CASE REPORT

Successful treatment of Takayasu arteritis with rituximab as a first-line immunosuppressant

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SUMMARY

Takayasu arteritis is a rare large vessel vasculitis which has traditionally been treated with high-dose steroids. There have been a small number of publications where biological agents have been used to manage refractory cases. To the authors knowledge, there are no publications using biological agents in combination with steroids as a first-line treatment in Takayasu arteritis. In this publication, we document the case of Takayasu arteritis, in a 39-year-old woman, where rituximab was used in combination with steroids as a first-line agent in the setting of poorly controlled bipolar affective disorder.

BACKGROUND

Takayasu arteritis (TA) is a large vessel vasculitis. It is a very rare condition, most commonly affecting young women from Asia and Eastern Europe. The annual incidence of TA is up to 3.3 per million in Asia compared to 0.8 per million in the UK.¹ The average age at diagnosis is 31 years and the average delay in diagnosis being documented at 17.5 months (range: 7–42 months).² TA is characterised by granulomatous inflammation of large vessel walls, with intimal fibrosis and vascular narrowing. The exact aetiology still remains unclear.

The diagnosis of TA can be difficult. Discrepancies in blood pressure and pulses are the commonest findings with ~80% having bruits.² Systemic inflammatory response does not always correlate with inflammatory activity in the vessel walls. It has been shown that only 71% of TA cases have elevated inflammatory markers, with the median erythrocyte sedimentation rate (ESR) being 45 mm/hour and median C reactive protein being 37.5 mg/L.² Therefore, when clinically suspected, one should consider MRI. In previous publications, the benefits of radiological imaging in the diagnosis of TA have been highlighted.³

The initial treatment usually involves high-dose intravenous steroids followed by a high dose of prednisolone, 1 mg/kg/day, tapered very slowly. The median steroid therapy duration is 22 months with 75% of cases being off treatment after 3 years.⁴ Patients with higher inflammation at onset tend to require more steroids, for longer and have more flares.⁵ Following steroids, most patients require an additional immunosuppressive agent. The commonest additional agents are methotrexate, azathioprine and mycophenolate mofetil. Among those who remain active with refractory disease anti-TNF therapy,⁶ tocilizumab⁷ and rituximab^{8–11} have been used with varying success.

In this report, we present the case of a young woman who was diagnosed with TA and successfully treated with rituximab.

CASE PRESENTATION

A 39-year-old woman presented with a 2-week history of myalgia, burning sensation in both feet, tenderness in the distribution of both temporal arteries and a generalised fatigue. She reported that her initial symptoms were of lower back pain radiating down her right lower limb. There was associated cramping and a burning sensation. These symptoms progressed to legs and shoulders with a subsequent difficulty in mobility over the following 3 days. A spiking fever developed 9 days after the initial onset of symptoms along with night sweats, flushing, retrosternal chest pain, tenderness at the lower edge of the mandible and 'sore eyes'. This was on a background of 20 years of poorly controlled bipolar affective disorder and an elevated body mass index. Her presenting medications were carbamazepine 400 mg PO mane and 600 mg PO nocte, lithium 800 mg PO nocte, lamotrigine 300 mg PO OD and venlafaxine 75 mg PO BD. She was a non-smoker, never used illicit drugs and drank 2 units of alcohol per week.

Initial clinical examination revealed tenderness in the distribution of the temporal arteries (right greater than left), questionable synovitis of the distal interphalangeal joints in the second and third digits of the right hand, tenderness at the lower edge of the mandible bilaterally and an unsteady gait. She was apyrexial with a blood pressure of 104/66 mm Hg and heart rate of 91 beats/min in normal sinus rhythm (recorded on one side only).

Presenting investigations confirmed a urinary dipstick positive for blood, a CRP of 389.9 mg/L, ESR of 126 mm/hour, urea 4.6 mmol/L, creatinine 60 mmol/L and white cell count $17.7 \times 10^9/L$ (neutrophils 14.9). Chest X-ray was normal. A provisional diagnosis of a vasculitis was recorded with the need to out-rule infection. A vasculitis screen was sent. Viral and bacterial septic screens were negative. A temporal artery biopsy on the day following presentation was negative for inflammation of the arterial, fragmentation and disruption of the internal elastic lamina. Rheumatoid factor (RF), anti-CCP antibodies, ANA, ENA and dsDNA were negative. p-ANCA showed an atypical stranding pattern and c-ANCA negative (MPO and PR3 negative). A subsequent CT imaging and MR angiography was consistent with a large vessel vasculitis rather than small vessel vasculitis. Based history, clinical findings, laboratory investigations and

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Figure 1 A graphical description of laboratory results in combination with medications given during the management of this case.

radiological findings, a diagnosis of Takayasu's arteritis was recorded. She received 3 days of 1 g intravenous methylprednisolone with a maintenance treatment of 40 mg prednisolone PO OD to follow. A treatment reassessment was carried out at that stage. Rituximab, as per the vasculitis protocol, was felt to be the most appropriate next treatment for this patient. This was given at weekly intervals for a total of four sessions.

Since being treated with rituximab, this patient has been maintained on azathioprine 100 mg PO OD in combination with prednisolone 7.5 mg PO OD. Figure 1 highlights serological markers and treatment interventions over time. Follow-up radiology confirms stable disease. She is now over 3 years since her initial treatment with rituximab.

DISCUSSION

Very few cases of TA being treated with rituximab have been reported in the literature. In 2008, Galarza *et al*¹¹ proposed the use of rituximab as the first-choice treatment for severe autoimmune rheumatic diseases. They reported 74 patients treated with rituximab for varying autoimmune rheumatic conditions. Two were TA but details are very limited and one treated successfully.

Hoyer *et al* published findings showing increased levels of CD19+/CD20-/CD27high B cells in patients with active TA.¹⁰ The authors successfully treated three patients, with refractory TA, with rituximab, using the RA protocol.¹² Later in 2012, Ernst *et al*,¹⁰ highlighted an additional case of refractory advanced TA being very successfully treated with rituximab. Ernst *et al* showed a very significant CRP and steroid sparing response to rituximab for their TA case.

The most recent publication was by Caltran *et al*¹¹ who highlighted two cases of the successful use of rituximab in treating TA. Both cases availed of multiple immunosuppressants, including anti-TNF therapy, before receiving rituximab as two infusions of 1000 mg, 15 days apart. Both patients have remained asymptomatic with disease remission, for over 2 years. They are maintained on mycophenolate mofetil.

Unlike the previous publications using rituximab for the treatment of TA, to the author's best knowledge, our case differs in that we used the vasculitis protocol documented in the pivotal

2010 Jones *et al*¹² publication in the *New England Journal of Medicine*. In addition, all previous cases used rituximab for refractory TA cases. Our case is different in that we used rituximab with prednisolone as a first-line regimen. We believe this to be the first published case using rituximab with prednisolone as a first-line immunosuppressant regimen and with the rituximab vasculitis protocol being used. The reason for our use of rituximab with prednisolone as a first-line immunosuppressant regimen was to achieve maximum disease control, as quickly as possible, with avoiding long-term high-dose steroids due to the history of bipolar affective disorder and avoiding any potential medication interactions with psychiatric medications.

Learning points

- ▶ Rituximab can potentially be used as a first-line immunosuppressant in the management of Takayasu arteritis (TA).
- ▶ Steroid sparing medication regimens are desirable in patients with mental health issues.
- ▶ The presentation of TA can be variable in signs/symptoms at presentation.

Contributors MBO and MJP interviewed and examined the patient, actively involved in patient care, carried out the review of patient records and result and prepared the manuscript. NO carried out the review of patient radiology and prepared the manuscript. UB interviewed and examined the patient, actively involved in patient care and prepared the manuscript.

Competing interests None declared.

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