Pegaspargase, a chemotherapy drug known to improve survival outcomes in acute lymphoblastic leukemia, is associated with a risk for hypersensitivity reactions. At a children's hospital in the midwestern United States, two patients developed unusual reactions consisting of disseminated urticaria about two weeks after their second dose of pegaspargase. Both patients then proceeded to have severe anaphylaxis with the third dose of pegaspargase. These cases highlight the importance of advanced practice nurses being alert for the occurrence of unusual and delayed reactions to chemotherapy administration.

AT A GLANCE

- Pegaspargase is linked to hypersensitivity reaction risk; hypersensitivity reactions typically occur within a few minutes to hours of the infusion.
- Disseminated urticaria, appearing about two weeks after a second infusion of pegaspargase, preceded anaphylactic reactions to a third infusion in two patients with acute lymphoblastic leukemia.
- Advanced practice nurses should be alert for delayed and unusual reactions to pegaspargase and consider the risks of hypersensitivity reaction in all patients.

KEYWORDS
pegaspargase; urticaria; hypersensitivity; pediatric; acute lymphoblastic leukemia

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Pegaspargase

Two pediatric case studies of delayed urticaria preceding anaphylactic reactions postadministration

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Asparaginase is a standard chemotherapy treatment for pediatric acute lymphoblastic leukemia (ALL) (Heo et al., 2019; Marini et al., 2019). Administration is associated with risk of hypersensitivity reactions (HSRs), including anaphylaxis, angioedema, cough, and local or diffuse erythema and urticaria (Burke & Rheingold, 2017; Pidaparti & Bostrom, 2012). These reactions occur in 3%–41% of patients receiving asparaginase (Burke et al., 2018). Reactions may be immediate or delayed and can vary in severity in relation to both patient- and treatment-related factors. Although anaphylactic reactions typically occur within minutes to hours, delayed reactions have been reported within a few days of administration (Burke & Rheingold, 2017).

There are five formulations of asparaginase: *Escherichia coli* (*E. coli*)–derived, pegylated (pegaspargase), *Erwinia*, calaspargase, and recombinant crisantaspase (Jazz Pharmaceuticals, 2019; Marini et al., 2019). Pegaspargase was created to decrease the incidence of HSRs, the development of neutralizing antibodies, and the frequency of administration (Heo et al., 2019). Known hypersensitivity to *E. coli* asparaginase increases the risk of pegaspargase reactions (Burke et al., 2018). Pegaspargase can administered by intramuscular or IV routes; both are associated with HSR risk (Beaupin et al., 2017; Burke et al., 2018; Hasan et al., 2017). Differences in reaction definitions, reporting, and patient risk may contribute to variations in reported reaction rates. In addition, reactions occurring outside the healthcare setting and those that are self-managed may be underreported (Beaupin et al., 2017).

At a children's hospital in the midwestern United States, two patients experienced disseminated urticaria about two weeks after their second dose of IV pegaspargase. Both patients subsequently developed anaphylaxis with the third pegaspargase infusion. Remaining alert for the occurrence of unusual and delayed reactions to pegaspargase is important as advanced practice nurses consider individualized reaction risk.

Case Study 1

Patient A is a two-year-old male diagnosed with very high-risk pre–B-cell ALL treated on the Children's Oncology Group protocol AALL1131. This protocol entails about three and half years of therapy for males, with phases including induction, consolidation, interim maintenance I, delayed intensification, and maintenance (Burke et al., 2019). Very high-risk patients also undergo a second interim maintenance phase. Pegaspargase is given once in induction, twice in consolidation, twice in delayed intensification, and twice in interim maintenance II (Burke et al., 2019). Patient A tolerated the first dose of IV pegaspargase without reaction. The second infusion was paused twice for a total of eight minutes, once for two short coughing episodes and once for sudden restlessness and irritability. He recovered quickly with each pause. The infusion was completed without additional issues or need for medications, but persistent vomiting and decreased intake developed soon after discharge. This