LETTER

A case report of neonatal alloimmune neutropenia in a neonate

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Dear Editor,

Neonatal alloimmune neutropenia (NAIN) is a rare but potentially life-threatening disease of the newborn. The incidence is about 0.5-2 per 1,000 live births. Anti-human neutrophil antigen (HNA) antibodies of the IgG immunoglobulin class are transported across the placenta and bind to the fetal neutrophils. It is unknown whether the antibodies only lead to increased destruction of mature cells or the inhibition of granulocytopoiesis. According to literature, neutropenia is usually self-limiting, and the duration varies from several weeks to 3-4 months. Neonates with neutropenia independently of the underlying disease are at high risk of developing severe and fulminant infections.

A male newborn, birth weight 3060g, was born from second uncomplicated pregnancy to a mother known to have hypothyroidism under treatment with levothyroxine, in the 38th week of gestation. The mother mentioned two previous abortions. Maternal toxoplasmosis, syphilis, varicella-zoster, parvovirus B19, rubella, cytomegalovirus, and herpes infection serology was negative, and her blood count was normal. The firstborn child was healthy. The newborn presented with pale skin and physical examinations revealed no abnormality. However, routine laboratory examinations due to neonatal jaundice on day three showed apart from G-6PD deficiency, severe neutropenia, white blood cells (WBC): 2,830 /μL (range: 3,800-10,500 /μL) with absolute neutrophil count (ANC): 100 /μL (range: 1,500-6,500 /μL). The values of other hematological and biochemical exams were within normal limits except for hemoglobin (9.3 g/dl; range: 14.0-18.0 g/dl). Blood and urine cultures were obtained, and the patient was put on antibiotics (ampicillin plus amikacin). Also, intravenous immunoglobulin (IVIG) was administered for two days (dose: 800 mg/kg/day). For the next two days, both WBC and ANC (3,000 /μL) increased. On days 5 and 9, recombinant human granulocyte colony-stimulating factor (rh-GCSF) therapy was given for three consecutive days (dose: 5 μg/kg/day). No further increase in ANC was noticed. Blood and urine cultures were negative. Ultrasonography of the abdomen and the heart, x-rays of the chest and the forearms, and chromosomal fragility testing were all normal. These exams were performed in order to exclude Shwachman-Diamond syndrome, osteopetrosis, transient erythroblastopenia of childhood, and anemia Fanconi. Due to the persisting neutropenia, a bone marrow study was performed, which revealed no pathological findings.

To further evaluate the etiology of neutropenia, blood samples were obtained from the patient and parents for granulocyte antibody screening. In the serum of the neonate was found to contain granulocyte specific antibodies against HNA-1b on CD16b. Polymerase chain reaction revealed that the antigen was encoded by FCGR3B*02 allele. This finding is typical for the diagnosis of neonatal immune neutropenia due to HNA antibodies. Patient ANC peaked at 1,500/μL on day 50 and was discharged home. Patient's neutropenia has been resolved at the age of four months, and currently, he is in excellent clinical condition.

This is the first report of NAIN in Greece in which the causative antibody was identified. According to international literature, a wide variety of antigens, including the HNA system, have been identified in NAIN. However, the antigens involved are unidentified in almost half of all cases. The majority of cases are mediated by antibodies that bind to HNA-1a, -1b, or -2a. Even though NAIN is a relatively rare condition, timely diagnosis can prevent severe complications. The issue of the choice and efficacy of specific therapy to increase the blood neutrophil count in the management of NAIN is not fully defined. Prophylactic antibiotic therapy, IVIG, and rh-GCSF are variable and may prove useful in some cases.

Conflict of interest

None.

References

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