Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 10/23/2019
Approved on: 01/30/2020

CASE REPORT

Congenital neutropenia: a case report

Ana Luiza Augusto[1], Carmen Lucia Santos[1], Jucilane Lima Ferruzi[1]

Keywords:
Neutropenia, Infection, Congenital Abnormalities.

Abstract

The term congenital neutropenia embrace a family neutropenic disorders, that can be permanent or intermittent, severe or pleasant, which can cause repercussions in other organ systems. Neutropenia can range from mild pyogenic infections to life-threatening sepsis, and each successive infection can leave permanent sequelae. The risk of infection is approximately inversely proportional to the circulating polymorphonuclear neutrophil count and is particularly high at counts below 0.2G/l. About half of the forms of congenital neutropenia, without extrahematopoietic manifestations and normal adaptive immunity, are due to mutations in neutrophil elastase. Some patients have severe permanent neutropenia and frequent infections early in life, while others have mild intermittent neutropenia. The difficulty in suspected diagnosis congenital neutropenia and, consequently, the time to start treatment can lead to infectious complications and put the patients' life at risk.

[1] University Hospital of the Federal University of Grande Dourados, Residency of Pediatrics - Dourados - MS - Brazil.

Correspondence to:
Ana Luiza Augusto.
Hospital Universitário da Universidade Federal da Grande Dourados. R. Ivo Alves da Rocha, 558 - Altos do Indaiá, Dourados/MS, 79823-501.
E-mail: ana_luizaga@hotmail.com

Residência Pediátrica; 2021: Ahead of Print.
DOI: 10.25060/residpediatr-2021.v11n3-217

This work is licensed under a Creative Commons Attribution 4.0 International License.

INTRODUCTION

Congenital neutropenia is a rare disease, with different degrees of heredity, which can be classified as mild, moderate or severe[1]. It usually manifests with recurrent infections from the first years of life, ranging from skin abscesses to sepsis[2].

The diagnosis is made based on clinical suspicion, associated with cytopenia demonstrated in laboratory tests and bone marrow aspiration, which shows the absence of mature neutrophils and interrupted maturation, especially in the promyelocyte phase, in addition to the molecular diagnosis[3].

The treatment aims to provide adequate antibiotic therapy for bacterial infections and the use of recombinant human hematopoietic growth factors, to increase the absolute number of defense cells, and, in the last case, a bone marrow transplant, thus ensuring better survival to the patient. patient[4].

CASE REPORT

Patient, female, born on July 17, 2013. She was admitted to the Pediatric Emergency Care (PAP) of the University Hospital of the Federal University of Grande Dourados (HU - UFGD) on 05/30/2017, aged 3 years and 10 months old, coming from Sete Quedas - MS, due to the presence of papule in the infra-umbilical region, pruritic, for 5 days, associated with pain, erythema and increase in local temperature, in addition to abdominal wall edema. Within 72 hours of onset, the patient developed oliguria and anasarca. She sought care at the hospital in the city of origin and was referred to the HU-UFGD.

Upon admission to the PAP, the patient had a regular general condition, pale 2+/4+, hydrated, eupneic, afebrile, with pain facies; rhythmic and normophonetic heart sounds, in two beats, without audible murmurs; vesicular murmurs present globally, without adventitious sounds; abdomen with the presence of cellulitis in a band in the region of the umbilical scar, with phlogistic signs.

The mother reported a previous medical history of numerous skin infections, requiring hospitalization for antibiotic therapy. At 15 months, he was hospitalized for treatment of pneumonia, in addition to episodes of skin infection and stomatitis treated on an outpatient basis.

The diagnostic hypothesis of cellulitis secondary to an accident by a venomous animal was raised; laboratory tests were collected (Table 1) and admitted to a pediatric ICU, where empirical antibiotic therapy was started with Ceftriaxone and Clindamycin. Due to the worsening of the condition, the antibiotic was changed to Piperacillin+tazobactam and, later, to Vancomycin and Meropenem.

The patient was transferred to the pediatric ward, where the lesion worsened. It was necessary to perform debridement of the periumbilical lesion, which did not show a purulent lesion, but fat necrosis. Due to the persistence of the laboratory worsening, antibiotic therapy was changed, at the suggestion of the infectology team, for Imipenem.

Table 1. Exams requested after admission to the PAP.

BLOOD COUNT		
HEMOGLOBIN	7.20 g/dL	
HEMATOCRIT	21.20%	
LEUKOCYTES	10.780/mm³	Rods: 13%,
		Neutrophils: 30% (3234/mm³)
		Eosinophils: 0
		Lymphocytes: 35%
		Monocytes: 21%

Source: Patient's chart.

After ten days of treatment and with improvement of the abdominal lesion, the patient then evolved with significant leukopenia, associated with severe neutropenia (Table 2), and Filgrastim was started. Even so, the evolution continued with progressive worsening of neutropenia. She was evaluated by the pediatric hematology team, and a hypothesis of drug-induced neutropenia was raised. Thus, Imipenem was discontinued and control tests performed within 48 hours , which maintained the presence of neutropenia.

Table 2. Exams requested in the Pediatric Ward.

BLOOD COUNT		
HEMOGLOBIN	10.20 g/dL	
HEMATOCRIT	30.40%	
LEUKOCYTES	6.900/mm³	Rods: 0%,
		Neutrophils: 2% (138/mm³)
		Eosinophils: 9%
		Lymphocytes: 69%
		Monocytes: 20%

Source: Patient's chart.

Due to improvement and clinical stability, the patient was discharged on 07/28/19, with outpatient return for investigation of the condition.

On 08/30/19 a bone marrow biopsy and myelogram were performed. The myelogram showed diluted bone marrow, with normocellular fragments, megakaryocytes in normal number and without morphological alterations, granulocytic series with maturation arrest in myelocytes and with the presence of immature cells in reduced number, erythroid series without morphological alterations, lymphocytic series without morphological alterations. Biopsy showing normocellular bone marrow for age, with discrete dysplastic alterations, slight increase in young forms of the granulocytic series, moderate eosinophilia, absence of fibrosis or siderosis, suggested immunohistochemistry.

The patient developed fever after the bone marrow biopsy procedure. Upon physical and laboratory examination, acute otitis media was diagnosed, associated with febrile neutropenia, and hospitalization was carried out for treatment with antibiotics for 10 days.

On 10/08/2017, he developed pneumonia and febrile neutropenia, requiring a new hospitalization for antibiotic therapy for 10 days. On 11/01/2017, immunohistochemistry was performed with inconclusive results. The patient was then referred for investigation at the Brazilian Group of Myelodysplastic Syndrome at the Hospital do Câncer de Barretos - SP, where the final report was: congenital neutropenia.

Due to the risk of progression to myelodysplasia, the patient was followed up with the pediatric hematology team. It was decided not to initiate recombinant hematopoietic growth factors, as they would present more risks than benefits, since the infections manifested were not serious and could, most of them are treated with antibiotic therapy on an outpatient basis.

DISCUSSION

Congenital neutropenia is a condition that makes affected individuals prone to recurrent infections. People with this condition have a deficiency of neutrophils, and given the age of the patient in this case, the values should be between 1,500 and 8,000/mm³, and had a value of 3234/mm³ when she was admitted to the Pediatric Emergency Department - different from what is expected according to the literature referring to the pathology - later evolving to 138/mm³ and keeping a count always below 1000/mm³.

In addition to quantitative abnormalities, many patients with congenital neutropenia show qualitative neutrophil disorders. A prominent finding in severe congenital neutropenia is the so-called "maturation arrest" in the differentiation of neutrophils, that is, patients present a persistent condition, as their progenitor cells manifest proliferative efficiency, however, there is an imperfection in the timing of the formation of promyelocytes for myelocytes[5].

The preferred sites of infection are highly variable, however, the most frequent are the skin and mucosa; ear, nose and throat; and the lungs. Stomatologic infections are very frequent after 2 years of age in patients with deep central neutropenia and are characterized by erosive, hemorrhagic and painful gingivitis associated with papules (oral boils similar to aphthae) of the tongue and cheek mucosa[2].

Congenital neutropenia is a condition that makes affected individuals prone to recurrent infections, being apparent at birth or soon after, being a rare disorder (1 to 2 per million)[6] that has multiple forms of genetic inheritance and may be autosomal dominant (most common), autosomal recessive (classical Kostmann syndrome), X-linked recessive and sporadic[7].

Among the most used treatments in congenital neutropenia, antibiotics are used, especially in severe cases that develop fever. Laboratory blood tests should be performed to identify the possible cause of the infection and during this time the patient is treated with intravenous antibiotics. Granulocyte Colony Stimulating Factor (G-CSF) which is administered via subcutaneous injections, stimulates bone marrow production and neutrophil maturation. The goal is to consistently bring the neutrophil count back to normal to prevent infections[4].

However, in the Clinical Protocol and Therapeutic Guidelines of the Ministry of Health (2010) it was observed that the use of Granulocyte Colony Stimulating Factor in patients with congenital neutropenia and Shwachman-Diamond syndrome may present a higher risk of developing myelodysplasia and myeloid leukemia. acute[8]. That is why the pediatric clinical staff chose not to submit the patient to this treatment, since most of the infections presented could be treated with antibiotic therapy.

CONCLUSION

Congenital neutropenia is a rare disease whose diagnosis is a challenge for pediatricians, since numerous differential diagnoses need to be ruled out, such as HIV, Leishmaniasis, Leukemia and drug reaction. In addition, it is a disease that requires strict monitoring of the patient, in view of the severity with which it can evolve and its possible complications.

REFERENCES

1. Skokowa, J.; Dale, D.C.; Touw, I.P.; Zeidler, C.; Welte, K. Severe congenital neutropenias. Nat Rev Dis Primers, v. 8, n. 3, 2017.
2. Stoppler, M.C. Neutropenia Symptoms, Causes, Levels, Defined, & Treatment. Informative Report, 2017.
3. Donadieu, J.; Fenneteau, O.; Beaupain, B.; Mahalaoui, N.; Chantelot, C.B. Congenital neutropenia: diagnosis, molecular bases and patient management. Orphanet J Rare Dis, v. 6, p. 1-28, 2011.
4. Yates, A. Severe congenital neutropenia. Nat Rev Dis Primers, v. 3, p. 17-32, 2017.
5. Burns DAR, Silva MAA. Imunodeficiências congênitas ou primárias. In: Burns DAR, Silva MAA, eds. Genética baseada em evidências – síndromes e heranças [Internet]. 2017; [acesso em 2019 Fev 03]; 593. Disponível em: https://docplayer.com.br/35014162-Imunodeficiencias-congenitas-ou-primarias-dennis-alexander-r-burns-monica-de-araujo-alvares-da-silva.html#show_full_text
6. Santos, L.F.M.; Mukai, A.O.; Bertoli, C.J.; Fernandes, T.A.R.; Suetugo, C.P. Relato de um caso de neutropenia congênita grave em um lactente jovem. Rev Paul Pediatr, v. 29, n. 4, p. 680-684, 2011.
7. Boztug, K.; Welte, K.; Zeidler, C.; Klein, C. Congenital neutropenia syndromes. Immunol Allergy Clin North Am, v. 28, p. 259-275, 2008.
8. Brasil. Ministério da Saúde. Consulta Pública Nº 7, de 11 de fevereiro de 2010. Protocolo clínico e diretrizes terapêuticas anemia aplástica, mielodisplasia e neutropenias constitucionais e mielodisplasia uso de fatores estimulantes de crescimento de colônias de neutrófilos.