Successful Treatment With Low-Dose Thalidomide in a Patient With Both Behçet's Disease and Complex Regional Pain Syndrome Type I

Case Report

Daniel W.T. Ching, MB, ChB, FRCP, FRACP, Alan McChintock, MPS, MPPharm, BPharm (hons), and Frances Beswick, MBBS, FRCA, PANZCA, PFPMA NZCA

Abstract

Thalidomide is a recognized treatment of Behçet’s disease. Low-dose thalidomide seems to be effective in the treatment of orocutaneous ulcers and is potentially safer with a lower incidence of adverse effects than higher doses. We wish to report a case of Behçet’s disease in a 33-year-old woman who responded well to thalidomide 50 mg 2 to 4 times per week. Her disease manifestations (severe orocutaneous ulceration, pseudofolliculitis, mild thrombophlebitis, positive pathergy response, and fatigue) were previously resistant to courses of prednisone, dapsone, colchicine, various types of mouthwash, and topical steroid preparations. She also gave a history of complex regional pain syndrome type I (CRPS I) over her left patella (severe pain, intermittent edema, hyperalgesia, allodynia, cold sensation, and loss of movement) after a fall onto her left knee 6 years previously. This had only partially responded to a variety of treatment modalities.

After starting thalidomide for her Behçet’s disease, the pain in her left knee unexpectedly disappeared. There are no studies showing that thalidomide improves neuropathic pain, probably by selectively blocking tumor necrosis factor-alpha production in activated macrophages. We believe this is the first report of successful use of thalidomide in a human being with CRPS 1, and we therefore recommend that thalidomide should be considered in the treatment of CRPS I.

Key Words: thalidomide, Behçet disease, complex regional pain syndrome

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A 33-year-old Caucasian housewife of Scottish descent presented with a 2-year history of recurrent, painful oral ulcers, occurring in crops lasting 1 to 3 weeks. She had been treated with various mouthwashes, including triamcinolone in oralbase, by an oral surgeon for 2 years. A gynaecologist had been treating her recurrent vulval and vaginal ulcers for 4 years, which were diagnosed as inflammatory and not infective ulcers. A dermatologist had been seeing her for a year for pseudofolliculitis; 2 episodes of mild thrombophlebitis, and a positive pathergy phenomenon had been observed after vencupuncture and intravenous cannula insertion.

She had been classified as having Behçet’s disease because of recurrent oral ulceration, recurrent genital ulceration, skin lesions, positive pathergy tests and having met all the diagnostic (classification) criteria set by the International Study Group except for eye lesions.

Her past medical history included a diagnosis of reflex sympathetic dystrophy, now called complex regional pain syndrome type 1 (CRPS 1) in her left patella 6 years previously. After a minor fall onto her left knee, she developed severe pain, intermittent edema, allodynia, dysaesthesia, hyperpathia, and loss of movement in her left knee. She had been treated by the pain clinic in 2 centers with sympathetic nerve blocks, therapeutic epidural block, intravenous pamidronate, self hypnosis, physiotherapy (pain retraining), hydrotherapy, transcutaneous nerve stimula-
Successful Treatment With Low-Dose Thalidomide

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fylaine because of gastrointestinal adverse effects. When her nerve conduction studies were performed towards the end of August 2002, they were still normal. We therefore restarted her on low dose thalidomide between 100 and 400 mg weekly, depending on her symptoms. Her orogenital ulcers disappeared promptly, and the ache in her left patella also disappeared upon restarting thalidomide.

DISCUSSION

Denman and colleagues used 50 mg of thalidomide 3 nights weekly in a series of 45 patients with Behçet’s disease and found this low dose effective in suppressing mucosal ulcers. It was well tolerated and did not cause neuropathy after a mean follow-up of 41 months. Two other studies have found thalidomide 100 mg daily as effective as higher doses in the treatment of aphthosis. A fourth study found the smallest dose of thalidomide needed to control the majority of orogenital ulcers was between 7 and 200 mg daily. Our patient found a total weekly thalidomide dose of 200 mg was sufficient in completely suppressing her orogenital ulcers. Despite this low dose, she started to experience paresthesia in her left forefoot and hands after 6 months of treatment.

A recent review found thalidomide is used in a variety of inflammatory conditions. It has a number of immunomodulatory, anti-inflammatory, and antiangiogenic mechanisms. Its efficacy in the treatment of Behçet’s disease might be the result of its tumor necrosis factor-alpha (TNF-α) inhibitory actions, and infliximab, a chimeric IgG1 monoclonal antibody directed against TNF-α, has been used recently to treat a case of Behçet’s syndrome, resulting in remission.

There is evidence that TNF-α is involved in the pathogenesis of CRPS 1, and thalidomide has been shown to block neuropathic pain in a rat model of chronic constriction injury of neuropathic pain. Etanercept, a recombinant tumor necrosis factor receptor (p75)-Fc fusion protein that competitively inhibits TNF-α, has recently been shown to
reduce hyperalgesia in a mice model of painful neuropathy. A
As far as we know, our patient is the first reported case of a patient with CRPS 1 who has been successfully treated with thalidomide. Thalidomide is relatively inexpensive compared with infliximab and etanercept, and our case suggests that a controlled trial on the use of thalidomide in CRPS 1 is warranted.

REFERENCES

When Thought Leaders Mislead: “Discoid Lupus is Not Related to SLE”
Daniel J. Wallace, MD
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As early as 1872, Kaposi noted that chronic cutaneous lupus can disseminate to systemic disease. However, this view was vigorously disputed by internists for years. In 1957, Harry Keil expressed frustration at trying to teach internists otherwise. As late as 1951, Beecher, discussing the collagen disease in Cecil and Loeb’s Textbook of Medicine, stated that in spite of its name, this disease (discoid lupus) bears no relation whatsoever to systemic lupus. During that decade, the first of many articles appeared which in essence showed what we now know: 5-15% of chronic cutaneous lupus evolves into systemic lupus over 5-10 years. In 1957, Reches reported that 61% of 100 Board Certified Internists replied that no relationship existed. But Dubois told me how much time he had to “waste” during that decade debating and teaching that there was a connection. Earlier editions of his textbook recounted these “battles” with “thought leaders” that took a whole generation to correct.

REFERENCES