs were normal. No obvious lymphadenopathy was found. Final impression showed features suggestive of leiomyoma.

## Laboratory Findings

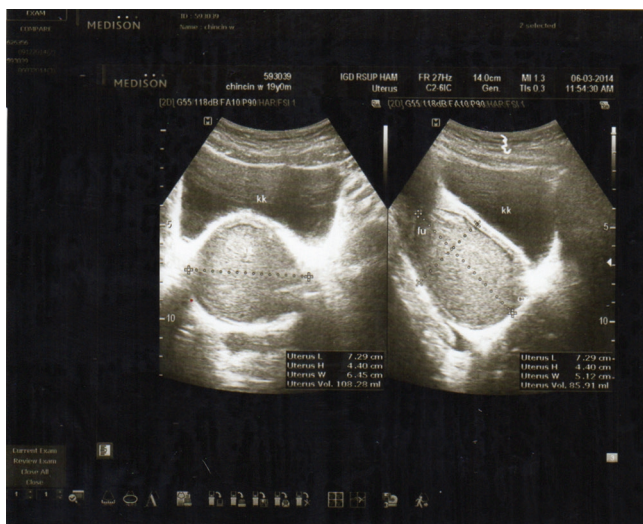
There was decrease in hemoglobin count (7.6 g/dL) with leukocytosis ( $15,800/\text{mm}^3$ ). Her platelet count was only  $8000/\text{mm}^3$ . Peripheral blood smear showed a normochromic normocytic anemia with immature cells of leukocyte (blast cell 10%) and was suggestive for acute leukemia.

The patient was then referred to the hematology division of internal medicine and subsequently underwent bone marrow puncture procedure, the results of which were found to be positive for acute lymphoblastic leukemia.

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**Figure 1:** Ultrasound revealing sign of leiomyoma of the uterine. Courtesy of Muhammad Fidel Ganis Siregar.

Blood transfusion was performed to treat anemia. Leuprolide acetate (3.75 mg) was injected for three cycles, with an interval of 28 days, to treat leiomyoma. Last follow-up showed that the patient still received medication and treatment from both gynecology and hematology divisions of internal medicine.

## Discussion

Literature shows that prolonged menstrual complaints may be encountered in cases with abnormal uterine bleeding, from which an etiology should be determined, whether structural or nonstructural. If a mass is suspected, a structural cause should be considered. Bleeding from other sites are also frequently found, consequently hematological disorders or other systemic diseases should be investigated.

Bleeding may cause a low hemoglobin count in a routine blood examination. However, if low hemoglobin was accompanied by leukocytosis and thrombocytopenia, a systemic hematological disorder such as leukemia must be considered. Coagulopathy disorders can be one of the causes of abnormal uterine bleeding. The suspicion of acute leukemia should be confirmed by examination of the bone marrow.

Acute myeloblastic leukemia (AML) is a disease characterized by neoplastic transformation and differentiation disorders of progenitor cells of myeloid series. If untreated, the disease will lead to rapid death within a few weeks to months after the diagnosis. Before 1960, only palliative treatment was available for patient with AML. Nowadays, rapid development of this disease treatment gives hope for AML patient to be cured. AML treatment progress achieved with chemotherapy regimen is better, high-dose chemotherapy with bone marrow transplant support and good supportive therapy such as more new-generation antibiotics and transfusion of blood components to cope

with the side effects of the treatment. In addition, for about two decades, in which other diagnostic techniques have also been developed, leukemia is detected by immunophenotyping and cytogenetic analysis, which produce a more accurate diagnosis.<sup>[1]</sup>

Theoretically, there are many coagulopathy disorders that cause abnormal uterine bleeding. The treatment of bleeding caused by coagulopathy is based on the improvement of the state of hematologic disorder, which automatically reduces bleeding complaints. Abnormal uterine bleeding treatment regimens such as nonsteroidal anti-inflammatory drugs cannot be given in this case because of the nature of anti-platelet itself as it can worsen the disturbance of platelets count because of the disease itself. Treatment options available might be gonadotropin-releasing hormone (GnRH) analog and the contraceptive pill. GnRH analog works by competing occupied GnRH receptors, causing suppression of the gonads and amenorrhea in patients. In contrast, treatment with oral contraceptives does not seem a wise choice in myoma uteri experienced by the patient because of the greater concentration of estrogen will increase the growth of myoma itself.

A study conducted at a single center in France showed that treatment with leuprolide may reduce vaginal bleeding in premenopausal patients receiving myelosuppressive chemotherapy. In this observational study, 21 women aged 16–50 years who received chemotherapy and were anticipated to experience thrombocytopenia (defined as platelet count  $<100 \times 10^3/\text{mm}^3$ ). An objective clinical evaluation of vaginal bleeding was performed, including hormonal examination such as the plasma level of estradiol, follicle stimulating hormone, and luteinizing hormone. The patients were initially treated with both progestin and GnRH analogs in accordance with the menstrual regularity and time since last menstrual period whenever possible. If myelosuppressive chemotherapy could not be scheduled or delayed, GnRH analog administration and progestin treatment usually began regardless of the menstrual cycle.<sup>[1]</sup>

After bleeding complaint is resolved, the issue will be the fertility, especially in cases of hematological malignancy requiring chemotherapy. One study conducted in Argentina in 2001 showed evidence that GnRH analog also protects the occurrence of premature ovarian insufficiency after chemotherapy and maintains fertility in patients.<sup>[2]</sup>

In these studies, patients were divided into three groups. The first group of premenarchal patients aged from 3 to 7.5 years undergoing polychemotherapy without GnRH analogs; the age of the second group of postmenarche women who received GnRH analogs before polychemotherapy was 14.7–20 years; the third group were postmenarchal patients aged 15.9 to 20 years who received polychemotherapy without GnRH analog. In the second group, leuprolide acetate injection was given a month before and during chemotherapy. To accelerate ovarian regression, a subcutaneous injection of 0.2 mg was given simultaneously. In the first group, patients experience spontaneous menarche between the ages of

12–17.9 years, followed by a normal ovulatory cycle. Three patients experienced pregnancy. After resolution of bleeding, both groups who received GnRH analog experienced a normal ovulatory cycle. Two patients experienced pregnancy. The third group experienced hipoestrogen hypergonadotropic amenorrhea. In conclusion, GnRH analogs are given before and during chemotherapy to improve ovarian function and protect fertility.<sup>[2]</sup>

Prophylactic therapy with GnRH analog appears to be effective in reducing episodes of severe vaginal bleeding during periods of thrombocytopenia and may be able to avoid the side effects observed with conventional hormone therapy, such as hepatotoxicity and venous thromboembolism. Most of the experimental data result from the use of leuprolide therapy. Overall, the test has no consistency with regard to dosage, dosage form, and administration schedule. However, because the effects of these agents are independent of the dose of the drug, it may not be a factor that affects the clinical outcome when the minimum concentration of the drug is maintained.<sup>[3]</sup>

These data indicate that the use of GnRH agonist for the prophylaxis of menorrhagia associated with thrombocytopenia is especially beneficial to those who are expected to have a prolonged period of thrombocytopenia (i.e., duration >30 days). Thrombocytopenia is almost always the case in the population with hematological malignancies. The effects include expected leuprolide gonadal suppression, which leads to the discontinuation of estrogen therapy. Therefore, it may be wise to consider supplementation with calcium and vitamin D in patients who received leuprolide for 6 months or more in order to prevent loss of bone mineral density and to prevent osteoporosis.<sup>[4]</sup>

## Conclusion

GnRH analog administration must be considered in patients having uterine leiomyoma with acute leukemia condition. This agent can not only decrease the volume and bleeding complaint caused by tumors but also improve ovarian function and protect fertility before and during chemotherapy in leukemia.

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