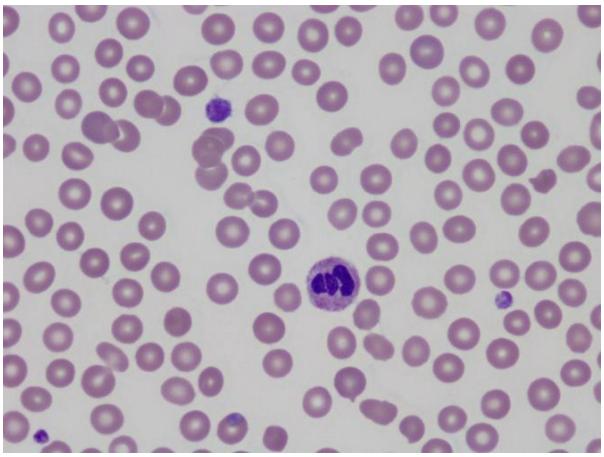
Partial DiGeorge (22q11.2 deletion) Syndrome

Specimen No 1376



DiGeorge Syndrome (DGS) also known as 22q11.2 deletion syndrome (22q11.2DS) is associated with a heterozygous deletion of the proximal long arm of chromosome 22. DGS has a wide range of clinical signs and symptoms related to defective development of the third and fourth pharyngeal pouch system during embryogenesis. The major clinical manifestations include congenital heart defects, particularly conotruncal malformations, neonatal hypocalcemia due to hypoparathyroidism, palatal abnormalities, thymic aplasia and subsequent immune deficiency, characteristic facial dysmorphisms and learning difficulties. It is associated with various immune abnormalities including immune cytopenias (thrombocytopenia, haemolytic anaemia, Evans syndrome), juvenile idiopathic arthritis and autoimmune thyroid disease.

Thymic hypoplasia in DGS results in a range of T cell deficits depending on the number of T cells present. Patients with DGS are divided into two subgroups; complete DGS and partial DGS depending on the level of immunologic function and degree of thymic hypoplasia. In complete DGS there is a complete absence of thymic tissue which results in profound immunodeficiency and is life threatening if not treated. In partial DGS patients have variable T cell counts and function which results in non-life threatening immunological function. The majority of patients, including our patient, have partial DGS.

Thrombocytopenia has been frequently reported in association with DGS however the exact etiology is unknown. One of the common causes of thrombocytopenia has been reported to be autoimmune thrombocytopenia (ITP). It has also been hypothesised that the cause of thrombocytopenia is due to decreased expression of GP1b or conotruncal heart defects. Macrothrombocytopenia has been reported to be linked to hemizygous deletion of GP1b-β gene on chromosome 22, which is also seen in the autosomal recessive platelet disorder Bernard-Soulier syndrome (BSS). Anaemia has been noted to be present in a variable number of patients with DGS and may be due to chronic inflammation, recurrent infections and rarely immune haemolytic anaemia. Recurrent infections due to immunodeficiency are commonly seen.

There are numerous causes of thrombocytopenia in pregnancy that vary with the duration of pregnancy, severity of thrombocytopenia and patient status. These can occur concurrently with DGS and must also be considered during pregnancy. Causes of pregnancy related thrombocytopenia include gestational thrombocytopenia or incidental thrombocytopenia, ITP, pre-eclampsia with severe features/HELLP syndrome (haemolysis, elevated liver enzymes and low platelet syndrome), thrombotic microangiopathy (TMA) including thrombotic thrombocytopenic purpura (TTP), complement mediated TMA and shiga toxin mediated haemolytic uraemic syndrome, disseminated intravascular coagulopathy (DIC) and acute fatty liver in pregnancy (AFLP). There are also a number of other causes of thrombocytopenia that may be discovered incidentally during pregnancy.

The patient in this case was diagnosed with DGS as a baby after she was found to have a cardiac abnormality known as Tetralogy of Fallot. The patient had previously undergone two repairs of her Tetralogy of Fallot and a valve replacement. The provided slides and results for this patient are from monitoring bloods taken during pregnancy for intrauterine growth restriction. Macrothrombocytopenia was found to be present which is known to occur with DGS/22q11.2DS, however other concurrent causes of thrombocytopenia needed to be considered. Features associated with other known causes were not seen on patient's blood film and the patient had normal coagulation profile and biochemical profile. As ITP could not be ruled out in this case, the patient's baby was also at risk of having ITP.

Precautions were therefore recommended which included avoiding instrumental delivery and monitoring baby's platelet count post-delivery. The patient had an elective caesarean section and required a platelet transfusion post-delivery.

References:

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