Behçet’s disease (BD) is a systemic inflammatory disease characterized by recurrent oral aphthae, genital ulcers, ocular inflammation and skin lesions. Involvement of large vessels, central nervous system, and gastrointestinal tract, and thrombotic events are less frequent but can be life threatening. Ocular complications of BD are some of the most devastating for patients with a major impact on quality of life. Eye involvement, which affects 50-90% of BD patients, is characterized by intraocular inflammation and occlusive retinal vasculitis. The etiology of BD is still unknown, but both genetic background and environmental factors are thought to be important in its pathogenesis. BD has long been regarded as an autoimmune disease; however, it has recently been found that it shares several clinical features with autoinflammatory diseases.

Autoinflammatory diseases are a group of inherited disorders caused by dysfunction of innate immunity and characterized by recurrent self-limited inflammatory attacks occurring at variable intervals without evident precipitating events. The inflammatory process most commonly involves the skin, serous membranes, joints, gastrointestinal tract and eyes, and is associated with elevated levels of acute phase reactants but relative lack of high-titer autoantibodies or antigen-specific T cells. The concept of “autoinflammatory” disease was introduced at the end of the 1990s and has grown rapidly in recent years as a result of advancements in molecular biology and genetics. Familial Mediterranean fever (FMF) is the prototype of this group of disorders which is characterized by recurrent painful attacks of fever and inflammation in the peritoneum, synovium, or pleura. FMF is an autosomal recessive disorder commonly found among individuals of Mediterranean descent and caused by MEFV gene mutations. This gene encodes pyrin, which normally assists in keeping inflammation under control by deactivating the immune response. Without this control, an inappropriate full-blown inflammatory reaction occurs.

Autoinflammatory and autoimmune disorders are both characterized by aberrant chronic activation of the immune system eventually leading to tissue inflammation. However, the pathogenesis underlying this damage differs such that the innate immune system directly causes tissue inflammation in an autoinflammatory disease, whereas activation of the adaptive immune system in autoimmune disease is responsible for the inflammatory process.

Although autoinflammatory and autoimmune diseases are currently divided into two different subgroups, regarding their similarities they might be considered as a single spectrum of disorders with a wide range of manifestations including pure autoinflammatory diseases at one end and pure autoimmune diseases at the other. Based on current evidence, BD does not easily fit under any one of these two pure ends. In fact, BD is at the crossroad between autoimmune and autoinflammatory syndromes. The following observations suggest that BD might have an autoinflammatory nature:

1. Increased activity of neutrophils and elevated levels of interleukin-1β in both BD and autoinflammatory diseases.
2. Recurrent episodes of remission and
exacerbation in BD similar to other autoinflammatory diseases.

3. Enhanced inflammatory responses and overexpression of pro-inflammatory cytokines are prominent features of BD, compatible with findings in other autoinflammatory disorders.\(^{12}\)

4. No specific autoantibody has been attributed to the pathogenesis of BD, contrary to other autoimmune diseases.

5. There are relationships between BD and some autoinflammatory diseases, especially FMF; both diseases are prevalent in the Mediterranean basin and are treated with colchicine.\(^{13}\) Moreover, genetic research has suggested that particular variants of the \textit{MEFV} gene are more common in people with BD which may be a susceptibility gene for it as well.\(^{14,15}\)

On the other hand, there is evidence in favor of an autoimmune nature for BD as well. For example, in common with other autoimmune diseases, BD shares class I MHC (HLA-B\(_{51}\)) association. Some symptoms of BD are treated with T-cell suppressing agents (e.g. Cyclosporine A). Furthermore, recent data suggest that a novel subset of T cells, Th17, plays a crucial role in pathogenesis of BD.\(^{16,17}\)

Autoinflammatory or autoimmune, the inevitable fact is that optimal management of BD; both treatment of inflammatory attacks and prevention of recurrences, has not yet been completely achieved. Sharing common features with autoinflammatory diseases suggests that targeting innate cells or their inflammatory mediators may be more effective than T-cell- or B-cell-directed therapies. Mounting evidence exists on the therapeutic advantages of biologic agents over conventional immunosuppressants, especially in sight-threatening Behçet’s uveitis. Interferon-a (IFN-a) has been reported to induce long-lasting remission in patients with ocular BD resulting in notable improvement in visual prognosis.\(^{18}\) Similarly, infliximab, a tumour necrosis factor a (TNF-a) antagonist, represents an important therapeutic advancement for patients with severe and resistant disease.\(^{19}\)

Ongoing or recently completed clinical trials (http://clinicaltrials.gov) report on the potential efficacy of other biologic response modifiers such as adalimumab (anti TNF-a antibody), anakinra (IL-1 receptor antagonist), tocilizumab (IL-6 blocker), secukinumab (anti IL-17 antibody), daclizumab (anti T-cell activated antigen monoclonal antibody), and rituximab (anti CD20 antibody).

Recent advances in our knowledge on the pathogenesis of BD pave the way for introduction of novel therapeutic modalities and lightening perspectives for overcoming this disabling disease.

**Conflicts of Interest**

None.

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