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CASE REPORT

Case Report: Vesiculopustular Eruption of Transient Myeloproliferative Disorder of the Newborn with Down Syndrome

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Abstract

Neonates with Down Syndrome (DS) have a greater predisposition to Transient Myeloproliferative Disorder (TMD), a hematologic disorder with transient proliferation of immature cells in peripheral blood and bone marrow. Some neonates with TMD present with skin manifestations characterized by diffuse erythematous papules, with crusts, vesicles and pustules, usually with early and prominent facial involvement. Despite the spontaneous remission of TMD over several months, some cases may need support care and, occasionally, chemotherapy. It is described the case of a newborn with Down Syndrome phenotype, male, that manifested such characteristics in the fifth day of life, and the instituted propaedeutics in a Neonatal Intensive Care Unit. The diagnosis is both clinical and laboratorial, and therefore was based in typical features. The used treatment involved conservatory measures of skin and mucosal care, avoiding trauma. It was observed an improvement of all lesions within one month of life. As a result, it is demonstrated the importance of differential diagnosis given the need for regular clinical follow up and eventually chemotherapy.

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INTRODUCTION

Neonates with Down syndrome (DS) have a unique predisposition for developing Transient Myeloproliferative Disease (TMD), a rare clonal myeloproliferation characterized by peripheral leukocytosis that can progress to acute myeloid leukemia (AML) or acute megakaryocytic leukemia[1]. Incidence varies from 4% to 10% in newborns with DS. The disease resolves spontaneously in most cases, but 20% of the affected newborns subsequentially develop acute leukemia, generally with characteristics of megakaryoblastic leukemia[2].

Studies and genetic research have revealed that most cases of TMD are not associated with somatic GATA1 mutations, initially found in patients with DS[3]. Only 5% of newborns have cutaneous manifestations of TMD in the form of diffuse erythematous papules with crusts, vesicles and pustules, generally with early prominent facial involvement[2]. The first case was reported by Schunk and Lehman in 1954[4].

This article reports the case of a newborn with a phenotype consistent with Down Syndrome, who presented with the classic signs of TMD while treated at a Neonatal Intensive Care Unit.

CASE REPORT

This report describes the case of a male full-term newborn with a phenotype consistent with Down Syndrome, birth weight of 2,665g, appropriate for gestational age, Apgar scores of 8/9, born from an elective cesarean section, provided adequate prenatal care. His mother had a history of gestational hypothyroidism and sporadic hypertensive spikes. The infant and his mother were discharged 72 hours after birth. When he was taken for a reassessment five days after birth, vesicular and pustular lesions were observed on both sides of the malar region of the face. A specific antibiotic regimen was started based on a diagnostic hypothesis of neonatal impetigo. Blood workup revealed a white blood cell count of 50,000 and no anemia, thrombocytopenia or presence of blasts; his liver function was normal; CSF analysis was also normal.

The lesions on the face grew in size and number, maintaining a vesicular-pustular characteristic, with some developing crusts (Figures 1 and 2). The hypothesis of neonatal herpes was considered and the infant was started on acyclovir despite the lack of laboratory confirmatory tests for herpes simplex. A Tzanck test did not show cytopathic changes consistent with viral infection.

Lack of improvement from the lesions, presence of a DS phenotype, and blood workup suggestive of myeloproliferative disease led to the consideration of transient myeloproliferative disease (TMD) and the adoption of an expectant approach to management. The newborn was discharged after 16 days of hospitalization and improved completely from the lesions by the time he was one month old.



Figures 1 and 2: Vesicular-pustular lesions in the malar region.

DISCUSSION

Neonates DS are more predisposed to developing TMD, a hematological disorder with transient proliferation of immature cells in peripheral blood and bone marrow. TMD can affect up to 10% of individuals with DS and is found almost exclusively in newborns and infants with trisomy 21. It can be indistinguishable from congenital leukemia, with spontaneous remission being the biggest difference between the two. However, up to 20% of patients with TMD may develop acute megakaryoblastic leukemia[5].

Mutations acquired in exon 2 of the gene encoding the transcription factor GATA1, located on the X chromosome, have been identified in leukemic blasts in the majority of patients with myeloid leukemia and transient leukemia, causing the exclusive expression of a shorter GATA1 protein (GATA1s). Two studies demonstrated that GATA1s does not result in leukemia in the absence of trisomy 21 in humans and mice. However, there is no established relationship between trisomy 21 and oncogenic GATA1s and which factors drive the transition from pre-leukemia to myeloid leukemia in only a portion of the affected children[6].

A small proportion of patients with DS and TMD develop skin rashes, referred to mainly as papules, vesicles and pustules[5]. Approximately 1 in 20 patients with TMD will develop a large number of pustular vesicles and/or papulovesicular rashes, usually starting on the face and later involving the trunk or extremities, in addition to areas of friction with the skin. There is a chronological coincidence between the onset of skin rashes and the development myeloproliferative disease. Although megakaryoblasts are not typically present in the epidermis, if vesicles are present, a positive myeloperoxidase stain of vesicular fluid may identify blast cells and aid in diagnosis[7].

Patients with DS and TMD may not present altered white blood cell counts. This is why peripheral blood tests

might be needed, particularly if skin lesions appear, in which a significant proportion of blasts may have irregular nuclei, open chromatin and cytoplasmic blebs, suggesting the presence of megakaryocytic blasts. Previous studies have demonstrated that blasts positive for cell surface marker CD34 and with partial co-expression of CD41 are associated with early megakaryocytic differentiation. Additional findings of CD117, CD7, CD56 and CD33 expression with low myeloperoxidase positivity are consistent with TMD or acute megakaryoblastic leukemia. When such factors are present, diagnostic investigation must include patient age, clinical condition, and the presence or absence of Down Syndrome, suggested by typical facies and confirmed with karyotyping[8].

Differential diagnosis considering benign conditions such as erythema toxicum neonatorum and transient neonatal pustular melanosis is required. The lesions may also arise from systemic diseases, exposure to infection or a family history of dermatoses, which call for in-depth investigation. The main pathogens include the herpes simplex virus, varicella-zoster virus, Staphylococcus aureus, streptococci, Listeria and congenital syphilis[8].

Skin rashes resolve spontaneously, without scars, simultaneously with the resolution of TMD, generally between one and two months of age, with an average of 6.5 weeks[2]. Although TMD spontaneously resolves over several months, support care may be required in some cases and a few patients may need chemotherapy. Symptomatic neonates with TMD, especially those with high blast counts or liver dysfunction, may benefit from low-dose cytosine arabinoside (cytarabine) due to the sensitivity of myeloblasts to TMD in this treatment[5]. Additionally, patients prescribed chemotherapy are at risk of developing tumor lysis syndrome. Treatment includes aggressive hydration and the drug rasburicase, used in the prophylaxis of acute hyperuricemia with the aim of avoiding kidney failure[7].

CONCLUSION

Although rare, the pustular rashes seen in TMD must considered in differential diagnosis to rule out other benign and infectious skin diseases, so that in-depth investigation is conducted and proper treatment prescribed. Chemotherapy is needed in cases where the disease does not resolve with expectant management.

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