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203.LYMPHOCYTES AND ACQUIRED OR CONGENITAL IMMUNODEFICIENCY DISORDERS

Severe Reaction to Rituximab in Children

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Background:
Rituximab is a chimeric monoclonal antibody used in various pathologies involving CD20-positive cells. While it is usually well tolerated, infusion-related reactions are frequent but usually mild. Severe reactions such as anaphylaxis and serum sickness nevertheless can occur. Rituximab-induced serum sickness (RISS) is a rare delayed hypersensitivity reaction that may be unrecognized, as it can be confused with severe infection or in some circumstances with primary disease flare-up. We aim to extend our knowledge about severe infusion related reactions to rituximab in children, focusing on RISS and anaphylaxis.
Objectives:
Our study objective was to study severe reactions to rituximab by evaluating all children and adolescents who received rituximab in our center.
Methods:
Children and adolescents who received rituximab between 2014 and 2021 at CHU Sainte-Justine, a tertiary and leading pediatric center in Quebec, Canada, were included in the study. Data was collected retrospectively from our electronic medical records in CHU Ste-Justine. The diagnostic criteria proposed by the World Allergy Organization in 2020 were used to classify patients in the anaphylaxis subgroup. Patients with RISS were included if they developed fever and at least rash and/or arthralgia, starting 1 to 30 days following rituximab infusion, and if no other confirmed diagnosis explained symptoms. The study was approved by local Institutional Review Board.
Results and discussion:
1534 rituximab infusions in 391 patients were analyzed. A severe infusion reaction to rituximab occurred in 14 patients (3.6%); none resulted in death. Rituximab was prescribed for an auto-immune disease in 61% of cases.
Seven patients presented with RISS (1.8%); all were treated for an auto-immune disease including 4 for immune thrombocytopenia (ITP). Mean time from rituximab to RISS was 9 days (ranging from 6 to 12 days). All RISS patients but one presented with the classical triad of fever, rash and arthralgia. Increased C-reactive protein or sedimentation rate was documented in all patients, and decreased complement in 83%. Three patients required admission to intensive care unit due to hemodynamic instability. Patients received corticosteroids and/or intravenous immunoglobulins; mean duration of RISS was 4 days (ranging from 3 to 6 days). Rituximab was reinfused after RISS in one patient; she presented an immediate anaphylactoid reaction after which rituximab was permanently discontinued. Patients who received lower doses of rituximab were less likely to present RISS compared to patients who received higher doses (risk ratio 0.14, CI 0.03-0.74, p=0.016). Although few ITP patients developed RISS, RISS was associated with a greater chance of achieving partial or complete ITP remission (risk ratio 3, CI 1.47-6.14, p=0.033). Such possible association was not observed in other diseases.
Seven patients developed severe anaphylaxis (1.8%), 3 of them reacted after the first dose (42.8%). Five of them were able to receive further rituximab infusion, using desensitization protocols.
Conclusion:
RISS is a rare hypersensitivity reaction in children. To this day, our study is the first to report more than 3 patients in a pediatric setting. RISS in children seems to be more frequent when rituximab is administered for an autoimmune condition, especially ITP. Although the classic triad of fever, rash and arthralgia appears more frequent in children than in adults, RISS should be considered in the differential diagnosis of any suggestive symptom developing within 30 days of infusion. Presence of biological inflammation and/or low serum complement can further support the diagnosis. In all patients, evolution was favorable within a few days with steroids. However, in contrast with anaphylaxis, RISS should be considered as a contraindication for further rituximab therapy.

Disclosures Deslandres: *Organon:* Other: Invited speaker; *Abbvie:* Other: Invited speaker; *Janssen:* Other: Invited speaker. **Pastore:** *Novartis:* Research Funding; *Forma Therapeutics:* Research Funding; *Agios:* Research Funding; *Vortex:* Consultancy, Other: eceived monetary compensation for participation at adboard; *NovoNordisk:* Consultancy, Other: eceived monetary compensation for participation at adboard; *Prinicipa pharmaceutics:* Research Funding.

OffLabel Disclosure: Rituximab is a monoclonal antibody targeting CD20-positive cells. It is often used off-label in pediatric or adult settings, mainly to treat auto-immune conditions or EBV replication in immunosuppressed patients.

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