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Infliximab in the Treatment of Ankylosing Spondylitis: A New Frontier

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Introduction

Ankylosing Spondylitis (AS) is a chronic, inflammatory, and often debilitating condition primarily affecting the axial skeleton, particularly the sacroiliac joints and spine. It is part of a broader category of diseases known as spondyloarthritis, which is characterized by inflammation of the joints and entheses (sites where tendons and ligaments attach to bones). AS typically manifests in early adulthood and is more common in men, often leading to significant pain, stiffness, and eventual fusion of the spine if left untreated. This condition can severely impact mobility and quality of life, making early intervention crucial for controlling inflammation and preventing irreversible damage to the joints.

In recent years, the treatment landscape for AS has expanded with the advent of biologic therapies. Among these, infliximab, a Tumor Necrosis Factor-Alpha (TNF-α) inhibitor, has emerged as a key therapeutic option. Infliximab works by targeting and neutralizing TNF-α, a pro-inflammatory cytokine that plays a central role in the pathogenesis of AS. By inhibiting TNF-α, infliximab helps to reduce inflammation, alleviate symptoms, and slow disease progression, offering new hope for patients with moderate to severe AS who have not responded to conventional therapies [1]. This article explores the role of infliximab in the treatment of ankylosing spondylitis, examining its mechanism of action, efficacy, safety, and place in the treatment paradigm for AS.

Description

The underlying cause of ankylosing spondylitis is not fully understood, but it is believed to involve a combination of genetic and environmental factors. The strongest genetic association is with the HLA-B27 gene, which is found in a large proportion of patients with AS. This genetic predisposition leads to an abnormal immune response, resulting in inflammation at the entheses and joints. Over time, the inflammation can cause cartilage damage and bone erosion, followed by new bone formation and eventual fusion of the spine. Chronic inflammation in the sacroiliac joints is often the hallmark of AS, but the disease can also affect peripheral joints, the eyes (uveitis), and other organs. TNF-α is a key cytokine involved in the inflammatory process of AS. It is produced by activated immune cells, including macrophages and T-cells, and contributes to the recruitment of other inflammatory cells to the site of inflammation. TNF-α also induces the production of other pro-inflammatory cytokines, amplifying the inflammatory response. In AS, elevated levels of TNF-α are found in the affected joints and tissues, driving the inflammatory cascade that leads to tissue damage, pain, and disability [2].

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Infliximab is a monoclonal antibody that specifically targets and neutralizes TNF-α. It binds to both soluble and membrane-bound forms of TNF-α, preventing it from interacting with its receptors on the surface of cells. This inhibition of TNF-α results in a reduction of downstream inflammatory signals, leading to decreased production of pro-inflammatory cytokines, reduced leukocyte infiltration, and ultimately, a reduction in inflammation and tissue damage. In addition to its effects on inflammation, infliximab also modulates the immune system in a way that may reduce the abnormal immune responses seen in AS. By targeting TNF-α, infliximab helps to balance the immune system, preventing the excessive inflammatory reactions that lead to chronic joint damage and the progressive disability associated with AS.

The efficacy of infliximab in treating ankylosing spondylitis has been well-documented in clinical trials and real-world studies. In a landmark study, infliximab significantly improved clinical outcomes in patients with moderate to severe AS who had failed to respond to conventional Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and Disease-Modifying Antirheumatic Drugs (DMARDs) such as sulfasalazine and methotrexate [3].

Infliximab has been shown to provide rapid relief of symptoms, including pain, stiffness, and fatigue. Patients often experience significant improvements in their ability to perform daily activities, such as walking and climbing stairs. Clinical studies have demonstrated improvements in physical function, as measured by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and other assessment tools. These improvements in mobility and daily functioning contribute to a better quality of life for patients with AS. Slowing Disease Progression: Long-term studies have indicated that infliximab can slow the structural progression of the disease, as evidenced by reduced spinal fusion and less joint damage over time. In some cases, the treatment has even resulted in the reversal of some inflammatory changes, particularly in the sacroiliac joints. Infliximab is effective in preventing the recurrence of acute inflammatory flare-ups, reducing the frequency and severity of these episodes [4].

While infliximab is generally well-tolerated, it is associated with certain risks, primarily due to its immunosuppressive effects. Common side effects include. Some patients may experience infusion-related reactions, such as fever, chills, or rash, during or shortly after the administration of infliximab. Because TNF-α plays a crucial role in the immune system's defense against infections, inhibiting TNF-α can increase the risk of infections, particularly respiratory infections and tuberculosis. Patients are carefully screened for latent tuberculosis before initiating therapy with infliximab. Infliximab may increase the risk of developing autoimmune disorders, including lupus-like syndromes and vasculitis, although these are rare. There have been concerns regarding the potential increased risk of malignancies, particularly lymphomas, with long-term use of TNF-α inhibitors. However, the overall risk remains relatively low, and the benefits of treatment often outweigh the risks for patients with severe, active AS.

Infliximab is typically reserved for patients with moderate to severe ankylosing spondylitis who have not responded adequately to conventional therapies, such as NSAIDs or DMARDs. It is often used in combination with other treatments to provide comprehensive disease management. Infliximab is administered through intravenous infusions, typically starting with a loading dose followed by maintenance doses every six to eight weeks. It is important to note that while infliximab can significantly improve symptoms and disease outcomes, it does not cure AS [5]. As such, treatment with infliximab is considered long-term, and regular monitoring is required to assess its

effectiveness and safety. Furthermore, some patients may experience a loss of response over time, which may necessitate dose adjustments or switching to another biologic agent.

Conclusion

Infliximab represents a new frontier in the treatment of ankylosing spondylitis, offering significant improvements in clinical symptoms, quality of life, and disease progression for patients with moderate to severe disease. By targeting and neutralizing TNF-α, infliximab helps to reduce the inflammatory processes that drive AS, providing a valuable therapeutic option for patients who have not responded to conventional treatments.

While infliximab is generally well-tolerated, its potential side effects, including increased susceptibility to infections and autoimmune reactions, require careful monitoring and patient selection. Despite these risks, infliximab has become an essential tool in the management of AS, particularly for those with aggressive disease or those at risk of severe disability. As research into biologic therapies continues to evolve, the role of infliximab in ankylosing spondylitis will likely be further refined. With its ability to significantly alter the course of this chronic and debilitating disease, infliximab offers patients with AS a promising pathway to better disease control, improved functional outcomes, and a higher quality of life.

Acknowledgment

None.

Conflict of Interest

None.

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