

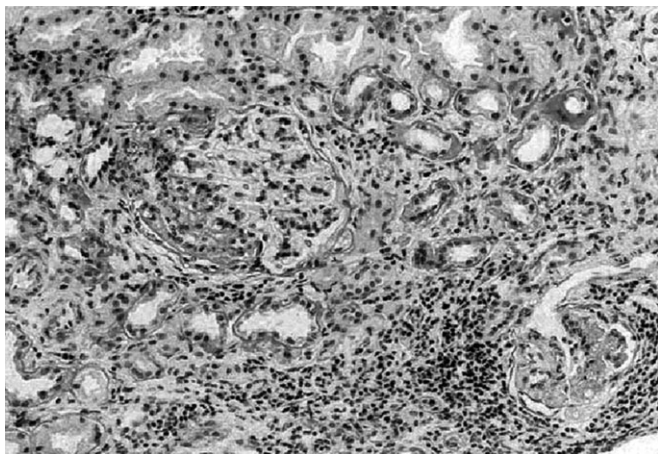


Fig. 1 Second renal biopsy: advanced glomerular sclerosis with cellular infiltration to interstitial tissue and degeneration of the renal tubules are seen (periodic acid–Schiff).

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Anaphylactic reaction to polyethylene glycol-conjugated asparaginase: Premedication and desensitization may not be sufficient

Justyna Walenciak, Wojciech Mlynarski and Beata Zalewska-Szewczyk

Department of Pediatrics, Oncology, Hematology and Diabetology, Medical University of Lodz, Lodz, Poland

Sahiner *et al.* presented two cases of anaphylaxis in response to polyethylene glycol (PEG)-conjugated asparaginase (PEG-asparaginase) that occurred despite desensitization and premedication.¹ L-Asparaginase (L-asp) is the key component of the treatment of some lymphoid malignancies. One of the main factors limiting its therapeutic efficacy is inactivation of the drug due to immune response that may occur in approximately 60% of patients.² At the beginning of the incorporation of the drug into treatment protocols it has been noticed that development of hypersensitivity reaction to L-asp is related to decreased serum activity of the enzyme, although some patients maintained serum L-asp activity despite development of anti-asparaginase antibodies.³ According to the treatment protocol in force in most European countries (AIEOP-BFM ALL 2009), any clinical allergic reaction to L-asp is an indication to discontinue treatment with the current preparation and to change the formulation. There are three preparations of L-asp available on the market: two are derived from *Escherichia coli* (a native and pegylated form of the

enzyme), and one is derived from *Erwinia chrysanthemi*. The Sahiner *et al.* cases raise the very important issue of lack of accessibility to certain formulations of the enzyme in some countries and the accompanying clinical implications. Clinically, overt allergy to native L-asp following hypersensitivity to PEG-asparaginase should imply *Erwinia* asparaginase treatment, but, as Sahiner *et al.* noted, this medication is not available on the Turkish market. This explains continuation of the treatment with PEG-asparaginase incorporating desensitization and premedication protocols. Although in some studies desensitization protocols are described to be effective against clinical symptoms of L-asp hypersensitivity, they do not resolve the question of decreased activity of the enzyme. In contrast, it has been shown that there is a group of patients who do not develop allergic reactions to L-asp, but they lack L-asp activity. This phenomenon is called “silent inactivation” and occurs in as many as 40% of patients, mainly in those at higher risk of treatment failure.⁴ Therefore the monitoring of serum drug activity enables selection of patients who not benefit from further treatment with certain drug formulations, and may be implemented for individualization of ALL therapy. In our opinion, serum L-asp activity monitoring is also extremely important when continuing the drug after hypersensitivity episodes. As has been described by Kawahara *et al.*, it is possible to reach therapeutic L-asp activity after subsequent doses of the drug along with anti-allergic medications.⁵ This

Correspondence: Justyna Walenciak, MD, Department of Pediatrics, Oncology, Hematology and Diabetology, Medical University of Lodz, 36/50 Sporna Street, 91-738 Lodz, Poland. Email: justyna.walenciak@live.com

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method is supported by authors from countries where not all L-asp formulations are available, but we believe that this should be followed by measuring the drug activity in order to find a group of patients who clearly benefit from this procedure.

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