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Case Report

An unlucky WHIMsical child – A case report

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ABSTRACT

Immunodeficiency in children often has the worst prognosis and there are varied primary and secondary causes for immunodeficiency. Warts Hypogammaglobulinemia, Infections, and Myelokathexis (WHIM) syndrome is a congenital immune deficiency that increases the likelihood of human papillomavirus infection (Warts), a low white blood cell count, hypogammaglobulinemia, and bone marrow myelokathexis. We present the case of a 3-year-old child brought by an orphanage caretaker with a history of recurrent swelling in both eyelids, multiple skin lesions all over the body, and recurrent respiratory tract infections. The child has been treated with native medications elsewhere with no improvement noted. Work up done for immune deficient states and bone marrow evaluation revealed myelokathexis with neutropenia/lymphopenia which made the possibility of WHIM syndrome. Treatment with colony stimulating factor has been initiated but could not be continued due to financial constraints. This report emphasis on the need for work-up to make early diagnosis and intervention of the disease as such than treating only their manifestations.

Keywords: Warts hypogammaglobulinemia, infections, myelokathexis syndrome, Warts, Hypogammaglobulinemia, Myelokathexis, Stye, Infections

INTRODUCTION

WHIM syndrome includes warts, hypogammaglobulinemia, infections, and myelokathexis among other manifestations. It is an autosomal dominant condition with a defect in the chemokine receptor (CXCR4). The abnormality in the chemokine is poorly understood and still awaits conclusive evidence. The clinical features and presentation are varied, and most patients during early childhood would have suffered from recurrent sinusitis, respiratory tract infections, cellulitis, urinary tract infections, and abscesses.[1,2] *Streptococcus*, *Staphylococcus*, *Haemophilus*, and *Klebsiella* are some of the most common organism causing infections. Immunodeficiency is attributed to neutropenia/lymphopenia, hypogammaglobulinemia, resulting in infections, and recurrent respiratory tract infections that lead to bronchiectasis. We report a 3-year-old child who presented with recurrent multiple styes in the eyelids and several skin lesions. Evaluation revealed findings favoring WHIM syndrome and treatment with granulocyte-macrophage colony-stimulating factor (GM-CSF) was initiated, the outcome was not fruitful.

CASE REPORT

A 3-years-old child was brought to the out-patient department by the caretaker of an orphanage with a history of recurrent swelling of both side eyelids with discharge. The history of native treatment for recurrent respiratory infections has been elicited with no clinical improvement.

On examination, the child was poorly built and nourished with multiple tender swelling in the right and left eyelids with pus pointing suggestive of stye. Several skin boils with pus discharge and excrescent lesions suggestive of warts also noted in lower limbs with few lesions over forearm. Possibility of immune-suppression was the first thought, with HIV testing being negative child has been worked up extensively. However, a history of primary and secondary immune-suppression among family could not be obtained. A complete blood count revealed a low white blood cell count with neutropenia, lymphopenia. On work-up, bone marrow examination revealed degeneration and hyper segmentation of mature neutrophils, hyperplasia of myeloid cells, and an overall reduction in precursor cells [Figure 1]. Based on the clinical findings of warts, recurrent infection and bone marrow examination with other evidence of hypogammaglobulinemia diagnosis of WHIM syndrome have been made. Further genetic testing was deferred due to non-availability of the resources. Antibiotics local application and systemic administration provided symptomatic improvement and started on GM-CSF 250 mg/m^2/day with drastic improvement in days after initiation of therapy. However, treatment could not be continued as planned due to financial constraints and non-availability of medication. On follow-up after a month, respiratory symptoms and styes reduced significantly, but the skin lesions were still active, for which medications were continued.

DISCUSSION

WHIM syndrome is a very rare congenital cause of immunodeficiency that has an autosomal dominant mode of inheritance. A gain in function mutation of CXCR4 is found in most cases and WHIM syndrome is the first disease associated with dysfunctional CXCR4.[3] Human papilloma virus infection with warts in the hands, trunk, and face is very common and it is proposed to be due to CXCR4 mutation. Hyperplasia with various cytoplasmic and nuclear changes suggestive of increased apoptosis in bone marrow called Myelokathexis is characteristic of WHIM syndrome. Despite increased bone marrow activity, severe neutropenia is noted in most patients, rendering them susceptible to bacterial infections. Studies reported lymphopenia, with significant reduction in B-lymphocytes than T-lymphocytes.[4,5] Infections with encapsulated organisms such as pneumonia and sinusitis are common due to hypogammaglobulinemia especially reduced immunoglobulin G (IgG) but also immunoglobulin M (IgM). Diagnosis of WHIM syndrome requires high clinical suspicion, as any patient with recurrent respiratory tract infections and skin lesions with multiple warts should arouse the thought of immune-deficiency and associated significant neutropenia, lymphopenia, IgG/IgM deficiency, and warrant a bone marrow examination to rule out WHIM syndrome. Early recognition and treatment will, improve the quality of life. Treatment with granulocyte colony-stimulating factor and GM-CSF apart from antibiotics has shown dramatic improvement over the condition and it has been reported that hypogammaglobulinemia may improve.[6] Mortality due to infection is not uncommon; however Epstein Barr virus associated lymphoma and lymphoproliferative disorders with mortality also been reported.[7] We report a 3-year-old child from orphanage who presented as recurrent stye with other clinical features suggesting immune-deficient states. Investigations revealed neutropenia, lymphopenia, hypogammaglobulinemia, and myelokathexis in bone marrow which pointed toward WHIM syndrome and was managed with GM-CSF though there were lot of financial constraints.

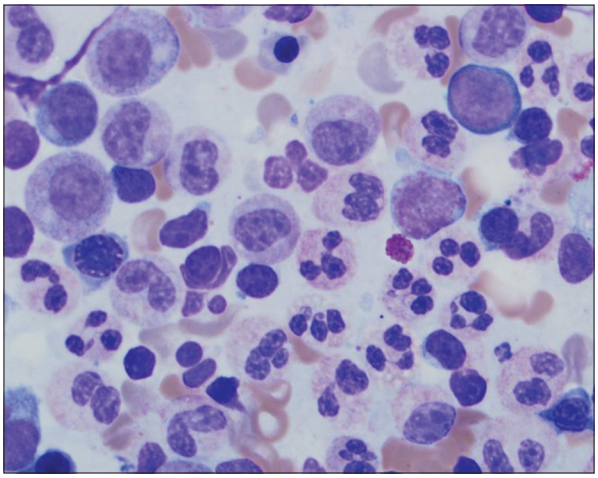

Figure 1: Bone marrow aspirate showing degenerated hyper segmented neutrophils with thin chromatin strands between segments and overall reduction of mature precursor cells.

CONCLUSION

WHIM syndrome is an inherited immunodeficiency which renders the patient susceptible to infections and treatment often requires GM-CSF and intravenous immunoglobulins in addition to only antibiotics. In our report, the child was managed with GM-CSF and close follow-up advised. This report emphasis on the importance of high suspicion and thorough clinical evaluation in these cases which can save lives.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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