Central retinal vein occlusion associated with thrombotic thrombocytopenic purpura/hemolytic uremic syndrome: Complete resolution is possible

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ABSTRACT
We aim to describe a case of central retinal vein occlusion associated with thrombotic thrombocytopenic purpura (TTP). The retinal vein occlusion resolved gradually as his TTP started to respond to medical treatment but significant macular edema persisted. Focal argon laser treatment resulted in complete resolution of the macular edema.

KEY WORDS: Central retinal vein occlusion, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura

Case History

We report a 45-year-old male who presented in January 2003 with a history of being ill 10 days previously with severe bloody diarrhea, which required hospital admission. Significant colitis was seen at endoscopy but stools were negative for infection. Histology was suggestive of either pseudomembranous colitis or ischemic colitis. He responded to supportive measures (metronidazole and corticosteroids) and was discharged home after one week.

Thereafter, he was well for two days. Then he became unwell, feeling weak and thirsty when he presented to the hematology department. Investigations confirmed the presence of a micro-angiopathic hemolytic anemia with hemoglobin 12.1 g/dL, platelet count 15 × 10^9 /L, and white cell count 10 × 10^9 /L. Lactate dehydrogenase (LDH) was raised to 900 U/L and coagulation screen was normal. Urea was 19 mmol/L, creatinine 208 micromol/L, and urinalysis revealed protein ++++. Stools were negative for infection (including specific cultures for E. coli 0157).

He was commenced on intravenous hydrocortisone (250 mg every six hours) with subsequent rapid improvement in his symptoms. A diagnosis of TTP/HUS was suspected and plasma exchange was started (the replacement solution for plasmapheresis in this disease is plasma or cryo poor plasma and not albumin as is the case with all other conditions requiring plasmapheresis). After daily plasma exchange for 33 days his platelet count increased to 126 × 10^9 /L. Renal functions returned to normal, although trace protein has persisted on urinalysis. LDH decreased to 598 U/L. Plasma exchange and steroids were gradually reduced over the next month. However, the LDH rose to 823 U/L, so oral cyclosporin-A (2.5 mg/kg a day in two divided doses) was introduced (March) but his condition was refractory to treatment.

In April, he developed sudden onset of blurred vision in his
left eye. Examination showed right visual acuity of 6/6 and left acuity of 6/60. There was no relative afferent papillary defect and fundoscopy revealed dot retinal hemorrhages, tortuous vessels and significant macular edema. Fundus fluorescein angiography showed changes consistent with central retinal vein occlusion. Given the climbing LDH and the new ocular signs, and after exclusion of an occult infection, plasma exchange was increased and intravenous rituximab (375 mg/m²) was also commenced. The platelet count and LDH started to improve after starting rituximab. A month after initiation of rituximab treatment, his left visual acuity improved to 6/24 and fundoscopy showed resolving hemorrhages but persistent macular edema. By June the retinal hemorrhages completely resolved and the macular edema was slightly reduced improving his left vision to 6/12. Focal argon laser treatment was given at that stage which resulted in complete resolution of the macular edema and his left vision was 6/6 in July.

Adjuvant therapy with rituximab and vincristine (slow intravenous infusion of 1 mg once a week) was even needed before his condition started to improve. His last plasma exchange was in August and since then his blood counts stayed stable and within normal limits and he did not have further relapses until his last visit in March '05.

Discussion

The mechanism of tissue damage in TTP is not fully understood. Endothelial cell injury and retinal vascular thrombosis are regarded to be important in the pathophysiology. Histopathology shows localized thrombi composed mainly of platelets in the involved and uninvolved vessels. Similar histopathologic findings have been reported for ocular manifestations of TTP. A milestone was reached with the discovery of defective degradation of von Willebrand Factor (vWF) by a newly described metalloprotease. Patients with TTP have severe deficiency of vWF-cleaving protease, whereas patients with HUS have normal levels. In most cases of nonfamilial TTP, an immunoglobulin-G antibody to the protease was identified. Histopathology and improve the patient's vision to normal.

References