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Case Report **Pharmacy**

Case Report on Ustekinumab-Induced Varicella Zoster Infection

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Abstract

Ustekinumab is a human monoclonal antibody typically used to treat moderate to severe plaque psoriasis, psoriatic arthritis, moderate to severe Crohn's disease, or moderate to severe ulcerative colitis (inflammatory bowel disease). Ustekinumab mediates the body's T-cell response by acting as an antagonist against interleukin-12 (IL12) and interleukin-23 (IL23). Although rare, the emergence of severe infections or exacerbation/reactivation of existing infections (bacterial, mycobacterial, fungal, viral) is possible for Ustekinumab. We report a case of a 29-year-old female patient who was prescribed Ustekinumab for Crohn's disease management. After the commencement of the drug for two doses she developed Varicella pneumonia with ARDS which was subsequently managed.

Keywords: Crohn's disease, Ustekinumab mediates, interleukin-12.

INTRODUCTION

Ustekinumab is a human immunoglobulin (Ig) G1 kappa monoclonal antibody directed against interleukin (IL)-12 and IL-23, which are cytokines in immune and inflammatory responses. It is a targeted biologic disease-modifying anti-rheumatic drug (bDMARDs) used in managing various inflammatory conditions that activate IL-12 and IL-23 signaling pathways. Ustekinumab is used for severe plaque psoriasis and active psoriatic arthritis, alone or in combination with methotrexate. In 2016, Ustekinumab was additionally approved for managing moderate to severe Crohn's disease in selected adult patients. The risk of viral infection is increased in immunosuppressed inflammatory bowel disease (IBD) patients. Varicella zoster virus (VZV) is of particular interest in IBD because of several reports of severe, disseminated and occasionally fatal varicella infection in immunosuppressed IBD patients. Patients should be screened for VZV immunity and vaccinated before commencing immunosuppression.

CASE REPORT

A 29-year-old female with a known case of Crohn's disease came to the hospital with chief complaints of fever and breathing difficulty. The patient developed varicella zoster infection 4 days before the current complications. She was suffering from Varicella pneumonia with ARDS. Her abnormal laboratory investigations included a drop in Hb (10.4), elevated CRP level (163) and a secondary infection was also identified (pseudomonas aeruginosa induced). She was managed with INJ.ACYCLOVIR and other antibiotics as well as mechanical ventilation to manage varicella-zoster associated ARDS. She improved with the treatment and was later discharged when deemed clinically stable. The patient is a known case of Crohn's disease and had been under regular follow-up for the same. Prior to the current incidence of varicella infection the patient was initiated on INJ.USTEKINUMAB 130MG for Crohn's management nearly one month before. She had already received two doses of the same, the last dose being 12 days prior to the varicella infection episode. Even though the patient was started on biological therapy, she was not given HZ vaccinations. Hence biological was restarted after the completion of varicella vaccines after the patient cured from the varicella infection. Upon further evaluation, the possibility of acquiring such subsequent infections can be correlated to the initiation of biological therapy (Ustekinumab) without prior administration of preventive vaccines.

DISCUSSION

Ustekinumab is an anti-IL12/23 IgG1 kappa human monoclonal antibody currently undergoing US Food and Drug Administration review for use as a psoriasis treatment. The candidate has also been evaluated in Phase 2 studies as a treatment for psoriatic arthritis, Crohn's disease, and multiple sclerosis. In large clinical trials, ustekinumab has proven effective for treating moderate-to-severe plaque psoriasis.

TNF-α antagonists may increase the risk of herpes zoster (HZ), as well as the duration and severity. Recently, the monoclonal antibody ustekinumab, blocking the p40 subunit of IL-12 and IL-23, has been introduced for treating moderate to severe plaque psoriasis. Two patients with severe psoriasis treated with ustekinumab developed severe contiguous multidermatomal HZ, 1 and 9 months after treatment initiation. The occurrence of HZ after the initiation of Ustekinumab suggests a causal relationship.

Ustekinumab is available for injection in pre-filled syringes and vials. The drug is administered by either subcutaneous injection or intravenous infusion. Crohn's disease and ulcerative colitis management are based on an initial intravenous weight-based infusion followed by a subcutaneous maintenance schedule.

Initial infusion dosage:

A. Weight < 55 kg: 260 mg (2 vials)
B. Weight 55 to 85 kg: 390 mg (3 vials)
C. Weight > 85 kg: 520 mg (4 vials)

In Crohn's disease and ulcerative colitis, recommended adult S/C maintenance dosage: 90mg subcutaneously eight weeks after initial intravenous administration and every eight weeks after that.

Infection with varicella zoster virus (VZV) causes varicella (chickenpox), which can be severe in immunocompromised individuals, infants and adults. VZV is the only human herpesvirus for which highly effective vaccines are available. After varicella or vaccination, both wild-type and vaccine-type VZV establish latency, and long-term immunity to varicella develops. However, immunity does not protect against reactivation. Thus, two vaccines are used: one to prevent varicella and one to prevent zoster.

Genetic defects in interleukin-12/23/17 immunity are associated with an increased risk of Staphylococcus aureus and herpesvirus skin infections. All biologics evaluated were positively associated with bacterial skin infections, herpes simplex, and herpes zoster.

Not many reports associated with Ustekinumab induced Varicella Zoster infections are available in the literature. This case report highlights an intresting observation of an Adverse drug event caused by a biological drug which was considered as just a contributive factor until now.

CONCLUSION

The use of biologicals in the treatment of inflammatory bowel disease (IBD) has revolutionized patient care, providing effective management of symptoms and improved quality of life. HZ vaccination should be considered prior to initiation of biological therapy mandatorily. However, it is essential to acknowledge and address the potential adverse events associated with these medications.

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