Case Report: Noonan Syndrome/Myeloproliferative Disease vs Juvenile Myelomonocytic Leukaemia Representing a Diagnostic Dilemma with Large Prognostic Differences

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Introduction

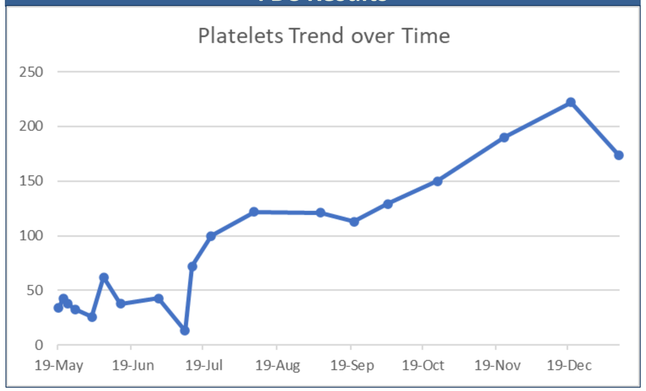
Noonan syndrome (NS) is an autosomal dominant syndrome affecting 1 in 1,000-2,500 most commonly due to mutations in the PTPN11 gene. It commonly presents with characteristic dysmorphic features, skeletal malformations and cardiac defects. Frequently associated haematological disorders include coagulation factor deficiencies, thrombocytopaenias and Myeloproliferative disorders with prevalence estimates from 20% to 34%.[1,2] Noonan Syndrome/ Myeloproliferative disorder (NS/MD) is a self-limiting disorder which presents similarly to Juvenile Myelomonocytic Leukaemia (JMML). In contrast, JMML has a median survival time of 10-12 months without hematopoietic stem cell transplantation and a lapse rate of 1/3 with treatment. We present a rare case of NS/MD without features of NS presenting a difficult diagnostic challenge.

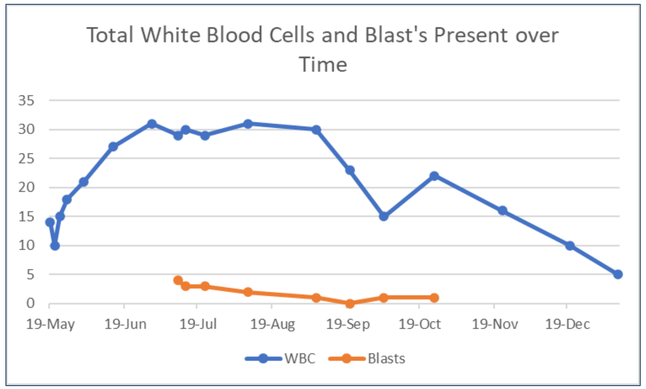
Our Case

Our patient is a dichorionic diamniotic twin 1 delivered by ELSCS at 37 weeks, birth weight 2.2kg. Admission to the neonatal unit was due to hypoglycaemia and suspected IUGR with bruising noted. A full blood count (FBC) was completed showing thrombocytopenia (Platelets: 35.1x10 9 /L). Weekly FBC revealed progressive leukocytosis (WBC: 31.5x10 9 /L) with associated leucoerythroblastosis and myeloid proliferation with 2% blast cells. Initially, these results were highly concerning for JMML. Twin 2's neonatal course and subsequent development has been unremarkable.

Due to high index of concern for JMML, bone marrow aspirate was conducted with cytomorphology results consistent with myeloproliferation or JMML. JMML screen was positive due to PTPN11 mutation. The mutation involved was in exon 3 c.2118>T. Follow-up germline PTPN11 was tested using hair follicles confirming germline mutation and a diagnosis of NS. Due to this underlying diagnosis, a watch-and-wait approach was taken and improvement of blast counts confirmed the NS/MD diagnosis.

FBC Results





Discussion

The diagnosis between NS/MD and JMML is challenging due to similarities in presentation but vital given the prognostic differences. PTPN11 mutations are associated with JMML in 35% of cases and with NS in 50% of cases.[3] Our case described a rare manifestation of NS with no other classical features leading to diagnostic confusion. Previous studies had linked mutation exon 3 c.2118>T with NS/MD in the past however rarity has limited statistical analysis of this information.[4] Literature review showed this to be the only case where no other syndromic features when myeloproliferative disorder initially presented.

Learning Points

- JMML is a leukaemia with poor prognosis. This case shows a rare relatively benign differential in a presentation similar to JMML.
- Due to the possibility of Noonan Syndrome germline PTPN11 genetic testing should be done in neonates with JMML due to PTPN11 mutations

References

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