A new treatment for polyarteritis nodosa

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Case

A 69-year-old male developed a temperature of 40°C, abdominal pain and florid lower limb purpura whilst holiday in Cyprus. Treatments for a lower respiratory tract infection and for presumed Henoch Schonlein Purpura were instituted. Within a week, he developed anuric renal failure and disseminated intravascular coagulation (DIC). He was treated by daily haemodialysis until his condition was sufficiently stable for transfer back to the UK.

On arrival, he was clinically stable with a blood pressure (BP) of 160/80 mmHg. The purpuric rash remained prominent despite treatment with steroids for over a week. Table 1 summarizes the initial laboratory investigations.

Within 8 h of admission, he developed sudden severe right-sided abdominal pain accompanied by hypoxia and a fall in BP to 110/60 mmHg. An urgent abdominal CT scan identified a 13×10 cm right perinephric haematoma (Figure 1) and renal angiography showed multiple aneurysms (Figure 2). A large bleeding aneurysm at the lower pole of the right kidney was embolized using microcoils. Following embolization, empirical treatment with high dose steroid (intravenous methylprednisolone 500 mg daily) was administered for the first 3 days. Subsequently, he received oral prednisolone (60 mg daily) and azathioprine (50 mg daily for 7 days and then increased to 100 mg daily for 2 days), but azathioprine was discontinued when his platelet count fell to 30×10⁹/l. The thrombocytopenia subsequently resolved. Several days later, he developed malaena, and gastroscopy revealed two superficial duodenal ulcers.

After 14 days, he developed further abdominal discomfort. A repeat CT scan and renal angiogram identified recurrent bleeding from the lower pole aneurysm, which was successfully re-embolized with microcoils. Two weeks after discontinuing azathioprine, oral cyclophosphamide (100 mg daily) was commenced but also had to be discontinued after nine days because of recurrent thrombocytopenia. As an alternative and novel treatment for PAN, the tumour necrosis factor-alpha-inhibitor (TNF-I), infliximab (5 mg/kg) was infused intravenously at fortnightly intervals. Forty days after the second renal angiogram, he experienced a third episode of haemorrhage from the same kidney. A repeat angiogram demonstrated that the source of bleeding remained the large aneurysm at the lower pole of the right kidney. The appearance of other small aneurysms identified on previous angiography had, however, significantly improved (Figure 3). Further embolization to the bleeding aneurysm was performed in an attempt to avoid nephrectomy.

After three infusions of infliximab, the patient’s urine output returned and he became dialysis-independent. Following further improvement in his general condition he was discharged home and on outpatient review, twelve months after presentation, remains well with a serum creatinine of 25 μmol/l.

Discussion

PAN is a rare necrotizing vasculitis that affects small to medium size arteries. Spontaneous perirenal haemorrhage, though a recognized complication of PAN, is rare. Conventional treatment with corticosteroids and cyclophosphamide dramatically improves the prognosis in this condition: five year survival in untreated and treated PAN is 13% [1] and 80% [2], respectively. Since, recurrent thrombocytopenia accompanied by bleeding from both the GI tract and the kidney prevented the use of azathioprine and cyclophosphamide in this patient, an alternative agent was sought. Infliximab, a chimeric TNF-alpha-inhibitor has been used with good effect in the treatment of rheumatoid arthritis, Crohn’s disease, antineutrophil cycloplasmic antibodies (ANCA) associated vasculitis and other inflammatory conditions.
Whilst, there have been several small studies reporting the effectiveness of infliximab in inducing remission in refractory ANCA positive vasculitis [3], this is the first reported case of PAN treated successfully with this agent. The most challenging issue in this patient was recurrent aneurysmal haemorrhage from the right kidney.

Whilst nephrectomy was considered, this carried significant operative risks because of profound thrombocytopenia, and would probably have committed the patient to lifelong dialysis-dependency. The use of microcoil embolization for perirenal haemorrhage in PAN has been reported previously [4], but to our knowledge this is the first report of the combined use of infliximab and microcoil embolization in this situation. It is of particular interest that serial angiograms showed marked improvement in the renal vasculature following treatment with infliximab.

**Conclusion**

This patient with PAN accompanied by life-threatening and recurrent renal haemorrhage showed a good response to treatment with a TNF-alpha-inhibitor. Whilst, infliximab was used in this case because conventional therapies were not tolerated, our results raise the possibility that it may have a role in the treatment of other patients with PAN, and should be considered when standard therapies are unsuccessful or contraindicated.

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**References**


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