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A possible case of serum sickness after ocrelizumab infusion – Commentary

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Abstract Serum sickness is a type III delayed hypersensitivity reaction which causes deposition of immune-complexes in the tissues. It has been reported with rituximab, and in this issue of the journal, there is a case report of a patient with relapsing remitting multiple sclerosis who developed a possible serum sickness after the third infusion of ocrelizumab. In this commentary, we discuss the current literature on serum sickness, and how to diagnose and manage it. We provide our opinion on this particular case, and encourage neurologists and patients to remain vigilant of such a possibility.

Keywords: Multiple sclerosis, ocrelizumab

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Moreira Ferreira et al.[1] have reported a possible case of serum sickness (SS) after the third infusion of ocrelizumab in a patient with relapsing remitting multiple sclerosis (MS). Although this is not novel considering the rare yet well-known SS with rituximab (a chimeric anti-CD-20 therapy),[2,3] this is the first reported possible case of SS with ocrelizumab.

SS is a type III delayed hypersensitivity reaction which causes deposition of immune-complexes in the tissues leading to activation of the complement cascade and inflammatory reaction.[4] It is a clinical diagnosis characterised by the clinical triad of fever, arthralgia and rash. Other symptoms include myalgia, malaise, fatigue, conjunctival hyperaemia and purpura. It can also cause proteinuria, haematuria, raised inflammatory markers, high immunoglobulin levels and reduced complement.[2,5]

The onset of symptoms tends to occur around 10 days after the first infusion of rituximab,[2,5] but reactions tend to occur quicker after subsequent infusions.[2]

When suspecting SS, the following tests are a basic guide to establish diagnosis and consider other possible differential diagnoses, including an extensive infection screen, immunoglobulins and complement levels, erythrocyte sedimentation rate/C-reactive protein, kidney and liver functions, vasculitis screen and a urine dipstick.[2]

Once SS is recognised, treatment should be commenced including paracetamol, non-steroidal anti-inflammatory drugs, anti-histamine and/or steroids. Plasma exchange therapy (PEX) may be considered as a last resort.[6] The prognosis of SS is excellent in the absence of significant complications.[2]

Although this case raises the suspicion that SS may be induced by ocrelizumab, which is a humanised anti-CD-20 therapy and is therefore less likely to cause SS compared to rituximab, it is certainly not a definite case of SS. The lack of typical clinical and laboratory features makes other causes, such as an infection, more likely. In addition, the use of PEX in this case is controversial considering the normal neurological examination, vital signs and laboratory tests 2 months down the line. PEX is rarely used in SS and usually reserved for refractory cases with evidence of end organ damage.

In conclusion, although this is not a typical case of SS, MS neurologists and patients should be vigilant of the possibility of SS when prescribing anti-CD-20 monoclonal therapies. Once suspected, investigations and treatment should be commenced and cessation of further infusions with the offending drug is recommended to avoid recurrent and more severe manifestations.[4]

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