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Hematological aberrations in Jacobsen syndrome

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Jacobsen syndrome is a rare genetic disorder associated with a deletion of the long arm of chromosome 11, which includes band 11q23.1 or 11q24.1. Genetic changes occur de novo in 85% of patients. The incidence of this disease is 1:100,000 births, and 70% of patients are girls [1]. One of the symptoms, occurring in 88.5% of patients, is thrombocytopenia, already present in newborns. Over time, the number of platelets increases, but the qualitative defect of thrombocytes remains, which can cause bleeding. These symptoms have been named Paris-Trousseau syndrome [1, 2]. Pancytopenia may also be observed from other hematological symptoms. Other symptoms include retardation of psychomotor development and intellectual retardation. Often, patients have a characteristic appearance of dysmorphic features [3]. Defects of the heart, kidneys or gastrointestinal tract have also been observed [4]. The described immunological deficits, such as a decrease in IgA, IgG and IgM, or even common variable immunodeficiency (CVID), may correlate with the described disease syndrome. Changes in T and B lymphocytes and natural killer cells have also been described [5]. People with Jacobsen syndrome have an increased incidence of cancer, which is characterized by greater aggressiveness and a poor prognosis.

We present the case of a boy from a first pregnancy with complicated respiratory infection and blood deficiency anemia, with birth weight 2,790 g, rated 10 points on the Apgar scale. On the 2nd day of life, the boy had thrombocytopenia 52 G/L and lymphopenia 1.91 G/L (Figures 1, 2). In addition, a conflict in the ABO blood group system was diagnosed. On the 18th day of life, the child was hospitalized because of jaundice. In follow-up studies, the number of thrombocytes progressed to 30 G/L. Alloimmune thrombocytopenia was excluded. The child was then given intravenous immunoglobulins (IVIg), which was followed by an increase in the platelet count to 80 G/L. A gradual decrease in hematological parameters was observed. A myelogram showed effective rich cell marrow with megaloblastic renewal. Blood count showed mild leukopenia and a platelet count of 85 G/L. Viral infections [human immunodeficiency virus (HIV), hepatitis C virus (HCV), hepatitis B virus HBV, parvovirus B19, human herpesvirus 6 (HHV6), adenoviruses, cytomegalovirus (CMV)] were excluded. Fanconi anemia, by the mitomycin C test for chromosomal fragility, was also ruled out. Neither anti-platelet nor anti-granulocyte antibodies were detected.

On the basis of the cytogenetic examination, monosomy of chromosomes 5 and 7, trisomy of chromosome 8, KMT2A rearrangement and *TP53* deletions were excluded. However, a deletion of a fragment of the long arm of chromosome 11 was found. In immunological tests, the levels of immunoglobulins IgG and IgA were normal, while that of IgM was slightly elevated. The distribution of lymphocyte subpopulations, both in percentage and absolute values, was pathological. We found a decreased percentage and a decreased absolute value of T-lymphocytes, predominantly CD3+CD4+, with an elevated percentage and a normal absolute number of B-lymphocytes. Facial dysmorphism, and a heart defect (patent foramen ovale) were noted. The patient was put under nephrological care due to dilation of the right renal pelvis and grade II vesicoureteral reflux.

On the basis of the overall picture, the patient was diagnosed with Jacobsen syndrome with the presence of Paris-Trousseau syndrome. In follow-up examinations, the platelet count ranged from 85–130 G/L. In addition, we observed leukopenia with CD3 lymphopenia, which are typical of this disease entity.

Thrombocytopenia, according to its definition, is a decrease in the platelet count below 100 G/L. It is the most frequent bleeding disorder in children. One of its most common forms is immune thrombocytopenia (ITP), with an incidence of 1.9–6.4 per 100,000 births [6]. In the neonatal

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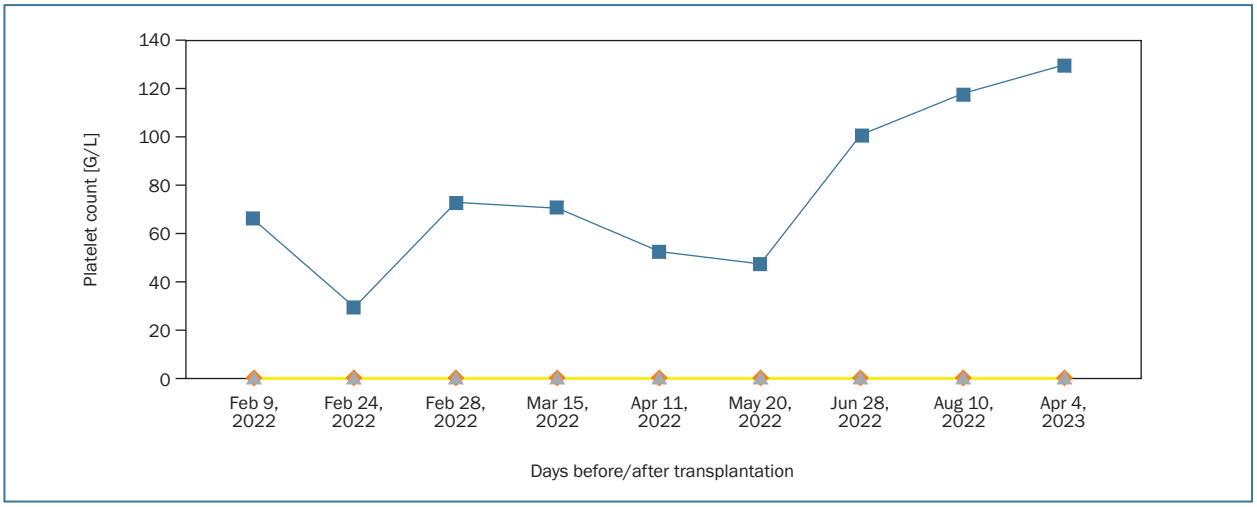

Figure 1. Platelet count depending on date of observation

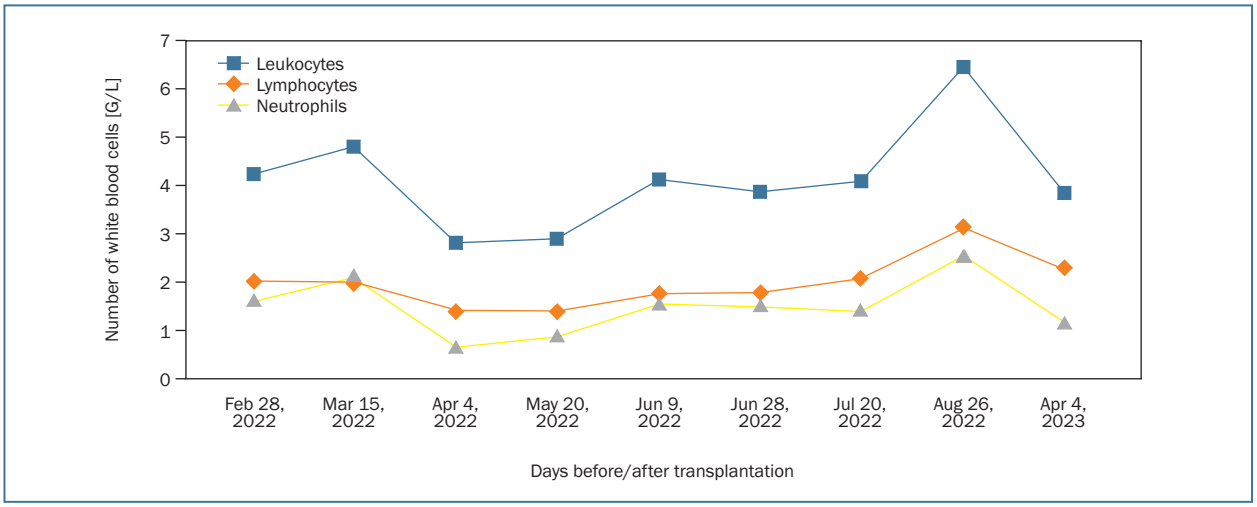

Figure 2. Number of white blood cells, including lymphocytes and neutrophils, depending on date of observation

period, alloimmune thrombocytopenia associated with antibodies in the mother's bloodstream is most common [6].

Jacobsen syndrome occurs with a frequency of 1:100,000 births. Diagnosis is based on clinical symptoms such as facial dysmorphism, intellectual development disorders, thrombocytopenia and genetic tests [1–4]. In our patient, from birth we observed facial abnormalities and thrombocytopenia. The lowest platelet count was 30 G/L, which increased with age to 130 G/L. We did not observe any life-threatening bleeding in him [7]. On this basis, we recognized Paris-Trousseau syndrome. In addition, we also recognized combined immunodeficiency, which is described in the literature as a syndromic syndrome of congenital immunodeficiencies [4]. Despite the descriptions of intellectual development disorder, our patient's psychomotor development is normal, and requires only speech therapy support. The final diagnosis of the disease was genetic testing showing a typical change for Jacobsen syndrome.

In conclusion, Paris-Trousseau syndrome is characteristic for Jacobsen syndrome. Thrombocytopenia associated with lymphopenia may be a manifestation of combined immunodeficiency syndrome, which we can detect in diagnostic tests. Both abnormalities are common in the deletion of chromosome 11.

Authors' contributions

AJ-G — sole author.

Conflict of interest

The author declares no conflict of interest.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

References

1. Mattina T, Perrotta CS, Grossfeld P. Jacobsen syndrome. Orphanet J Rare Dis. 2009; 4: 9, doi: 10.1186/1750-1172-4-9, indexed in Pubmed: 19267933.
2. Favier R, Douay L, Esteva B. A novel genetic thrombocytopenia (Paris--Trousseau) associated with platelet inclusions, dysmegakaryopoiesis and chromosome deletion AT 11q23. C R Acad Sci III. 1993; 316(7): 698–701, indexed in Pubmed: 8019893.
3. Nacinovich R, Villa N, Redaelli S, et al. Interstitial 11q deletion: genomic characterization and neuropsychiatric follow up from early infancy to adolescence and literature review. BMC Res Notes. 2014; 7: 248, doi: 10.1186/1756-0500-7-248, indexed in Pubmed: 24742288.
4. Penny LA, Dell'Aquila M, Jones, MC. Clinical and molecular characterization of patients with distal 11 q deletions 1995 am J. Am J Hum Genet. 1995; 56(3): 676–683, indexed in Pubmed: 7887422.
5. Dalm VA, Driessen GJ, Barendregt BH, et al. The 11q terminal deletion disorder Jacobsen syndrome is a syndromic primary immunodeficiency. J Clin Immunol. 2015; 35(8): 761–768, doi: 10.1007/s10875-015-0211-z.
6. Donato H. Neonatal thrombocytopenia: a review. I. Definitions, differential diagnosis, causes, immune thrombocytopenia. Arch Argent Pediatr. 2021; 119(3): e202–e214, doi: 10.5546/aap.2021.eng.e202, indexed in Pubmed: 34033425.
7. Ichimiya Y, Wada Y, Kunishima S, et al. 11q23 deletion syndrome (Jacobsen syndrome) with severe bleeding: a case report. J Med Case Rep. 2018; 12(1): 3, doi: 10.1186/s13256-017-1535-5, indexed in Pubmed: 29307309.