Case report

An eight day old male presented to the Special Care Baby Unit of University of Port Harcourt Teaching Hospital with a three day history of fever, poor sucking, convulsions, and excessive crying, and a two day history of intermittent gum bleeding. He had been admitted soon after birth in a private hospital and treated for presumed sepsis with intramuscular ceftriaxone and gentamicin and later discharged home on the second day of life on daily intramuscular ceftriaxone (had seven doses before presentation). Two days prior to presentation, four pearl-like swellings were noticed on the lower gums. The swellings which were excised in the private clinic were intermittently bleeding at presentation.
Pregnancy which was supervised in the private hospital and generally uneventful except for intermittent fever treated with antimalarials. The mother had no skin rash during pregnancy and she took only the routine antenatal drugs (folic acid and fesolate). There was no history of prolonged rupture of membrane or peripartum pyrexia. Labour was at term and was difficult because of face presentation and the child cried weakly at birth. He was resuscitated by suctioning. The birth weight was 3.6Kg.

He was on exclusive breastfeeding and had received no immunizations yet. He was the 4th of 4 children; 3 males and 1 female with 3 alive. One male child died at 5 days of age from severe neonatal jaundice. There was no history of bleeding disorder in the other siblings or in the mother's family.

On examination, he was crying excessively and had submucous haemorrhagic swellings on both sides of upper and lower gums, bilateral subconjunctival haemorrhage with chemosis, jaundice, generalized petechial rashes, and significant axillary lymphadenopathy. No cataract was seen. Neurological examination revealed the child in opisthotonic position with occipitofrontal circumference of 31.5cm, flat normotensive anterior fontanelle, and poor sucking reflex. The heart rate was 136/minute, with a grade 4 machinery murmur maximal at the 2nd left intercostal space by the parasternal border and a palpable thrill in the same area. He had a non tender hepatomegaly of 5cm and a splenomegaly of 4cm. Both kidneys were ballotable and only the left testicle was felt in the scrotum.

There were no skeletal abnormalities. The initial working diagnoses were (1) Overwhelming septicaemia with meningitis and Disseminated Intravascular Coagulopathy (DIC) and (2) Acyanotic Congenital Heart Disease Patent Ductus Arteriosus. Differentials included congenital rubella syndrome, intracranial haemorrhage and Thrombocytopenia absent radii (TAR) syndrome.

Results of investigations done on admission showed a packed cell volume of 44%, platelets of 100x10^9/L and a white blood cell count of 24x10^9/L (neutrophils 65%, lymphocytes 33% and monocytes 2%). Coagulation profile showed prothrombin time of 45seconds, activated partial thromboplastin time of 65seconds and a thrombin time of 20seconds. The blood culture yielded no growth.

On the 8th day of admission, he started bleeding spontaneously again from all the venepuncture sites with easy bruising at points of contact with napkin/plaster which were also bleeding freely. A repeat full blood count showed a packed cell volume of 33%, platelets of 25x10^9/L and a white blood cell count of 4.8x10^9/L (neutrophils 36%, lymphocytes 52% and metamyelocytes 12%). The blood film showed macrocytosis of the red cells and the white cells showed relative lymphocytosis, band forms with neutrophil left shift. Another single volume EBT was given and the bleeding once again controlled. He subsequently remained stable until the 16th day on admission when he once again started bleeding from venepuncture sites and became very pale. He received a 3rd exchange blood transfusion. Subsequently, he made remarkable improvement, was no longer irritable, neck retraction receded and he started suckling from the mother’s breast.

He was jointly managed by the neonatologists and the haematologists who also agreed with the diagnosis of DIC secondary to overwhelming sepsis. He received intravenous fluid, intravenous ceftaxidime and was also given intravenous Vitamin K. On the 5th day on admission, he was found to be bleeding from the umbilical stump as well as vomiting frank blood. He also had a rapidly enlarging subcutaneous right sided neck swelling, ecchymoses, and was bleeding from both old and recent venepuncture sites. He received an urgent single volume exchange blood transfusion (EBT) with fresh whole blood. The bleeding was controlled and the right sided neck swelling receded.

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bicarbonate 27mmol/L, urea 5.4mmol/L and creatinine 85umol/L. The abdominal ultrasound however still showed accentuated renal parenchymal echoes with bilateral loss of corticomedial differentiation. At one year of age, he had achieved only social smile, had poor weight gain (weighed 6.8kg) and an occipitofrontal circumference of 50cm. A repeat cranial ultrasound showed dilated third and fourth ventricles in keeping with a communicating hydrocephalus for which the neurosurgeons placed him on Acetazolamide while awaiting ventriculoperitoneal shunting. The heart murmur is still present and he is awaiting a definitive Echocardiography and possibly corrective surgery at a cardiac centre.

**DISCUSSION:**

Plasma activities of most coagulation proteins are low at the time of birth, and only reach adult levels at about 6 months postnatally. Despite this quantitative and qualitative deficiency in the hemostatic capacity, there is a low incidence of either inappropriate bleeding or clotting in the term infant. However, when challenged by an extraordinary condition like infection, the neonatal hemostasis can be easily overwhelmed. This appears to be the case in our patient. Infection upsets hemostasis by either directly inducing thrombocytopenia (through adherence of bacterial products to platelet membrane, immune mediated destruction of platelets, decreased platelet production from infected bone marrow), hepatic dysfunction and shock or by activation of coagulation cascade which leads to consumption of the clotting factors.

Viral infections like cytomegalovirus and rubella are also noted to release neuraminidase, leading to sialic acid loss from platelet membrane, intravascular platelet aggregation and degeneration of megakaryocytes. Associated splenomegaly with hypersplenism and excessive destruction of platelets also plays an additional role. It is not clearly certain whether our patient had purely bacterial or congenital viral infection or both, but the features were highly suggestive of congenital rubella syndrome include maternal fever in pregnancy, petechiae rash, microcephaly, jaundice, hepatosplenomegaly, murmur of patent ductus arteriosus, lymphadenopathy, thrombocytopenia, and a negative blood culture. Viral studies and rubella IgG/IgM antibody titer are not available in our hospital to confirm this. The blood culture was negative but this was not surprising as the child was already on parenteral cephalosporins before presentation. Infection, however, can be indirectly inferred if there is thrombocytopenia, leucopenia (WBC <5000/mm³) or leucocytosis (WBC =24000/mm³), and most of the circulating polymorphs are immature forms like band forms, stab, and metamyelocytes, neutrophil left shift, and toxic granulation. These were all seen in our patient. Bacterial antigen detection studies like counterimmunoelectrophoresis or latex agglutination are also helpful in identifying the pathogenic bacteria because microbial antigen remain detectable for several days after the initiation of antibiotics, whereas cultures may be negative. It was also difficult to rule out meningitis in the infant since the severe thrombocytopenia and deranged clotting profile did not permit a lumbar puncture. Microthrombi, macrothrombi, emboli and hemorrhage in the cerebral vasculature are all responsible for the non-specific neurologic symptoms and signs displayed by patients with DIC.

The site of the bleeding may provide an indication of the hemostatic abnormality. Qualitative or quantitative platelet disorders usually present with mucocutaneous bleeding like petechiae, ecchymoses, purpura and gastrointestinal bleeding, whereas bleeding into joints and potential spaces such as fascial planes is most commonly associated with coagulation factor deficiency. In DIC, patients demonstrate both mucocutaneous bleeding and bleeding into deep spaces because platelet abnormality and coagulation factor abnormalities are both present.

There was no family history of bleeding tendencies in the mother’s brothers nor did the mother have thrombocytopenia, thus excluding the possibility of an inherited coagulation problem even though assay for factor VIII could not be done. Radiological presence of the radius also rules out Thrombocytopenic Absent Radii (TAR) syndrome, a rare autosomal recessive disorder characterized by congenital heart defects, thrombocytopenia at birth, bilateral agenesis of radii, but thumbs are always present. Clinically both bleeding and thrombotic problems may occur in DIC, and widespread microvascular and macrovascular thrombosis (including renal vein thrombosis) particularly contributes to multiorgan damage. This may explain the renal involvement in our patient.

As DIC is a secondary process, the management includes prompt and effective treatment of the underlying cause in addition to replacement therapy with blood components. The thrombocytopenia is usually treated with platelet concentrates while fresh frozen plasma is utilized to replace the depleted coagulation factor. Cryoprecipitate however is a better
source of fibrinogen. Neither of these blood components is available in our centre. Heparin may also be indicated to prevent conversion of fibrinogen to fibrin and to inhibit further thrombogenesis until treatment of the underlying primary disease or replacement therapy is able to reverse the trigger. Heparin is particularly helpful when thrombosis threatens to cause irreversible tissue injury like acute cortical necrosis of the kidney or digital gangrene. Some studies however did not demonstrate any survival benefit from administration of heparin.

Decreased concentrations of antithrombin III is thought to contribute to heparin resistance in the neonates. Recently, there is considerable interest in the use of protein C concentrates, which has been shown to be of benefit in sepsis associated DIC in children and adults, but there is only limited information on the use of this agent in the neonatal period.

**Conclusion:** DIC is a life threatening condition which in the neonate can be both dramatic and rapid. As it is a secondary process, the survival of patients will depend on vigorous treatment of the underlying disorders so as to curtail the triggers of blood coagulation as well as replacement of the consumed coagulation factor. Lack of appropriate diagnostic facility and blood components for replacement therapy are limitations in a deprived medical facility.

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**References:**