

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

**The case of SLE associated Sneddon-Wilkinson pustular disease successfully and safely treated with infliximab**

**This is the author's manuscript**

*Original Citation:*

*Availability:*

This version is available <http://hdl.handle.net/2318/64027> since

*Terms of use:*

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)



# UNIVERSITÀ DEGLI STUDI DI TORINO

***This is an author version of the contribution published on:***

***Lupus***, volume 18, 2009, DOI: 10.1177/0961203309103053

*Naretto C. et al., volume 18, Sage, 2009, pp. 856–857*

***The definitive version is available at:***

**<http://lup.sagepub.com/content/18/9/856>**

## **The case of SLE associated Sneddon-Wilkinson pustular disease successfully and safely treated with Infliximab**

C Naretto(1,2), S Baldovino(1,2), E Rossi(3), M Spriano(3) and D Roccatello(1,2)

1Master di II livello sulle Malattie Rare, Università di Torino, Italy;

2 Centro Universitario di Ricerche di Immunopatologia e Documentazione su Malattie Rare (CMID), Giovanni Bosco Hospital, Torino, Italy and

3 Sezione di Ematologia, Ospedale Universitario S. Martino, Genova, Italy

Correspondence to: Carla Naretto, CMID, Centro di Ricerche di Immunopatologie, Documentazione su Malattie Rare, Giovanni Bosco Hospital, p.zza del Donatore di Sangue 3, Torino 10152, Italy.

Email: [cmid@iol.it](mailto:cmid@iol.it)

Conflict of interest statement

No competing interest declared

Letter to the editor

The case of SLE associated Sneddon- Wilkinson pustular disease successfully and safely treated with infliximab.

Sir,

We are reporting on the case of a patient with a 5-year history of Sneddon-Wilkinson's disease (SWD) associated with systemic lupus erythematosus (SLE) who was successfully treated with infliximab.

SWD is characterised by a superficial, flaccid and aseptic vesiculo-pustular eruption that mainly affects middle-aged women. It can be associated with auto- immune systemic diseases such as SLE.(1)

Current therapeutic approaches to SWD include dapsona, steroids, phototherapy and retinoids. The use of antitumor necrosis factor alpha (TNF- $\alpha$ ), such as infliximab, is described as a possible rescue therapy for nonresponders.(2)

A 37-year-old woman was referred to our Centre (CMID) in April 2007, with a history of SLE since 1982. From the time of diagnosis until 1997, she had been treated with steroids and immunosuppressant drugs, including azathioprine and methotrexate. In 1997, the patient experienced an ischaemic stroke. The concomitant detection of anti-cardiolipin antibodies (ACAs)

and lupus anticoagulant (LAC) suggested a diagnosis of antiphospholipid syndrome (APS) secondary to SLE. The patient was given warfarin (target INR: 3.0). Because of a concomitant increase in levels of antinuclear antibodies (ANA) with homogenous pattern and anti-double strand DNA antibodies (dsDNA-Ab) together with the appearance of antineutrophil cytoplasmic antibodies with perinuclear pattern and clinical symptoms, including arthralgia, weakness and paraesthesia, bolus doses of 500 mg cyclophosphamide were intravenously infused every other week for a cumulative dose of 3 g. In March 2004, because of the difficulty in maintaining the therapeutic range of INR and frequent occurring of haemorrhages, warfarin was replaced by low doses of aspirin, which are still being administered.

In January 2002, very itchy cutaneous lesions appeared all over the body just sparing face. No systemic symptoms were present, and laboratory tests, including dsDNA-Ab, ACAs and LAC were normal or negative. Histologically, the lesions were characterised by subcorneal neutrophil infiltration with negative direct immunofluorescence. A diagnosis of SWD was made.(1)

Over the following years, the patient was treated with dapsone (50 mg/day), steroids (prednisone 25 mg/day), retinoids (30 mg/day) and hydroxychloroquine (400 mg/day), with only partial and transitory control of the cutaneous manifestations, but multiple (and sometimes severe) adverse effects, such as haemolytic anaemia secondary to dapsone therapy. Mycophenolate mofetil, cyclosporine and colchicine were also used, but no improvement was observed. Phototherapy was not recommended by the dermatologists because of the potential risk of inducing SLE flare.(3)

In April 2007, due to the severity of the cutaneous lesions, the patient agreed to begin a rescue therapy. At that time, despite continuing administration of prednisone (25 mg/day) and azathioprine (100 mg/day), a SLEDAI score of 5 was determined.

On the basis of the implications of proinflammatory cytokines, especially TNF- $\alpha$ , in SWD,4 infliximab was administered intravenously, at 5 mg/kg, at weeks 0, 2, 6, 14 and 22, and then every other month without any adverse effects. Of interest, within 24 h after the first infusion of infliximab the patient's overall condition improved dramatically and the pustules disappeared. Prednisone was tapered until a final dose of 5 mg/day and azathioprine until 50 mg/day within 3 months. No other drugs were administered.

Six months after beginning infliximab, the disease remains in remission except for mild blister pusses on the lower limbs (Figure 1). Noteworthy, no lupus flares were observed, and serological findings were not modified by anti-TNF- $\alpha$  antibody therapy.

Despite the known effects of anti-TNF- $\alpha$  antagonists on antinuclear antibodies titres,(5,6) ANA levels, which were positive at a low titre at the beginning of therapy, did not increase during the following 6 months, whereas dsDNA-Ab levels, which were negative at the beginning, remained negative after 6 months. Of interest, SLEDAI score was improved, and after 6 months of therapy it was as low as 1.

The Pubmed index reports two cases of SWD successfully treated with infliximab.(7,8) Etanercept was also found to be effective for this rare form of dermatosis.(9) All these patients presented with idiopathic, non-SLE-associated disease and showed prompt reversal of skin lesions.

Our patient is unique in that she represents the first reported case of an SWD associated with systemic lupus erythematosus, a condition which makes questionable the therapeutic option of anti TNF- $\alpha$ . Our patient was made aware of the potential risk of an immune exacerbation. However, the breadth of the skin lesions and the lack of success with standard therapies made her agree to start with such a rescue therapy. Infliximab was effective at keeping the pustular manifestations under control in this patient without affecting the ANA and dsDNA-Ab titre at least during the 6 months of follow-up. Moreover, the SLE-DAI score documented some effects on decreasing lupus disease activity, as described.(6)

The use of infliximab as rescue therapy in this case suggests that this innovative drug can be effective, at least in unusual cases of SLE.

1. Reed J, Wilkinson J. Subcorneal pustular dermatosis. *Clin Dermatol* 2000; 18: 301–313.

2. Alexis AF, Strober BE. Off-label dermatologic uses of anti-TNF- $\alpha$  therapies. *J Cutan Med Surg* 2005; 9: 296–302.

3. Hasan T, Nyberg F, Stephansson E, et al. Photosensitivity in lupus erythematosus, UV photoprovocation results compared with history of photosensitivity and clinical findings. *Br J Dermatol* 1997; 136: 699–705.

4. Grob JJ, Mege JL, Capo C, et al. Role of tumor necrosis factor- $\alpha$  in Sneddon-Wilkinson subcorneal pustular dermatosis. A model of neutrophil priming in vivo. *J Am Acad Dermatol* 1991; 25:944–947.

5. Ramos-Casals M, Brito-Zeron P, Munoz S, et al. Autoimmune diseases induced by TNF-targeted therapies: analysis of 233 cases. *Medicine* 2007; 86:242–251.

6. Aringer M, Steiner G, Graninger WB, Hofler E, Steiner CW, Smolen JS. Effects of short term Infliximab therapy on autoantibodies in systemic lupus erythematosus. *Arthritis Rheum* 2007; 56:274–279.

7. Bonifati C, Trento E, Cordiali Fei P, Muscardin L, Amantea A, Carducci M. Early but not lasting improvement of recalcitrant subcorneal pustular dermatosis (Sneddon-Wilkinson disease) after infliximab therapy: relationships with variations in cytokine levels in suction blister fluids. *Clin Exp Dermatol* 2005; 30:662–665.

8. Voigtlander C, Luftl M, Schuler G, Hertl M. Infliximab (anti-tumor necrosis factor alpha antibody): a novel, highly effective treatment of recalcitrant subcorneal pustular dermatosis (Sneddon-Wilkinson disease). *Arch Dermatol* 2001; 137: 1571–1574.

9. Berk DR, Hurt MA, Mann C, Sheinbein D. Sneddon-Wilkinson disease treated with etanercept: report of two cases. *Clin Exp Dermatol* 2008; Aug 9.