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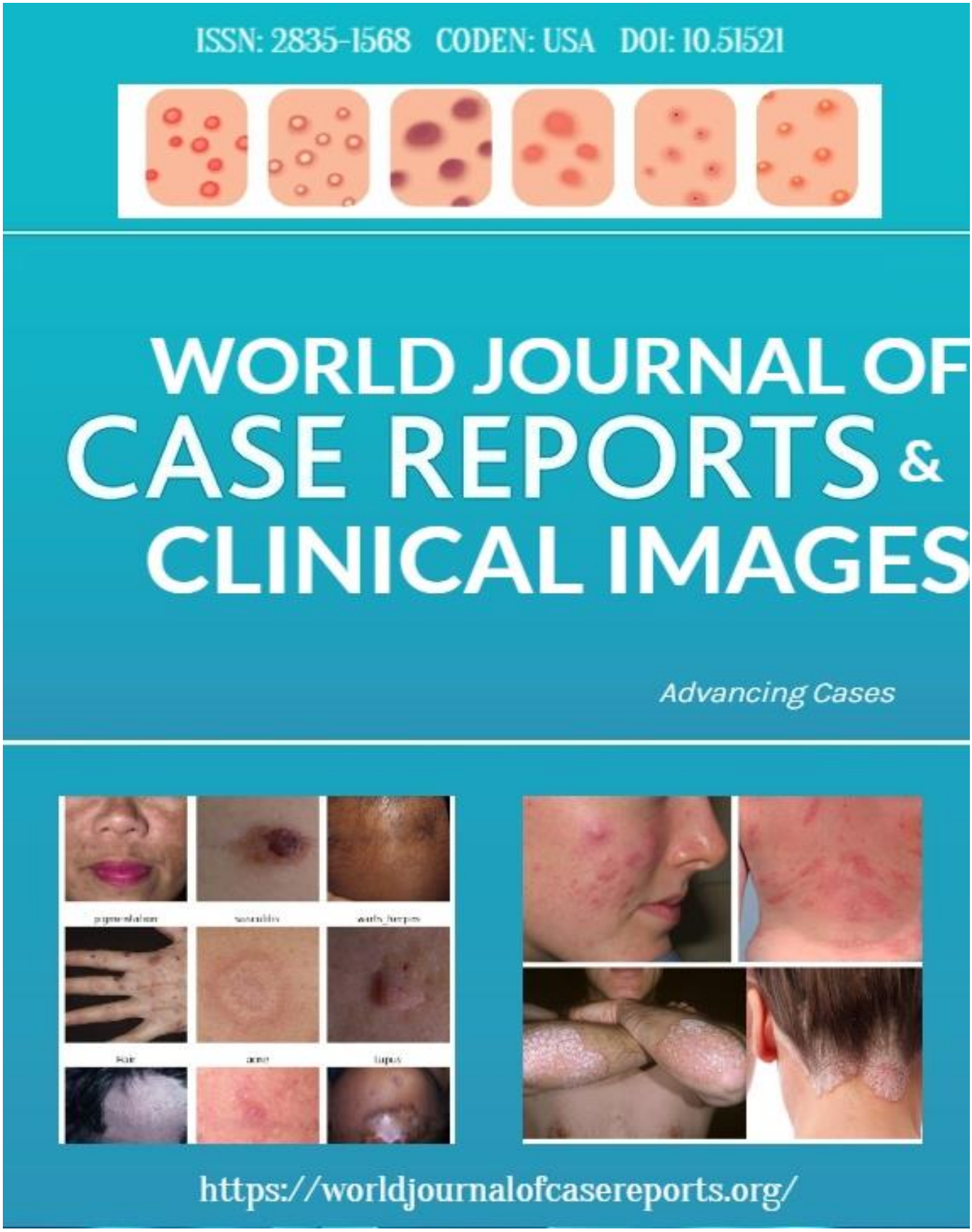

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CLINICAL IMAGE

A Case Demonstrating the Diagnostic Dilemma when Molecular Mutations do not fit the Morphology in the Classification of an MPN

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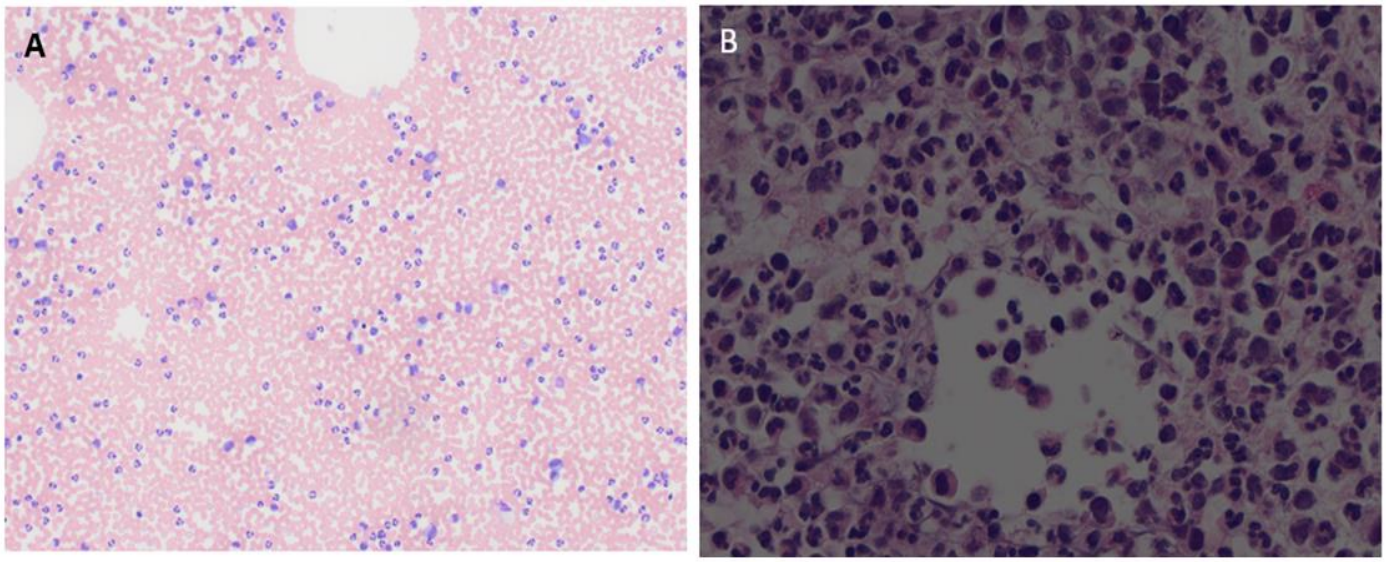
Abstract

Myeloproliferative Neoplasms (MPN) classification has been revolutionised by mutational analysis. This broad category of disorders still can cause diagnostic difficulty's especially when morphology doesn't fit with the mutations found.



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Case Presentation

We report a case of a 67-year-old Caucasian male presenting with night sweats and headache. He had a past medical history of type 2 diabetes. A full blood count (FBC) was performed, and results showed a Haemoglobin (Hb) 133g/L (normal 130-170g/L), Total White Cell Count (WCC) $107.7x10^9$/L (normal $4\text{-}10x10^9$/L), Platelet count (PLT) $83x10^9$/L (normal $150\text{-}410x10^9$/L), Absolute Neutrophil Count (ANC) $57x10^9$/L (normal $2\text{-}7x10^9$/L). A blood film was reviewed which showed a significant neutrophilia with no blasts, no basophils and no dysplastic features seen. A diagnosis of CML was excluded with the absence of BCR ABL.

Bone marrow aspirate Image A showed predominantly neutrophils (>90% of nucleated cells) with no excess of blasts or any dysplastic features. Cytogenetics showed a normal karyotype (46XY) and no clonal abnormality or evidence of the Philadelphia chromosome. Bone marrow trephine Image B was hypercellular and also showed mainly mature neutrophils with no excess of blasts. The morphological features were suggestive of chronic neutrophilic leukaemia.

Interestingly his NGS bloods returned and was negative for CSF3R but positive for ASXL1, KRAS, SRSF2 and TET2. NGS also found CUX1 of unknown significance.

Despite being negative for CSF3R he fulfilled the rest of the criteria for Chronic Neutrophilic Leukaemia as his peripheral blood and bone marrow aspirate/trephine have shown mainly mature neutrophils with no excess of blasts with no evidence of dysplasia and no other cause found.

CNL can be difficult to diagnosis as it has many overlying features with other myeloproliferative disorders such as atypical Chronic Myeloid Leukaemia (aCML). Recent developments with molecular sequencing have aided the diagnosis of CNL with most cases displaying a mutation in colony stimulating factor 3 receptor (CSF3R) [1,2]. The two main mutations are T618I and more rarely T615A. Colony stimulating factor stimulates granulopoiesis and encourages differentiation of granulocytes to mature neutrophils which are characteristic of CNL. Despite being present in the majority (~80%) of cases, CSF3R is not the only driver mutation in CNL and many others can also be present adding to the complexity of the condition such as in this case where ASXL1, KRAS, SRSF2, TET2 and CUX1 are positive [3].

The CUX1 gene is a tumour suppressor gene that is located on chromosome 7. It has been identified in myeloid neoplasms (AML, MPN) and are common in Myelodysplastic Syndrome. It has been noted that CUX1 mutations have been described in low risk MDS or AML whereas CUX1 deletions have been described in high-risk AML and MDS [4,5]. It has been noted that CUX1 mutations can occur in MPN however there are currently no cases describing CUX1 mutations in CNL. This case was labelled as an MPN-U and demonstrates the difficulty with the classification of myeloid malignancies when the mutations do not match the morphology.

Conflict of Interest: Not Declared any conflict of interest

Ethical Consideration: None

Acknowledgements: None

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