Behçet’s disease: Treatment of mucocutaneous lesions

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ABSTRACT

Oral and genital ulcers, and cutaneous vasculitic lesions are considered hallmarks of the disease, and often precede other manifestations. Mucocutaneous lesions figure prominently in the presentation and diagnosis. Therefore, their recognition may permit earlier diagnosis and treatment, with beneficial results for prognosis. This review overviews the current state of knowledge regarding the therapeutic approaches including local and systemic agents for the treatment of mucocutaneous lesions of BD.

Introduction

Behçet’s disease (BD) is a chronic, relapsing, systemic vasculitis of unknown aetiology. The disease was first described in 1937 by Hulusi Behçet as a trisymptom complex, characterized by recurrent oral ulcers, genital ulcers and uveitis (1). Nowadays BD is considered as a multi-systemic inflammatory disease with vascular, articular, gastrointestinal, urogenital, pulmonary and neurologic involvement (2,3). Although several immunological abnormalities have been demonstrated, the exact mechanism of the inflammatory changes occurring remains to be elucidated. The most probable hypothesis is that of an autoimmune reaction set off by infectious agents such as herpes simplex virus 1 or streptococcus species in genetically predisposed individuals (4).

Mucocutaneous lesions constitute the hallmark of the disease. The high frequency of oral ulcers (OU), genital ulcers (GU) and cutaneous lesions at any time in the course of the disease, or as onset signs confirm the importance of these clinical features for the diagnosis (5). OU (92-100%), GU (57-93%), cutaneous lesions (38-99%), ocular lesions (29-100%) and arthropathy (16-84%) are the most frequent features of the disease among the prevalent countries. OU represent the onset feature of the disease in the majority of the patients worldwide (47-86%) (5, 6). GU (0-18%) and cutaneous lesions, especially erythema nodosum-like lesions (0-19%), have also been reported as onset lesions (6). In a recent study (7), we have shown that OU (85%), GU (21.7%), and articular symptoms (16.7%) were the most common onset manifestations, and synchronous onset of the clinical manifestations (OU and GU 15%, and OU and articular symptoms 10%) is not an uncommon feature of the disease.

Oral and genital ulcers are characterized by recurrent and painful ulcerations of the oral mucosa and genital skin/mucosa. They are identical to recurrent aphthous stomatitis (RAS) in appearance, but they tend to be more frequent and occur in crops. The cutaneous lesions of the disease are varied and include erythema nodosum-like lesions, papulopustular lesions, superficial thrombophlebitis, extragenital ulcerations, reactivity of the skin to needle prick or injection (pathergy reaction) and other cutaneous vasculitic lesions e.g. Sweet’s syndrome-like, pyoderma gangrenosum-like, erythema multiforme-like lesions, palpable purpura, subungual infarctions, hemorrhagic bullae, furuncles, and abscesses (5).

BD has a chronic course with unpredictable exacerbations and remissions. Clinical manifestations of BD, with the exception of eye symptoms, tend to improve with time (8, 9). Serious complications such as central nervous system involvement and sight threatening eye disease are rarely observed at late onset, especially in cases of onset at 40 years of age or more (10). Recent studies (11) suggest that besides considerable morbidity, the disease confers an increased mortality, mainly because of central nervous system, pulmonary as well as large vessel involvement and bowel perforation. There is evidence that increased morbidity and lethal outcome is often due to delayed diagnosis and treatment. Yazıcı et al. (12), in their
2-year, randomised, placebo-controlled and double blind study, reported that in those patients enrolled the study without eye involvement, azathioprine was significantly better than placebo in preventing the development of eye disease. In a previous study (7), we have shown that the duration between the onset sign (OU) and the fulfillment of diagnostic criteria was 3.77 ± 4.43 years. On the other hand, the duration between the time point of fulfilment of diagnostic criteria and the diagnosis was around 3 years (2.83 ± 2.3 years). Our study indicated that the disease is often diagnosed with a delay of several years, and in the majority of patients, mucocutaneous lesions especially OU appear before potentially severe organ involvement occurs. Since the changes in the skin and mucous membranes may represent the initial signs of BD, familiarity with the mucocutaneous spectrum of the disease and prompt recognition is imperative. Current evidence suggest that early treatment, to some extent, may control, and perhaps, change the course of the disease. In general, no therapeutic agent results in cure of the disease. The choice of treatment is generally based on the clinical presentation and the site affected. However, the main aim of the treatment should be the prevention of irreversible organ damage, especially, during the early, active phase of the disease. No standard therapy has yet been established for the treatment of mucocutaneous lesions, and a wide spectrum of therapeutic agents have been used, with varying success. The therapeutic agent for the treatment of mucocutaneous lesion should address both healing and the prevention of new lesion development.

This review overviews the current state of knowledge regarding the therapeutic approaches including local and systemic agents for the treatment of mucocutaneous lesions of BD. With regard the treatment, our recommendations were mainly based on controlled studies. However, we also presented some small case studies and even isolated reports to help guide the clinician since there have been still limited number of controlled studies on BD. Most of the studies performed in this area include limited number of cases for investigation. Absence of standardized outcome measures for the disease is another problem. The disease runs a course of exacerbations and remissions which may also cause a limitation in the evaluation of the treatment results.

**Topical treatment**

The majority of experience in the treatment of OU comes from the studies performed in patients with RAS. As we mentioned before, OU of BD are identical to RAS in appearance. Therefore, therapeutic remedies related with RAS, to some extent, can be applied to OU of BD.

**Corticosteroids**

Although controlled studies are still lacking, the efficacy of topical corticosteroids is indisputable based on their favorable and widespread use. Topical corticosteroids suppress the inflammation associated with the formation of aphthae. Many studies suggest that they are effective both OU and GU especially when they are used in the early stage of these lesions. They reduce the pain severity and accelerate the healing duration of OU and GU.

Triamcinolone acetonide cream 0.1% in Orabase is one of the most widely used topical corticosteroids for OU. Triamcinolone spray can also be used as an effective alternative. Prednisolone tablets in 20 ml water can be used as rinse four times daily like those of dexamethasone elixir (0.5 mg/5 ml) especially for patients with multiple OU. Ghate and Jorizzo (13) reported the effectiveness of potent corticosteroid gels, 5-10 times daily. Potent corticosteroid creams are also effective in GU. Corticosteroids in conjunction with antibiotics can be used to decrease the severity of GU attacks (14). The same combination can also be used for extragenital ulcers and PPL. Major OU or GU can be treated by intraläsional triamcinolone, 5-10 mg/ml which is given to the base of the ulcer from the adjacent mucosa. Topical anaesthetics can be applied to decrease the pain before this application (13, 15, 16). Two double-blind, placebo-controlled studies (17,18) with corticosteroids, Betamethasone-17-benzoate gel and Beclamethasone dipropionate aerosol have shown significant reductions in ulcer duration and pain severity compared with placebo in patients with RAS. However, both studies indicated that corticosteroids have no effect in the frequency of OU.

Topical medications are easily washed away from the ulcerated mucosa. Various adhesive vehicles in combination with the drug are developed to solve this problem. Patients should be advised to use topical corticosteroids at least thrice daily while ulcer persist and to initiate the treatment during the early stage of lesion development. To increase the effectiveness of the treatment, prolonged contact of the corticosteroid with ulcerated mucosa should be instructed. To ensure maximum effect, patients should massage the medication on the ulcer for about 30-60 seconds with their finger or coat a cotton-tipped applicator and hold it against the ulcer for up to a minute (19). This approach can be suggested for those ulcers limited in number and located in easy-to-reach areas of the oral mucosa. Otherwise, medications like oral rinse or mouthwashes should be preferred. In any circumstances, eating and drinking should be avoided for a minumum of 30 minutes after corticosteroid use. It should be kept in mind, chronic topical corticosteroid use may facilitate overgrowth of Candida. Therefore, patients should be followed and antifungal agents should be added to the treatment prophylactically when necessary.

**Antimicrobial agents**

Antimicrobial agents including antibiotics and antiseptic agents are used to control microbial contamination and secondary infection.

1. **Antiseptics (hexetidine, chlorhexidine, listerine)**

In general, they reduce the pain in OU. However, It is not clear whether they shorten the healing time. Four controlled studies (20-23) have been performed related with these compounds in patients with RAS. In two of the studies (22, 23), no significant differ-
ences in pain severity and duration of OU have been reported between groups of drugs (Hexetidine mouthrinse, chlorhexidine mouthwash) and placebo. Two studies (20, 21) noted the effectiveness of the listerine mouthrinse and chlorhexidine gel on the pain severity and duration of OU. In two of the studies (21, 23), total ulcer number has been found to be decreased in drug groups. In three of the four studies, significant benefits throughout the treatment course have been reported in both drug and placebo groups, and this effect has been explained by patient awareness and improved oral hygiene (20, 22, 23). It is wise to remember that chlorhexidine has a bitter taste and cause brown discoloration of the teeth and tongue when used longer than 2 weeks, which may limit its long-term use.

2. Antibiotics

Tetracycline. Tetracycline has been widely used in RAS and OU of BD for years because of its antichemotactic and antimicrobial effects (16). Tetracycline 250 mg capsule can be dissolved in 5 ml of water or flavored syrup and is held in the mouth for about 2 minutes before swallowing. It can be used four times daily. The drug can also be used in combination with diphenhydramine hydrochloride to provide a topical anesthetic effects. Burgess et al. (24) recommend the less concentrated formulation of the tetracycline, 250 mg in about 180 cc water, since the more concentrated solution of the tetracycline may cause erosion and stain the enamel of the teeth.

Three placebo-controlled studies (25-27) related with tetracycline and chlor-tetracycline have reported a significant decrease in pain severity and duration of OU in patients with RAS. However, the frequency of OU did not show a difference. A marked side effect is not observed when the drug is not used longer than 5 days, otherwise dysgeusia, thrush, angular cheilosis, burning and soreness of throat may occur.

Cephalxin. 250-500 mg capsules of the drug can be dissolved in 30-50 ml of water, and can be used like those of tetracycline (16). Cephalxin also has anti-inflammatory effects.

Penicillin G. Recently Kerr et al. (28) reported the effectiveness of topical application of 50 mg penicillin G potassium troches in RAS. Authors, in their double-blind, randomized and placebo-controlled trial of 100 patients, noted a significantly earlier ulcer healing and pain relief in patients receiving active drug than those in the placebo and no-treatment arms.

Sucralfate

Previous studies have reported encouraging results from the use of sucralfate suspension in patients with RAS (29), chemotherapy-induced oral mucositis (30), and vaginal ulceration (31). The mechanism of action of sucralfate is still not fully known. It binds to ulcerated tissue and forms a barrier, and augments healing in the gastrointestinal tract ulcers. In a randomised, double-blind and placebo controlled study (32), we have shown that sucralfate suspension (1g/5ml), 4 times daily, for 3-month duration as mouthwash, decrease significantly the frequency, healing time and pain of OU, and healing time and pain of GU in patients with BD. The effectiveness of the sucralfate on the OU frequency and healing time continued during the post-treatment period in decreasing order. These results indicate that the continuous use of sucralfate suspension has a protective effect against the development of OU. Because of this reason, it can be given prophylactically for OU of BD. Therefore, sucralfate suspension may well be a therapeutic alternative, especially for OU.

Amllexanox

Amllexanox has anti-inflammatory and antiallergic activities. It inhibits leukotrienes and histamines, and suppress the formation and release of inflammatory mediators from mast cells, neutrophils and mononuclear cells. Amllexanox, in 1996, has been approved as the first treatment for aphthous ulcers in the U.S.A. Previous controlled studies (33, 34) suggest that the drug accelerates the healing and decrease the pain severity of ulcers in RAS. However, it does not reduce the frequency of ulcers. Amllexanox is used in oral paste (5%) 4 times daily (after meals and at bedtime) for 4-10 days. Only 2.1% of those 991 patients with RAS who used the drug reported adverse events including stinging, dryness, bumps on the lips and mucositis (35).

Aminosalicylic acid

In a double-blind and placebo-controlled study of 22 patients, Collier et al. (36) have shown that aminosalicylic acid (5% creme) three times daily for up to 14 days reduce the duration and pain severity of ulcers in patients with RAS.

Anti-inflammatory agents (benzydamine, diclofenac)

Benzydamine is a topical nonsteroidal anti-inflammatory drug with anti-inflammatory, analgesic, antipyretic and local anesthetic activity. In general, this formulation shows a transient local anesthetic effect on aphthous lesions. It is wise to keep in mind that benzydamine may cause allergic reactions (37). Another anti-inflammatory agent, diclofenac 3% in hyaluronan 2.5% has been reported to reduce the pain severity of aphthous lesions in a randomised, double-blind, single dose study of 60 patients (38). The preparation showed a stronger analgesic activity than lidocaine 3% gel.

Anaesthetics

Anaesthetics (lidocaine 2.5%-5%, mepivacaine 1.5%, tetracaine 0.5-1% gels or mucosal ointments) are widely used as gels or mucosal ointments 2 to 3 times a day. They are particularly effective on the pain severity of ulcers. They can cause the development of sensitivity (5).

Silver nitrate

Silver nitrate sticks have been used for the treatment of OU for years. However, application of this agent may cause discomfort for the most of the patients. 5% Silver nitrate solutions can be better tolerated, and widely used in recent years (37). It seems likely that this agent only relieve the pain, but it is not effective on the duration and frequency of OU.

Colony stimulating factor (CSF)
Recombinant human granulocyte/macrophage-CSF was used to treat a large genital ulcer with multiple intralesional application of 300 μg amnute around the ulcer. The treatment resulted in complete healing in two weeks (39). We used topical granulocyte-CSF, Filgastrim, for the OU (4x120 μg/day, for 5 days) and/or GU (4x30 μg/day, for 5 days) of 7 patients with BD. We observed beneficial effects on the healing duration and pain severity of ulcers (40).

Other drugs

Interferon alpha. In a randomised, double-blind study (41), interferon alpha (IFN-α) 2c hydrogel has been found not to be effective for OU, although the previous open study (42) reported the beneficial effects of the compound.

Doxymycin. The topical treatment of aphthous lesions with doxymycin in isobutylcyanoacrylate led to stronger reduction of pain than placebo in a randomised study with 31 patients (43).

Cyclosporin A. In a controlled study (44) of 24 patients, Ergun et al. reported that the effectiveness of Cyclosporine A (CyA) in Orbacase on OU is not different from the placebo.

Prostaglandin E2. In a double-blind study (45) of 35 patients with RAS, topical application of prostaglandin E2 (0.3 mg gel, twice a day for 10 days) resulted in significant reduction of the number of new lesions, however, no beneficial effect could be detected regarding the healing speed of existing aphthous lesions and the pain feeling compared to placebo.

Other measures

In addition to the above-mentioned treatment approaches to OU, patients should be advised to maintain good daily oral hygiene. These patients should avoid irritating agents such as acid, crusty, hard, spicy or salty nutrients and alcoholic beverages. Erythema nodosum-like lesions are treated topically like those of classic erythema nodosum. Wet dressings, water- or saline-soaked cotton gauze or cloth compresses are used for inflammatory as well as oozing, weeping, crusted, bullous, eroded, or ulcerated skin diseases. Aluminium acetate 3-5% (Burow’s solution) is one of the widely used agents for wet dressings. Evaporation from the dressing soothes and dries by cooling the skin surface and causing vasoconstriction which is responsible from the antiinflammatory effects. They can be applied for 10-20 minutes and repeated during the day for 3-5 days in early stage of erythema nodosum-like lesions. This approach is also helpful for the treatment of thrombophlebitis. All therapy should be combined with rest in bed.

PPL and extragenital ulcers can be treated with antibacterial or combined preparation of antibacterial and corticosteroid creams.

Systemic treatment

Patients with severe mucocutaneous disease or those who are unresponsive to the topical treatments require systemic approaches to control their disease. Systemic treatment should also be given for those ulcers developed in oropharynx, a location resistant to topical treatment, and for major ulcers that frequently do not respond topical treatments. Systemic treatment should also be thought in young, male patients presenting with severe mucocutaneous lesions to prevent the development of serious organ involvement.

Corticosteroids

Corticosteroids are effective choices in almost all mucocutaneous lesions. They can be given as monotherapy or in combination with other drugs such as colchicine, IFN-α or azathioprine. There have been many enthusiastic reports of their efficacy in the mucocutaneous lesions of BD. However, satisfactorily controlled trials are still lacking. On the other hand, well-known side effect profile of corticosteroids in higher doses limits their long term use. Corticosteroids do not improve the long term outcome in BD (46). We recommend prednisolon 40-60 mg/d for 1-2 weeks and then taper the dosage gradually over 4 weeks.

Colchicine

Colchicine inhibits the enhanced chemotactic activity of neutrophils (47). Colchicine (0.5-2 mg/d p.o.) has been widely used almost for all lesions of the disease, and promising results have been reported especially after the year of 1975 (48, 49). However, first placebo-controlled study (50) suggested that the drug is effective only for erythema nodosum-like lesions and arthralgia. Yurdakul et al., in a recent randomised, double-blind and placebo controlled study, (51) revisited the issue and have shown that colchicine reduces the occurrence of GU, erythema nodosum-like lesions, and arthritis among women, and occurrence of arthritis among men. Oligozoospermia, amenorrhea or dysmenorrhoea, malaise, hair loss, gastrointestinal complaints (nausea, vomiting, diarrhea) and hematologic side effects are the main adverse effects of colchicine.

Calguneri et al. (52) have found superior combined use of colchicine and benzathine penicillin 1.2 MU/3 weeks than colchicine alone. Combined treatment was effective in reducing frequency and duration of OU and erythema nodosum-like lesions and the frequency of GU.

Dapsone

Dapsone (100-150 mg/d p.o.) also inhibits the enhanced chemotactic activity of neutrophils and can be used as an alternative compound to colchicine. In an open study (53), the beneficial effects of dapsone have been reported. Quick relapses have been observed after discontinuation of the dapsone treatment. In a double blind, placebo-controlled study (54) of 20 patients, Sharquie et al. reported significant reductions in the oral and genital ulcer parameters as well as the incidence of other cutaneous and systemic manifestations in dapsone-treated patients. Hemolytic anemia and methemoglobinemia which can be severe in patients with glucose-6-phosphate dehydrogenase deficiency are the main side effects, and may significantly limit their use.

Levamisole

Levamisole is an antihelmintic agent, and is used widely both in RAS and BD patients for years because of immuno-
potentiating effects. Lehner et al. (55) evaluated the efficacy of levamisole in a double-blind, cross over study, and reported an improvement in OU and GU together with arthritis and uveitis. In an open study, De Merieux et al. (56) reported that levamisole is effective in OU, GU and ocular inflammation.

In RAS, 6 placebo controlled studies (57-62) have evaluated the efficacy of the levamisole. The duration in these studies was ranging from 6 weeks to more than 6 months. Levamisole was given every one to two weeks with a dose of 150 mg/ thrice daily for 1-3 days a week. In three of the studies (57, 61, 62), the frequency and the duration of OU showed a significant decrease compared with placebo. Significant subjective improvement has been reported in 5 of these studies (57-61). Taste disturbances and nausea are the major adverse effects of levamisole. Neutropenia, flu-like symptoms, skin rash and urticaria have also been reported.

**Interferon**

Interferons are known as a cellular response to the foreign constituents of microbes, tumors and antigens. Besides their immunomodulatory effects, ability to augment the decreased activity of patient’s natural killer cells, capacity to inhibit IL-8 synthesis and secretion from endothelial cells, suppressive effects on gamma delta T cells, and the antiviral activities of interferons, together with the putative association between BD and viral infection, particularly herpes simplex virus 1, have been suggested to explain their therapeutic potential in BD (63). Tsambao et al. (64) first introduced the systemic application of IFN-α 2a in three patients with BD who showed complete or almost complete remission. Since then a number of uncontrolled studies (65-68) have been published, using IFN-α 2a or IFN-α 2b, and giving the agent either daily or three times weekly. Promising results have been reported especially with IFN-α 2a. In a review of this literature, Zouboulis and Orfanos (69) concluded that a majority of patients showed a worthwhile improvement in mucocutaneous lesions, arthritis and ocular manifestations. A two-month treatment, at least, is likely to be necessary to increase the effectiveness, and the disease generally relapses upon discontinuation. In a recent randomised, double-blind and placebo controlled study, (63) we have shown that interferon-α 2a treatment with a dose of 6 MIU, thrice weekly, for 3 months is an effective alternative particularly for the management of mucocutaneous lesions of BD, and its effect decreases gradually after the cessation of treatment. IFN-α 2a treatment decreased significantly the duration and pain of OU, and the frequency of GU and PPL. The mean frequency and duration of erythema nodosum-like lesions, thrombophlebitis, and articular symptoms also showed a decrease. The primary side effects of IFN-α 2a therapy are flu-like symptoms (fever, chills, headache, fatigue, myalgia etc) that start a few hours after the initiation of the therapy, and continue less than a day. Nausea, vomiting, anorexia, diarrhea, loss of weight, hematologic changes, transient raising of hepatic transaminases are seen less frequently.

**Thalidomide**

Thalidomide has recently been approved for the treatment of male and sterilised as well as post-menopausal women with BD in the U.S.A. (70). The drug was shown to selectively inhibit TNF-α synthesis. In a randomised, double blind, placebo controlled study with 63 patients (71), a remission of OU and GU and PPL was detected in 22% of the patients over 8 weeks. During the 6-month treatment, 30% of the patients remained free of lesions. However, the effect of thalidomide is temporary, and discontinuation of the treatment results in recurrence of the OU and GU, therefore a maintenance treatment with 50 mg/d to 50 mg twice a week is required. Peripheral neuropathy with acral paraesthesia was found clinically in 6% and electrophysiologically in 22% of the patients who received thalidomide 100-300 mg/d over 6 months. Thalidomide therapy, however, was associated with exacerbation of erythema nodosum. Central nervous system signs with sleepiness and headaches as well as xerostomia and constipation can occur. Teratogenic risk of thalidomide limits the clinical application.

The effectiveness of the thalidomide is lost about 20 days after discontinuation of the drug. In an uncontrolled study with 43 patients, Denman et al. (72) reported the effectiveness of thalidomide with a dose of 50 mg thrice weekly for about 17 months. In addition, this dose schedule did not cause any evidence of neuropathy.

**Azathioprine**

Azathioprine shows an anti-inflammatory effect by suppressing both cellular and humoral immune responses. In a randomised, double-blind and placebo controlled study of 73 patients (12), azathioprine (2.5 mg/kg body weight/d p.o.) have been found to be an effective choice in OU, GU and thrombophlebitis besides ocular inflammation and arthritis. The treatment resulted in a decrease in the frequency of OU, GU and thrombophlebitis. Azathioprine was found to be significantly better than placebo in preventing the development of new eye disease. Therefore, authors concluded that the drug can be used profilactically to prevent the eye involvement in young, male patients presenting with severe mucocutaneous lesions. Sterility, myelotoxicity, immunosuppression, opportunistic infections and liver disease are the main side-effects.

**Cyclosporin A**

CyA is an immunosuppressant agent which selectively inhibits T lymphocytes. CyA is registered for the treatment of BD uveitis in Europa. The drug is also capable of markedly ameliorating mucocutaneous lesions; however, it should be reserved for the most severe cases because of its significant long-term adverse effects such as renal failure, hypertension, neurologic toxicity, hirsutism. There have been several reports of the effectiveness of CyA. In a controlled study of 96 patients with recurrent uveitis, CyA, 10 mg/kg/d has been shown to be superior to colchicine, 1 mg/d in decreasing frequency...
and severity of OU, GU and PPL, besides ocular attacks (73). In another controlled trial (74), 26 patients treated with CyA with a dose of 5 mg/kg/d have been compared with 50 patients receiving conventional therapy, systemic corticosteroid alone or combined with azathioprine. CyA treatment was found to be more effective in reducing OU, GU, cutaneous lesions, thrombophlebitis as well as articular symptoms and neurologic symptoms. There are also quite enthusiastic, but uncontrolled and open studies which report promising results. Avci et al. (75) have found that CyA is effective on the frequency, number, size and depth of OU and GU. The drug was also decreased the frequency of erythema nodosum-like lesions, PPL and thrombophlebitis. Cantini et al. (76) noted that the drug is an effective choice in the treatment of thrombophlebitis.

Methotrexate

Methotrexate (7.5-20 mg/1x week p.o. over 4 weeks) has been reported to induce an improvement of a severe mucocutaneous involvement (13,77). However, its use should be reserved for severe cases. Methotrexate is not recommended in pregnancy and lactation, and severe bone marrow depression, liver dysfunction, acute infections, renal insufficiency, and mucositis are important side-effects of the drug.

Anti-tumour necrosis factor-alpha

Recent trials of anti-tumour necrosis factor (TNF) (78-81) for BD have shown encouraging results in the treatment of recalcitrant OU and GU besides gastrointestinal and ocular symptoms. Two such compounds have shown favourable results on preliminary tests: infliximab (a chimeric anti-TNF monoclonal antibody), and etanercept (a dimeric fusion protein of the p75 TNF receptor and IgG). In a recent double blind, placebo controlled study (82) of 40 male patients with BD, etanercept has been reported to be beneficial in decreasing the number of OU, erythema nodosum-like lesions and PPL as well as arthritis episodes. However, recurrences developed in some patients 3 months after etanercept was stopped.

In conclusion, as a high incidence of vital organ involvement, as well as the increased mortality especially in young male patients has been recorded in patients with BD, continuous surveillance and good management of the disease is warranted. In this respect, patient-based organizations that now are allied with cognizant physicians should be encouraged. Treatment of the mucocutaneous lesions of BD has become much more effective in recent years. Because of recent advances in understanding the pathogenesis of the disease underlying, and availability of a wide spectrum of therapeutic agents, alleviation of most symptoms, or control of the disease and, perhaps, modification of the course of the disease are now possible.

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REVIEW


