RITUXIMAB INDUCED SERUM SICKNESS – IN A CASE OF RELAPSED PRIMARY MEMBRANOUS NEPHROPATHY

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Background

Serum sickness is a "type III" or immune complex-mediated hypersensitivity disease, caused by immunization of the host by heterologous serum proteins and subsequent illness caused by formation of immune complexes.

Serum sickness with Rituximab has been described in various studies. There is no case report of Rituximab induced serum sickness in primary membranous nephropathy Relapse patient after second dose with no any evidence of serum sickness or adverse reaction in previous doses

INTRODUCTION

- Serum sickness term first described by von Pirquet and Schick, in his book ‘Die Serumkrankheit’ in 1905.

- Triad of symptom of fever, rash, polyarthralgia after administration of anti-toxin (horse serum) for the treatment of diphtheria and scarlet fever.

- Delay between administration of the horse serum and the development of the symptoms of serum sickness, and the delay was shorter with subsequent dose.

- Serum sickness is a "type III" or immune complex-mediated hypersensitivity disease.

- The classic clinical syndrome of serum sickness is caused by immunization of the host (human) by heterologous (nonhuman) serum proteins and subsequent illness caused by formation of immune complexes.

- Following primary immunization with a protein antigen, IgM antibodies typically begin to develop 7 to 14 days later, and IgG antibodies appear a few days after IgM

- If the foreign protein is still present in the circulation when these antibodies appear, the antigen and antibodies may combine to form immune complexes.

- Rituximab (an anti-B cell chimeric mouse monoclonal antibody)
- Prescribed in various regimen for Membranous nephropathy, primary, as IV 375 mg/m^2 once weekly X 4 doses;
- Repeat cycle at 6 months (Fervenza 2010)

or

1,000 mg (flat dose) on days 1 and 15;

may repeat cycle at 6 months (Fervenza 2008)

or

375 mg/m^2 once weekly for 2 doses (Dahan 2017)

or

375 mg/m^2 once weekly for 4 doses (Ruggenenti 2012; Ruggenenti 2015)

or

375 mg/m^2 as a single dose and repeated at least 1 week later only if circulating B cells >5/mm^3 were detected (Ruggenenti 2012; Ruggenenti 2015).

- Serum sickness with Rituximab has been described in various studies

- There is no case report of Rituximab induced serum sickness in primary membranous nephropathy Relapse patient after second dose with no any evidence of serum sickness or adverse reaction in previous doses.

❑ CASE DETAILS

- We received a patient 48 yr male, nondiabetic, nonhypertensive, with primary Membranous nephropathy with Renal biopsy tissue PLA2R positive.

- He presently to us with fever, severe polyarthralgia with h/o administration of injection Rituximab 500 mg one week back.

- He had past h/o failed response to modified Ponticelli & partial remission when with CNI(Tacrolimus) plus steroid.

- Past h/o 1 dose of Rituximab 2 ½ yr back, without any h/o immediate or delayed adverse drug reaction as well no serum sickness

- He didn’t have any lymphadenopathy rash, increase in proteinuria, gastrointestinal symptoms, oral ulcer, alopecia, genital lesion, any other recent drug or vaccine exposure, no h/o insect bite or animal bite.

- He was evaluated for any systemic disease leading to same symptom & tropical infection.

- All reports came normal with no growth in Blood c/s with RA factor negative with negative test for Dengue, anti CCP negative (1.7 RU/ml), ESR 36, CRP 77.6 raised, normal C3, C4.

- In view of typical clinical presentation, he was diagnosed as Serum sickness though because of very dark skin colour no rash could be found.

- He was started on inj Methylprednisone 125 mg for 3 days, in view of severe debilitating polyarthralgia with inability to move even in bed.

- After 1st dose of steroid itself, his symptom completely subsided.

❑ CONCLUSION

- There is a risk factor with previous sensitization and need to explain the patient risk , symptoms & precaution before drug administration, during hospital stay and even after discharge.

- We should also rule out other differential diagnosis.

- Symptoms are usually mild & easy to manage.

❑ DISCUSSION

- Serum sickness is "type III" or immune complex-mediated hypersensitivity disease, characterized by fever, an urticarial or morbilliform rash demonstrating leukocytoclastic vasculitis, arthralgia/arthritis, gastrointestinal disturbances, lymphadenopathy, and proteinuria.

- often diagnosed based on clinical grounds, and generally a biopsy is not warranted to make diagnosis

- Differential diagnosis need to rule out, showing urticarial or morbilliform rash, fever, and arthralgias but does no evidence of cutaneous or systemic vasculitis.
    - Drugs - antibiotics (such as amoxicillin, cefaclor, cephalexin, and trimethoprimsulfamethoxazole).
    - Biologic immune modulators (such as infliximab, omalizumab, and rituximab).

THANK YOU