

## Systemic allergic dermatitis caused by the solvent of Eligard®

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Javier Ruiz-Hornillos<sup>1</sup>, Aythamy  
Henríquez-Santana<sup>1</sup>, Antonio  
Moreno-Fernández<sup>1</sup>, Inés Gonzalo González<sup>2</sup>  
and Sonsoles Rojo Sánchez<sup>2</sup>

<sup>1</sup>Allergy Department and <sup>2</sup>Dermatology  
Department, Hospital Infanta Elena,  
Valdemoro, Madrid

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Eligard Injection Kit® (Astellas Pharma, Madrid, Spain) is a gonadotropin-releasing hormone agonist. It works by decreasing the levels of certain hormones produced by the testes and ovaries. It is injected subcutaneously into the abdomen or into the arm as a depot injection. Eligard contains leuporelin acetate as the active ingredient. The delivery system consists of a biodegradable polymer (poly DL-lactic-co-glycolic acid), diluted in a solvent (*N*-methyl-2-pyrrolidone).

We report here a case of systemic allergic contact dermatitis caused by the solvent of Eligard.

### Case Report

An 80-year-old man with prostatic adenocarcinoma presented with eczematous lesions on his upper chest, extending down to the abdomen. Over the following 2 days, the eczema spread to his neck, face, back, arms, and legs. No other cutaneous abnormality or lymphadenopathy was found. He had been given injections of leuporelin acetate into the abdomen every 3 months, for a period of 9 months. The eruption appeared 12 hr after the third injection of Eligard. These symptoms disappeared 15 days after treatment with systemic steroids.

A biopsy was consistent with dermatitis. An allergic contact dermatitis was suspected and patch tests were performed with the European baseline series (TRUE Test®, Stallergenes Ibérica, Barcelona, Spain) active ingredient of Eligard (leuporelin acetate 1%, 10%, and 50% pet.), solvent ('as is'), and Eligard (leuporelin acetate + poly DL-lactic-co-glycolic acid and *N*-methyl-2-pyrrolidone) 'as is'. Readings



Fig. 1. (a) Patch tests D4: 1. Delivery system ('as is'); 2. Leuporelin acetate 50% pet.; 3. Eligard (leuporelin acetate + solvent) 'as is'; 4. Leuporelin acetate 10% pet. (b) Flare-up of dermatitis at D3

were made on D2 and D4 according to the ICDRG guidelines. Patch testing was positive to the solvent (poly DL-lactic-co-glycolic acid and *N*-methyl-2-pyrrolidone) at D4 (++) and Eligard at D4 (+). Leuporelin acetate and the other contact substances yielded negative results (Fig. 1a). On D3 a dermatitis of the upper chest had recurred, as well as reactivation of the eczematous lesions on the abdomen (Fig. 1b). Patch tests were performed on five control subjects, with negative results.

Two months after patch testing, after informed consent, subcutaneous challenge test was performed. The patient tolerated leuporelin acetate in another diluent.

### Discussion

Cutaneous adverse reactions due to leuporelin acetate include pruritus, urticaria, photosensitivity, injection site reactions, flare-ups, granulomas (1), and leucocytoclastic vasculitis (2). There have been no reports of systemic allergic dermatitis due to this drug. More localized reactions to leuporelin acetate have also been reported, and a conclusion that a sterile abscess was probably a response to the polymer used as a vehicle (3, 4).

Copolymers have been underestimated as to their sensitizing capacities.

Allergic contact dermatitis has been described (5, 6); however, the nature of the hapten is unknown.

We have demonstrated that the patient fulfils the criteria of systemic allergic dermatitis (7) and that this was induced by a component of the solvent mixture poly DL-lactic-co-glycolic acid and *N*-methyl-2-pyrrolidone from a leuprolin acetate depot injection. This is the first report of such a case.

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### Address:

Javier Ruiz-Hornillos  
Hospital Infanta Elena  
Unidad de Alergia  
Avenida Reyes Católicos 21  
CP: 28340 Valdemoro  
Madrid  
Tel: +34 9189 48410 ext 2030  
Fax: +34 9189 48544  
e-mail: jrhornillos@gmail.com