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Tacrolimus Induced Pseudo-Pelger-Huet Anomaly - A Case Report

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Abstract

The case of Psedo Pelger Huet anomaly in a patient with chronic kidney disease was reported. The recognition of this anomaly is clinically important as it is a marker of granulocytic dysplasia seen conventionally in myelodysplastic syndrome (MDS) where neutrophils are bilobed. The patient was planned for renal transplant and was given Tacrolimus. The peripheral blood smear and bone marrow examination essentially identified the anomaly preventing unnecessary investigation. The rarity of such case reports makes the article interesting and useful for practicing pathologists/ hematopathologist and oncologists.

Keywords: Pelger Huët anomaly, Tacrolimus, Peripheral blood smear.

Introduction

Pelger-Huët anomaly (PHA) was first described by Karl Pelger in 1928.[1] It was discovered as autosomal dominant granulocytic segmentation anomaly by G.J. Huët in 1931.[2] Pelger Huët cells are morphologically abnormal neutrophils characterized by abnormal condensation of chromatin, hypolobation and round, oval, peanut shaped, coffee bean shaped or symmetrically bilobed nucleus (dumb bell shaped) with normal cell size and cytoplasmic granules.[3] The morphological abnormality of neutrophil does not affect their function.[4] neither does it causes neutrophila however it may result in increased band forms on peripheral blood smear.[5, 6]

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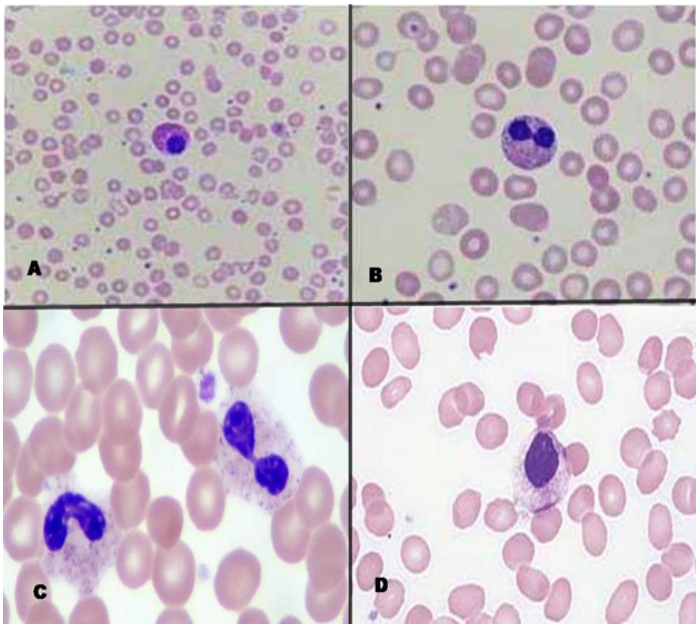
Case History

The case highlights the imperative role of peripheral blood smear examination for diagnosis of morphological abnormalities of various blood cell lines. The diagnosis of Pelger Huët anomaly was done entirely on morphological grounds and the pathologist were not aware of Tacrolimus administration to the patient. Once the morphological abnormality was identified a detailed drug history was sought from patient which eventually led to Tacrolimus as the causative factor. The literature search further confirmed the role of Tacrolimus in inducing Pelger Huët anomaly.

We received prepared bone marrow aspiration smears from a 25-year-old male patient planned for renal transplantation. Past medical history was significant for end stage renal disease. It is our protocol to examine a complete blood count for all outside patients undergoing bone marrow examination or for cases where prepared smears are received in the department. An automated complete blood count (CBC) demonstrated Hemoglobin- 98g/L (reference range 130-170g/L), white blood cell count 3.2 x 10 9/L (reference range 4-10 x 10 9/L) Platelet count 60 x 10 9/L (reference range 150-450 x 109/L), Absolute neutrophil count 1.2 x 10 3/L (reference range 2-7 x 103/L). A concurrent peripheral blood smear showed few unilobed neutrophils with clumped

chromatin and pink cytoplasm raising doubts of Pelger Huët anomaly. (Figure-A,B,C D) On communication with the clinician we found that the patient was receiving Tacrolimus in combination with Azathioprine in dose of 0.2mg/Kg/day. A literature search supported our findings of Pelger Huët anomaly in Tacrolimus recipients.

Figure 1



Discussion

This abnormality can be present in congenital or acquired forms. The acquired form referred as Pseudo Pelger Huët anomaly (PPHA) is seen in Myelodysplastic syndrome, Acute Myeloid Leukemia, infections like Tuberculosis, Mycoplasma and drugs.[4,7] The drugs commonly implicated in development of this morphological anomaly are in patients of transplant medications like Tacrolimus, ganciclovir, co-trimoxazole, Itraconazole, fludrabine, lorezepam, rituximab & citralopam.[7] In medication induced pseudo Pelger Huët anomaly neutrophils are unilobed, hyposegmented and show excessive nuclear clumping.[7] These changes are reversible in neutrophils as neutrophils resume their normal morphology on drug dose reduction or discontinuation.[8] Acquired Pelger Huët anomaly is a marker of granulocytic dysplasia seen conventionally in myelodysplastic syndrome(MDS) where neutrophils are bilobed. [4] Therefore it is of extreme importance to differentiate Pseudo Pelget Het anomaly in MDS/ Acute Myeloid Leukemia, or possible myeloproliferative disorder form other acquired causes to prevent unnecessary investigation. [8,9]

The morphological abnormality in hereditary Pelger Huët anomaly is attributed to genetic defect in the lamina B receptor which is usually present on chromosome 1q 41-43 and is responsible for the abnormal trafficking of the heterochromatin and nuclear lamins which are scaffolding proteins that control shape of nuclear membrane.[10] As it is a recent discovery the underlying mechanism of acquired Pelger Huët anomaly requires further studies.

Tacrolimus inhibits an enzyme calineurin required for production of IL-2 by T cells. [11] IL-2 in turn affects recruitment and activation of T-Helper cells [7] other cytokines involved in cytotoxic T cells, Natural killer cells and B cell activation. The exact role of Tacrolimus is unclear in causing the anomaly, but possibilities of its involvement include profound T cell suppression, cytokine effects on neutrophil maturation, direct toxicity or unusual hypersensitivity.[12]

Conclusion

Thus, one should examine direct peripheral blood smear in any case with normal total WBC count with significant left shift. A peripheral blood smear examination by pathologist and awareness of drug induced Pseudo Pelger Huët anomaly by clinician can prevent unnecessary work up leading to improved patient care.

Acknowledgments

None

Conflicts of interest

The author declares that there is no conflicts of interest.

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