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Novel prenatal diagnosis of protein C deficiency and primary prophylaxis with protein C concentrate: A case series

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Background: Severe protein C deficiency (SPCD) is a rare inherited thrombophilia that has high morbidity and mortality. Currently, standard treatment includes protein C concentrate and anticoagulation acutely followed by long-term secondary prophylaxis with chronic anticoagulation.

Objectives/Goal: To describe a case series of siblings diagnosed with severe protein C deficiency and the use of primary prophylaxis.

Methods/Design: Case series.

Results: A 2 day-old term male presented with progressive apneic episodes that required mechanical ventilation. Brain magnetic resonance imaging (MRI) was performed that showed cerebral edema and limited diffusion consistent with right-sided sub-acute infarct and thromboembolic stroke (see Figure 1). Additionally, he had extensive venous thrombosis involving the inferior vena cava on ultrasound. Coagulation labs were remarkable for protein C activity of 12 percent (28-54 percent normal). He was started on long-term anticoagulation with enoxaparin, which was continued at discharge. About six months later, he was found to have persistent low protein C level at 37 percent (60-130 percent normal), so genetic testing was performed. Results demonstrated a compound heterozygous mutation (c.699G>T; c.326_330dup). Along with these genetic findings, he had a protein C level of 51 percent (60-130 percent normal) at 12 months of age, so he was diagnosed with SPCD. He was continued on chronic anticoagulation. Since then, he has had no further thrombosis or complications. Following his diagnosis, his mother became pregnant and had in utero testing with amniocentesis. Genetic testing showed that he had the same mutation as the first patient, which was concerning for SPCD. Due to this prenatal diagnosis, treatment was initiated immediately after birth to provide primary prophylaxis. Initial labs revealed protein C activity of 6 percent (24-44 percent normal). Protein C concentrate of 66 units per kilogram (goal of 60-80 units per kilogram) was given every twelve hours and titrated to achieve protein C activity trough of 25 percent. He had no thrombosis and had one bleeding complication (hepatic hematoma). He was transitioned to anticoagulation with enoxaparin and discharged to home.

Conclusion: SPCD has proven to be a difficult disease to study due to its scarcity, but it remains clinically significant and devastating to patients. This case series highlights a potentially clinically relevant genetic variant and demonstrates effective primary prophylaxis.

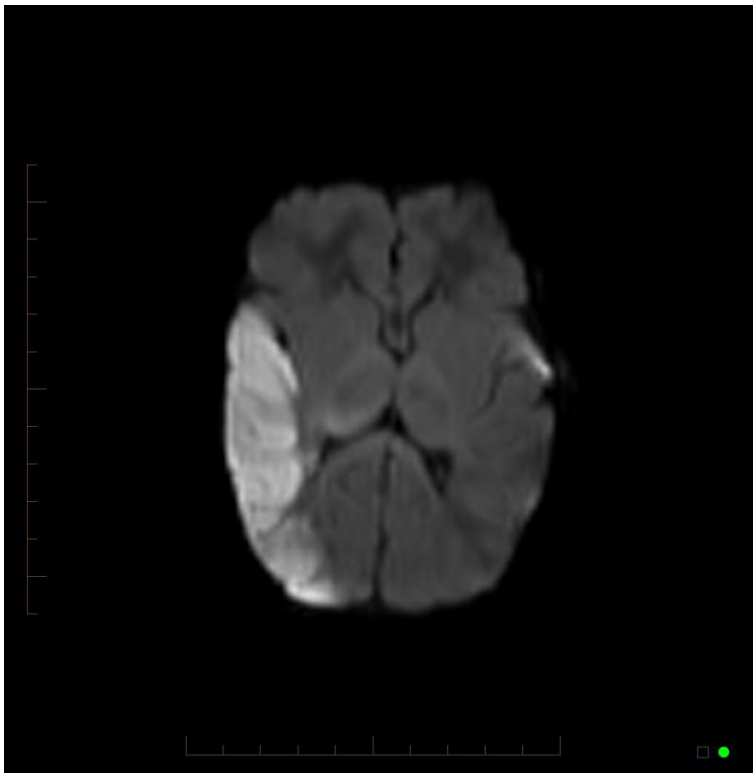

Figure 1