Case report

A mixed immunoblistering disorder exhibiting features of bullous pemphigoid and pemphigus foliaceus associated with *Spirulina* algae intake

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An 82-year-old healthy woman presented with bullae, partly hemorrhagic, on the trunk and extremities (Fig. 1), secreting erosions, and submammary macerations (Fig. 2). The blistering disease developed over a 2-year period, during which she reported taking no drugs. She did, however, begin using a food supplement containing the blue–green alga *Spirulina platensis* 1 year before the onset of the eruption.

At admission, the Nikolsky sign was positive. The first biopsy showed a subepidermal bulla with a denuded surface and sparse perivascular lymphocytic infiltrate with scattered eosinophils (Fig. 3). The second biopsy, taken during admission, demonstrated an intra- and subcorneal vesicular dermatitis with slight superficial acantholysis. Direct immunofluorescence disclosed immunoglobulin G (IgG) and C3 at the dermoepidermal junction. Indirect immunofluorescence was also positive at the dermoepidermal junction. A salt split test demonstrated IgG, IgM, and C3 on the upper side of the bulla. Immunoblotting of the serum was negative and showed no pemphigoid or pemphigus antigens. Enzyme-linked immunosorbent assay (ELISA) for desmoglein 1 and 3 antibodies was negative.

Diagnostic investigations for neoplasia, Wood's lamp exposure of urine, purified protein derivative (PPD), and antinuclear antibody (ANA) were negative.

With a diagnosis of mixed immunoblistering disorder exhibiting features of bullous pemphigoid and pemphigus foliaceus, prednisone 60 mg was started and gradually tapered, and topical treatment was begun with creams containing silver sulfadiazine and triamcinolone/neomycin. Suspecting the involvement of *Spirulina* in the disease, the food supplement was stopped. With this treatment, the patient steadily improved with no appearance of new blisters.

An *in vitro* interferon-γ release test with the *Spirulina*-containing food supplement, conducted to explore the connection between the agent and the eruption, yielded a slight increase in interferon (19%). The result was considered to be borderline, but, in view of the clinical picture and the fact that the patient was being treated with 20 mg prednisone at the time, the test can be considered as positive.

Three months after completion of the prednisone treatment, and with avoidance of the *Spirulina*-containing supplement, the patient was free of lesions with no recurrences.

**Discussion**

There have been a few reports of the use of herbal supplements to treat autoimmune disorders, but almost none on the exacerbation of autoimmune disease by immune-enhancing herbal supplements. Although many herbal supplements are touted for their immunostimulatory properties, the literature on the interactions of herbal supplements with autoimmune dermatologic disease is scarce.

We describe a case of a woman who developed an immunoblistering disease after ingesting a food supplement containing the blue–green alga *Spirulina platensis*. Our case is the second report of an immunoblistering disorder associated with *Spirulina* algae intake. The first report by Lee and Werth describes two cases: a 57-year-old man with known pemphigus vulgaris who experienced a severe flare-up of the disease after starting a food supplement containing ginseng, *Ginkgo biloba*, and *Spirulina platensis*; and a 45-year-old woman who developed dermatomyositis after intake of a supplement containing organic cayenne pepper, methylsulfonylmethane, and the algae *Aphanizomenon flos-aquae* and *Spirulina platensis*.

*Spirulina* is a microscopic filamentous cyanobacterium (blue–green alga) that has a long history of use as food. For the last 20 years, *Spirulina* has been produced commercially...
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for food and specialty feeds,4–6 and is sold widely in health food stores and mass-market outlets around the world.

One ingredient in blue–green algae is the blue phosphorescent protein pigment phycocyanin, which functions as a light-absorbing substance together with chlorophylls; it may also be used as a coloring agent or a synthetic dye in a number of foods and cosmetics.7

The immunomodulatory effect of Spirulina on humans was first shown in a study in 1982,8 which documented an increase in lymphocyte activity attributed to phycocyanin in a case–control study in cancer patients. Phycocyanin was also found to induce characteristic apoptotic features,9 which may have led directly to acantholysis and blister formation in our patient.

Spirulina stimulates mainly the innate immune system and acts on effector cells, as evidenced by interferon-γ (IFN-γ) production and cytolysis. The secretion of interleukin-1β (IL-1β), IL-4, and IFN-γ increases to nearly 2.0, 3.3, and 13.6 times basal levels, respectively.10–13 Enhanced immunoglobulin A (IgA) has been observed in lymphoid cells and saliva after Spirulina intake.14,15

Other in vitro animal and human studies support a role for Spirulina platensis in increasing the activity of macrophages, natural killer cells, and neutrophils, and promoting the production of IL-1 and tumor necrosis factor-α (TNF-α).16 IL-1 and TNF-α have been implicated in the pathogenesis of acantholysis.14

We suggest that the special dynamic clinical and histologic picture, with mixed features of two entities, could be attributed to the general augmentation of the immune system by the algae supplement. Alternative mechanisms include an adoptive immune reaction directed at specific epitopes in the Spirulina product, which are similar to targeted epidermal cell attachment molecules, or simply an idiosyncratic reaction.

References


