

Course of Chronic Idiopathic Leukocytosis in Pregnancy

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ABSTRACT Leukocytosis is defined as having a leukocyte count over 10.000/mm³ in adults. Showing a progressive increase during pregnancy, peripheral leukocyte count may rise up to 20.000 – 30.000/mm³ at birth. A 32-year-old G2P1 patient whose leukocytosis continues for about 15 years, was referred to our hospital due to a WBC of 35.000/mm³ at gestational week 30. We found out that the patient's mean preconceptional WBC had been 15.000/mm³ and her mean WBC went up to 20.000/mm³ at early pregnancy. The patient was diagnosed with idiopathic leukocytosis by haematology department and LMWH Clexane 0.4 1x1 (**Enoxaparin** 0.4 ml, Sanofi- Aventis) was given subcutaneously during the course of pregnancy. Her WBC was 16.300/mm³ at postpartum day 10. The patient's WBC was 12.000/mm³ at postpartum week 6 (after using LMWH) and 14.800/mm³ at postpartum week 8. We think that when the results of the two pregnancies are examined in this rarely seen case and chronic idiopathic leukocytosis is monitored together with LMWH, the potential negative effects on maternal, fetal, and neonatal outcomes (due to predisposition to thrombotic process) can be diminished.

Keywords: Leukocytosis; LMWH-DOCA conjugate; pregnancy

Showing a progressive increase during pregnancy, peripheral leukocyte counts may rise up to 20.000-30.000/mm³ at birth. It has been demonstrated that this increased leukocyte count may be associated with increased estrogen and cortisol levels and that “leukocyte activation” occurs due to the phenotypic and metabolic changes in leukocytes.^{1,2} In this case report, we intend to show the antepartum and postpartum outcomes of a pregnant woman with chronic, idiopathic leukocytosis.

CASE REPORT

A 32-year-old G2P1 patient with a 15-year diagnosis history of high white blood count (WBC) (chronic idiopathic leukocytosis) was referred to our hospital due to a WBC of 35.100/mm³ at gestational week 30. We learned that the patient's mean preconceptional WBC had been 15.000/mm³ and that her mean WBC increased to 20.000/mm³ in early pregnancy. Her screening tests were negative, and fetal well-being tests were normal. No risk factors were found in her medical history or in her genetic, hematological, or radiological evaluations. She did have a history of liver hemanangioma and high cholesterol. She reported smoking about three cigarettes daily during her present pregnancy. An obstetric ultrasound scan showed a single vital fetus whose size was compatible with her gestational week. Dur-

ing the abdominal ultrasound taken to exclude hepatosplenomegaly (HSM), an image was seen suggesting a 5-mm stone in her gallbladder, but there was no HSM. As her WBC was $23.100/\text{mm}^3$ in the complete blood count that was done for checking purposes, her medical history was questioned in more detail. By haematology department for a period of approximately 15 years, an exact diagnosis of idiopathic leukocytosis could not be made. Her family history revealed that her sister had also a high leukocyte count. The peripheral smear performed at the initial visit showed that the leukocyte percentage distribution was within normal limits. In the flow cytometry that was carried out to exclude chronic lymphocytic leukemia (CLL) (as her total lymphocyte count was $5.000/\text{mm}^3$), there were no findings compatible with that condition (CD3, 7, 5, 19, 20, 22, 33, 34, 45). The results of the Philadelphia chromosome (Ph chromosome) analysis carried out for chronic myeloid leukemia (CML) were reported to be normal. Since no splenomegaly or lymphadenopathy was observed in her radiologic imaging and no infection or pathology to explain the leukocytosis was found, the patient was diagnosed with idiopathic leukocytosis. A low molecule weight heparin (LMWH) plus enoxaparin sodium (Clexane® 0,4 Anti-XaIu/0,4 MI) 1*1 therapy was started for her.

The patient's early pregnancy screening tests were known to be negative, and there were no findings in her antepartum well-being tests that would suggest gestational diabetes, hypertension, or fetal growth retardation in the course of her pregnancy. At gestational week 39, she was administered a cesarean delivery, due to a previous cesarean section.

The patient gave birth to a healthy baby girl weighing 2950 gram. The patient began LMWH therapy to last six weeks postpartum against thromboembolism prophylaxis. Her WBC was $16.300/\text{mm}^3$ at postpartum day 10. Because of the JAK2 V617F gene mutation analysis, which was recommended by the hematology department for any myeloproliferative disease, turned out to be negative, bone marrow aspiration and biopsy examination were proposed. The patient did not

agree with these procedures. The patient's WBC was $12.100/\text{mm}^3$ at postpartum week 6 (after using LMWH) and $14.800/\text{mm}^3$ at postpartum week 8.

DISCUSSION AND CONCLUSION

In adults as having a leukocyte count over $10,000/\text{mm}^3$; leukocytosis can be classified as neutrophilic, lymphocytic, monocytic, eosinophilic, or basophilic depending on its primary and secondary causes. Neutrophilic causes can be classified as false negativity, and with primary and secondary causes.³ Although pregnancy and delivery are known to be among the causes of neutrophilia, a differential diagnosis should consider secondary causes such as infection, inflammation, stress, heavy exercise, smoking, drug use (e.g., glucocorticoids, epinephrine), Cushing disease, hyperthyroidism, eclampsia, asplenia, heat stroke, and solid tumors; anomalies such as hereditary neutrophilia, myeloproliferative diseases; chronic myeloid leukemia (CML), chronic neutrophilic leukemia (CNL) and polycythemia vera (PV); and primary causes such as leukemoid reactions.³⁻⁷ The secondary causes were excluded from the differential diagnosis of our patient due to her leukocytosis diagnosis approximately 15 years prior. No findings were encountered in her pathological examination with respect to hepatosplenomegaly (HSM) and lymphadenopathy (LAP) to suggest infection, inflammation or rheumatologic diseases (i.e., rheumatoid arthritis, Crohn's disease and ulcerative colitis). Other parameters such as hematocrit and platelet values were normal in her hemograms. In our genetic, immunological, and hematological investigations towards primary causes, we did not find any splenomegaly, LAP, or genetic condition that can be associated with hereditary neutrophilia that may involve an autosomal dominant inheritance pattern.^{7,8} As for chronic myeloid leukemia, we did not encounter the presence of immature cells in the peripheral smear, Philadelphia chromosome (Ph chromosome), or a low LAP score that can be compatible with CML.^{8,9} We also did not observe Ph chromosome positivity, HSM, or high vitamin B12 and uric acid, which are associated with CML in our patient.⁸ The JAK2 V617F gene mutation analysis we carried out to

search for any myeloproliferative diseases (e.g., PV) turned out to be negative.¹⁰

The disease is diagnosed with total exclusion of other situations causes leukocytosis and family history. During the diagnosis, it should be shown that there are no infections, rheumatic diseases, inflammatory diseases and other hematological diseases that will lead to leukocytosis from the patient. Peripheral smear, jak-2 mutation, Ph chromosome and bone marrow examination should be performed in terms of excluding hematologic diseases. These tests can be performed immediately in patients with long-standing leukocytosis. The increase in leukocyte count and peripheral spread may be influenced by the gestational process and other tests are not affected by the gestational process.

As the patient did not agree to undergo the bone marrow aspiration and biopsy examination that were proposed upon receiving a negative result from her gene mutation analysis, we diagnosed her with chronic idiopathic leukocytosis. The presence of similar leukocytosis in her sister seemed to support this diagnosis. Although the secondary causes of leukocytosis improved after the targeted treatment, the primary causes, either congenital or idiopathic, prevailed from time to time.³

Our aim here was to evaluate the antepartum and postpartum results of a pregnant woman with chronic idiopathic leukocytosis in pregnancy where the immune function exhibits changes. Chronic idiopathic leukocytosis is a rare benign condition and does not require treatment. Since

there is not enough data related to the effect of disease on the pregnancy, it is thought that pregnancy loss due to thromboembolism is the only possible condition that the patient may have on the fetus and LMWH prophylaxis is given to prevent pregnancy loss. We think that, when the results of the two pregnancies are examined in this rarely seen case, and chronic idiopathic leukocytosis is monitored together with LMWH, the potential negative effects on maternal, fetal, and neonatal outcomes (due to predisposition to thrombotic process) can be diminished.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: İçel Anıl Saygı, Uğur Keskin; **Design:** İçel Anıl Saygı, Mehmet Ferdi Kınıcı, Selim Sayın; **Control/ Supervision:** Kazım Emre Kardeşahin, Ulaş Fidan; **Data Collection and/or Processing:** Selim Sayın, Mehmet Ferdi Kınıcı; **Analysis and/or Interpretation:** İçel Anıl Saygı, Uğur Keskin; **Literature Review:** İçel Anıl Saygı, Ulaş Fidan; **Writing the Article:** İçel Anıl Saygı, Uğur Keskin, Kazım Emre Kardeşahin.

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