Pregnancy in Cyclic Neutropenia

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Abstract
We present a patient with cyclic neutropenia who had two successful pregnancies during which the disease improved. Following one of the deliveries severe endometritis and wound dehiscence of the episiotomy developed and neonatal pemphigoid was seen.

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Introduction
Cyclic or periodic neutropenia is a rare hematological disease of unknown etiology. It can be considered a stem cell defect and is characterized by regular oscillations in blood neutrophil count, and in many cases is associated with oscillations of other circulating blood cells. The neutropenic episodes recurring at approximately 3-week intervals are accompanied by aphthous stomatitis, fever, malaise, adenopathy, and occasional cutaneous infections [1, 2].

There are only few reports on the association of cyclic neutropenia and pregnancy [3–6]. These data, however, suggest a high rate of obstetrical complication [5, 6]. At present we report a patient with cyclic neutropenia who had two successful pregnancies.

Case Report
A 32-year-old woman, gravida 1, para 0, presented at the antenatal clinic with the first pregnancy in 1977. She had had multiple past admissions to various hospitals because of the symptoms of well-documented cyclic neutropenia occurring at 28-day intervals. Her disease was characterized by furunculosis, stomatitis, fever and transient arthralgia often recurring in the premenstrum. Her past history included recurrent furunculosis first noted at 6 months of age, diphtheria at the age of 2 years, tonsillectomy at the age of 11, bronchopneumonia recurring at least once every year. At the age of 12, frequent episodes of aphthous stomatitis and gingivitis began to appear. At this time the white blood cell count (WBC) was found to be between 3.0 and 6.0 × 10⁹/1 and once with 12% neutrophils. Onset of the menstrual cycle occurred at the age of 12. One year later cyclic granulocytopenia was established and the onset of neutropenic period was found to coincide with the late premenstrum (fig. 1). Platelets, reticulocytes, hemoglobin level, erythrocyte sedimentation rate, liver and kidney function tests were normal. The Coombs’ tests were negative. The immunoelectrophoretogram detected an increase in the IgG fraction. Bone
marrow biopsy taken in the neutropenic period showed maturation arrest of the granulocyte series at the promyelocyte stage. At the age of 27, cholecystectomy was performed in the postmenstrum after the premenstrual agranulocytosis (0.7 × 10^9/1 neutrophils) and the previous bone marrow finding had been confirmed. During the severe symptoms the patient received vitamins, occasionally antibiotics and prednisolone. The severity of the disease varied and there were also premenstrual and menstrual periods when the patient was asymptomatic. Her family history was unremarkable.

During the first pregnancy the patient first experienced a decrease in the severity of symptoms, then they fully disappeared and the prenatal course was uneventful. During pregnancy she received vitamins and iron. The WBC ranged between 4.0 and 9.0 × 10^9/1, and the granulocyte count was always over 2.0 × 10^9/1. The parturition started at 38 weeks of gestation with premature rupture of the fetal membranes and 12.5 h later it was ended with vacuum extractor for secondary inertia. She was delivered of a 2,900-g male infant with normal hematological values who was afflicted by pemphigoid. The patient’s neutrophil count amounted to 4.2 × 10^9/1 on the day before delivery. Two days subsequently she had, however, fever and the wound of the episiotomy turned infiltrated and painful. WBC was 6.0 × 10^9/1, granulocyte count 3.6 × 10^9/1, erythrocyte sedimentation rate 120 mm/h. Tetracycline therapy was instituted. Over the next days the WBC increased to 20.0 × 10^9/1, leukemoid reaction accompanied with gross toxic granulation (myelocyte = 11%, metamyelocyte = 11%, band = 27%, segmented = 38%, lymphocyte = 11%, monocyte = 2%) appeared and endometritis purulenta developed. The hemoglobin was 9.0 g/dl, the platelet count 220 × 10^9/l. The therapy was supplemented with an aminoglycoside antibiotics, vitamins, uterotonics and transfusion of packed red cells. Following a 4-day period of septic fever the patient recovered but her episiotomy wound slowly healed subsequent to dehiscing. The mother as well as the baby were discharged in good health 3 weeks after delivery. The patient breast-fed for 3 months during which she had again stomatitis and fever.

![Fig. 1. Changes in the blood neutrophil count over a representative 60-day study period. M = menses. S = symptoms.](image-url)
Haifa year later she became pregnant again. The prenatal course was uneventful and she received iron, folic acid and vitamin B12 throughout the pregnancy. The patient did not experience the symptoms of her disease during the second pregnancy. The labor initiated at a zenith of the neutrophil count in the 41st week of gestation. A healthy female infant weighing 3,600 g was born whose hematological values were normal. Hemorrhage presented in the third stage of labor due to adherent placenta and a blood loss of 800 ml was measured. The patient received transfusion and antibiotics. The episiotomy wound healed well. Neither puerperal nor neonatal complication was seen. Throughout the pregnancy the WBC ranged between 3.0 and 6.0 × 10⁹/ℓ, with neutrophils over 1.5 × 10⁹/ℓ. The patient breast-fed for 4 months. Three weeks postpartum the stomatitis and malaise presented again.

Since then the patient has been suffering from the attacks of cyclic neutropenia but her children have been healthy. Meanwhile she had a further pregnancy which was electively terminated for nonmedical reason. At this time, immediately before the termination she was symptom free and had WBC of 2.8 × 10⁹/ℓ with 1.6 × 10⁹/ℓ neutrophils.

Discussion
According to the early observations there is a controversy as to whether the symptoms in a patient with cyclic neutropenia deteriorate or ameliorate during pregnancy [3–5]. Our report supports the observation of others that the symptoms of the neutropenia improve or disappear during the pregnancy [4–6], and on the other hand, the amplitude of oscillations in neutrophil count decreases during pregnancy [6]. This change in pregnancy can be attributed to the increased level of steroid hormones since similar finding has been noted during the administration of prednisolone [1], testosterone [7] or estrogen [6]. The first postpartum episode of neutropenia, however, was noted to be accompanied with more severe symptoms than the previous and subsequent episodes [4, 6]. We did not notice the postpartum worsening of the usual symptoms in the patient with cyclic neutropenia but a wound healing problem as well as an intrauterine infection that manifested in neonatal pemphigoid and severe puerperal endometritis were particular in the present case.

Fetal complications such as stillbirth and preterm birth reported by others [5,6] were not confirmed by our case report.

The present case seems to be peculiar because the neutropenic period coincided with the late premen-strum; furthermore, the puerperal endometritis and wound dehiscence were accompanied with a leukemoid reaction. Our report has demonstrated that the cyclic neutropenia improves during pregnancy but both postpartum maternal and neonatal complications can occur.

References