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Kostmann's Neutropenia: A Case Report

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Abstract

Kostmann syndrome, or severe congenital neutropenia, is a rare condition in children marked by a neutrophil count of less than 500/mm^3. This congenital agranulocytosis, an autosomal recessive genetic disorder, is often first identified by a neonatal infectious syndrome. The deficiency in neutrophils increases susceptibility to bacterial and fungal infections. Prior to the availability of hematopoietic growth factors, the disease was associated with significant morbidity and early mortality. We present the case of a 17-month-old boy who was admitted to the pediatric emergency department at Hassan II University Hospital in Fes with skin abscesses.

Keywords

Kostmann Syndrome, Severe Congenital Neutropenia, Skin Abscesses

1. Introduction

Congenital neutropenias are a heterogeneous group of hereditary diseases, with the most common being severe congenital neutropenia or infantile agranulocytosis, first described over 50 years ago by Rolf Kostmann [1]. This rare autosomal recessive disorder is characterized by neutropenia observable at birth, with a low neutrophil count (<500/mm^3) and no associated lymphocyte deficit. Clinically, it presents with recurrent bacterial infections, including pneumonia, skin abscesses, deep organ abscesses, and septicemia [1] [2]. Previously rapidly fatal, the prognosis has improved somewhat with the use of granulocyte colony-stimulating factor (G-CSF). We will report the case of a young patient with Kostmann syndrome and compare our findings with those in the literature.

2. Clinical Case

A 17-month-old boy was admitted in 2020 to the pediatric department of Hassan II University Hospital in Fes for the management of skin abscesses that had

appeared two days prior, accompanied by fever. He is the only child of his parents, who are not consanguineous. His medical history includes treatment for three episodes of urinary tract infections.

On general examination, the infant appeared in relatively good condition, conscious, febrile at 39˚C, with a respiratory rate of 35 cycles/min, and a heart rate of 107 beats/min. There was a growth delay, with a weight of 7 kg (−3 standard deviations [SD]) and a height of 76 cm (−2 SD). On skin examination, there were multiple erythematous nodules with a rounded shape, regular contours, and firm, fluctuating consistency. Some nodules had fistulized to the skin and were covered in hemorrhagic crusts, located on the lower abdomen and in the left supraclavicular fossa (**Figure 1**). Oral examination was normal. Both pleuropulmonary and the otorhinolaryngological examinations revealed no abnormalities. Examination of other systems showed no particularities.

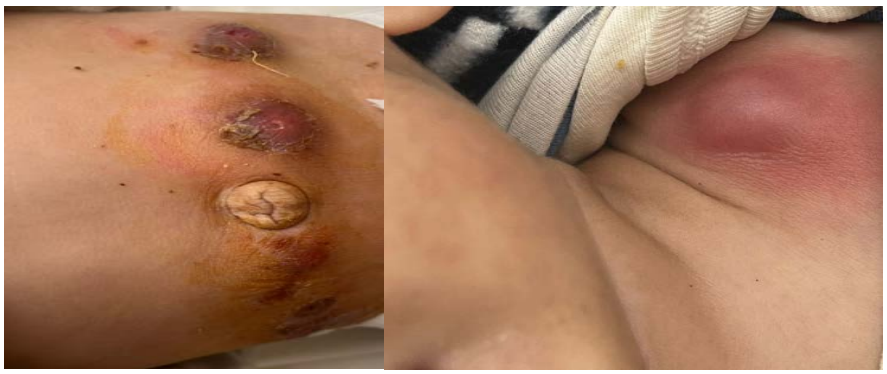

Figure 1. The locations of skin abscesses in our patient.

The biological assessment showed a complete blood count (CBC) with hypochromic microcytic anemia, hemoglobin (Hb) at 5.6 g/dL (11.1 - 12.9 g/dL), mean corpuscular volume (MCV) at 48 fL (72 – 87 fL), mean corpuscular hemoglobin concentration (MCHC) at 31 g/dL, and reticulocyte count at 60,000/µL. Severe neutropenia was present with a neutrophil count at 80/µL (3,500 - 6,000/µL), normal lymphocytes at 4,120/µL, and monocytes at 2,450/µL. Platelet count was 473,000/µL, with no blasts on the blood smear. C-reactive protein (CRP) was 95.9 mg/L. Neutropenia was consistent across all CBCs. Immunoglobulin levels were normal for the age (IgA at 3.47 g/L, IgM at 3.03 g/L, IgG at 24.32 g/L), and serology for acquired immunodeficiency was negative. Lymphocyte subset testing was not performed due to family financial constraints. A bone marrow examination revealed erythroblastic hyperplasia with no significant cytological abnormalities and hypoplasia of the granulocyte lineage, with evidence of maturation blockage and 15% blasts.

Therapeutic management included ceftriaxone (100 mg/kg/day) and vancomycin (10 mg/kg every 6 hours) for 15 days. The patient's condition improved with defervescence, healing of skin lesions, and normalization of infectious markers including CRP, though neutropenia persisted. Following the infection episode, the

patient was started on G-CSF (Neupogen®) at 5 µg/kg/day. Genetic testing was recommended for the family. Five months later, the patient presented with pneumonia and unfortunately, the outcome was marked by death.

3. Discussion

Kostmann syndrome is an autosomal recessive condition with a prevalence of 1 to 1.7 cases per 333,300 people, corresponding to an annual incidence of approximately 1 case per 250,000 live births [3]. At present, severe congenital neutropenia has been linked to mutations in only four genes. These mutations can be categorized into two main groups. The first group is characterized by mutations in the ELA-2 gene, which are associated with severe neutropenia (<200/mm^3). The second group is more varied and does not involve ELA-2 mutations; instead, mutations in the GFI1 gene, the HAX1 gene, and activating mutations in the Wiskott-Aldrich syndrome (WASP) gene have been found. These four types of mutations follow different inheritance patterns: autosomal dominant for ELA-2 and GFI1, autosomal recessive for HAX1, and X-linked recessive for WASP. All these mutations result in a reduced production of neutrophil [3].

It is characterized by a defect in myelopoiesis with a circulating neutrophil count of less than 500/mm^3 [4]. This deficiency in neutrophils, which are essential for host defense, results in recurrent bacterial and/or fungal infections. The most common sites of these infections are cutaneous-mucosal, odontostomatological, ENT, pulmonary, and gastrointestinal. Upon discovering such a presentation, a comprehensive biological assessment is necessary to rule out several differential diagnoses, including lymphocytic immunodeficiencies and autoimmune neutropenias.

Bone marrow examination reveals a blockage in granulopoiesis, with halted maturation at the promyelocyte and myelocyte stages [4]. Genetic counseling is essential and should consider both the family history and the responsible mutation. Prenatal diagnosis can be offered if the genotype is known.

Each infectious episode warrants hospitalization for better infection control. Indeed, this disease exposes children to severe infections, both systemic and localized, leading to death before the age of two in 40% to 50% of cases prior to the introduction of granulocyte growth factors. These growth factors help correct neutropenia in over 90% of cases [5]. Thus, Carlsson *et al.* demonstrated that treatments with recombinant human hematopoietic growth factors, such as glycosylated (lenograstim) or non-glycosylated (filgrastim) granulocyte colony-stimulating factor (G-CSF), significantly extend life and improve the quality of life for patients [6]. These growth factors help restore neutrophil levels close to normal, thereby reducing the risk of infections. The rate of severe infections is now around 10% over a 10-year period.

The vital and functional prognosis closely depends on the quality of care, the promptness of treatment during a severe infection, and the possibilities of a bone marrow transplant, especially in cases of malignant transformation.

4. Conclusion

Kostmann syndrome is a rare disease whose prognosis is significantly influenced by the quality of care, the speed with which severe infections are treated, the use of growth factors, and the possibility of a bone marrow transplant, especially in cases of malignant transformation.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Kostmann, R. (1956) Infantile Genetic Agranulocytosis (agranulocytosis Infantilis Hereditaria) a New Recessive Lethal Disease in Man. *Acta Paediatrica*, **45**, 309-310. https://doi.org/10.1111/j.1651-2227.1956.tb06875.x

[2] Dale, D.C., Cottle, T.E., Fier, C.J., Bolyard, A.A., Bonilla, M.A., Boxer, L.A., *et al.* (2003) Severe Chronic Neutropenia: Treatment and Follow-up of Patients in the Severe Chronic Neutropenia International Registry. *American Journal of Hematology*, **72**, 82-93. https://doi.org/10.1002/ajh.10255

[3] Boisramé-Gastrin, S., Lelièvre, J., Le Moine, P. and Pers, J. (2010) Syndrome de Kostmann et cavité buccale: Présentation d'un cas et revue de la littérature. *Médecine Buccale Chirurgie Buccale*, **16**, 45-51. https://doi.org/10.1051/mbcb/2009037

[4] Carlsson, G., Andersson, M., Pütsep, K., Garwicz, D., Nordenskjöld, M., Henter, J., *et al.* (2006) Kostmann Syndrome or Infantile Genetic Agranulocytosis, Part One: Celebrating 50 Years of Clinical and Basic Research on Severe Congenital Neutropenia. *Acta Paediatrica*, **95**, 1526-1532. https://doi.org/10.1080/08035250601087607

[5] Dommergues, J.-P. and Bader-Meunier, B. (2002) Les Cytopénies Constitutionnelles. *Journal de Pédiatrie et de Puériculture*, **15**, 401-409. https://doi.org/10.1016/s0987-7983(02)83115-2

[6] Carlsson, G. and Fasth, A. (2001) Infantile Genetic Agranulocytosis, Morbus Kostmann: Presentation of Six Cases from the Original "Kostmann Family" and a Review. *Acta Paediatrica*, **90**, 757-764. https://doi.org/10.1080/080352501750315663