Results: A full-body CT scan demonstrated the presence of multifocal lymphadenopathy, alveolar infiltrates suggestive of diffuse alveolar haemorrhage, and haemorrhage in both kidneys and the left adrenal gland; anti-coagulation was held, despite the INR being within the patient’s baseline therapeutic levels. He was admitted with a working diagnosis of CAPS and possible zoster infection. Appropriate immunologic workup was requested. He was prescribed intravenous acyclovir, antibiotics, pulse dose of glucocorticoids, and IVIG. Bronchoscopy with bronchoalveolar lavage revealed the presence of haemosiderin-laden macrophages. The rash resolved, and the patient’s condition improved. He was discharged with glucocorticoid tapering regimen, hydroxychloroquine, aspirin and warfarin.

Antibody titers were taken prior to IVIG administration at presentation, and at 4 weeks. High VZV IgG titers found at presentation regressed over four times on follow-up. Furthermore, at 4 weeks the patient had developed IgM antibodies against both VZV and HSV. These findings confirmed a concurrent infection.

Conclusion: This is the first report of coexisting HSV/VZV infection associated with CAPS. A literature review identified a total of 28 patients with coexisting HSV/VZV infection, whereas only one case of CAPS triggered by HSV was identified[1]. This case illustrates that concurrent infection can occur in the absence of immunosuppressive therapy in patients with APS, serving as a trigger for hemorrhagic CAPS. Simultaneous treatment with antiviral against herpesviruses, glucocorticoids and IVIG may mitigate the inflammatory cascade associated with CAPS.

REFERENCES:

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AB0649 INFECTION PROFILE OF IMMUNE-MODULATORY DRUGS USED IN AUTOIMMUNE DISEASES: ANALYSIS OF SUMMARY OF PRODUCT CHARACTERISTIC DATA

INTERMEDIATE RESULTS

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Background: Accurate information on immune-modulatory drugs, including infections, is required to guide prescribing decisions. The “summary of product characteristics” (SmPC) by the European Medicines Agency (EMA) provides a useful repository of information on adverse events e.g. infections, from clinical trials and post-market pharmacovigilance (1).

To date, no comparison has been undertaken on reported infection frequencies across SmPCs for immune-modulators.

Objectives: To compare infection frequency, site and type across the most commonly-prescribed immune-modulatory drugs used to treat IMIDs, using information provided by SmPCs.

Methods: A drug was included if licensed in Europe for treatment of one of the following: rheumatoid arthritis, axial spondyloarthritis, connective tissue disease, autoimmune vasculitis, autoinflammatory syndromes, inflammatory bowel disease (Crohn’s and ulcerative colitis), psoriasis, multiple sclerosis and other rarer conditions.

The Electronic Medicines Compendium (EMC) was searched for commonly prescribed immune-modulatory drugs used for the above indications. SmPC documents were manually searched for information on infection frequency, extracted from sections 4.4 and 4.8. Infection frequency was recorded as per convention in the SmPC: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/10000); very rare (<1/10000) (1), for each drug. Information was further extracted on infection site (e.g. respiratory, skin etc), type (e.g. bacterial, viral etc) and individual pathogenic organisms.

25% of included SmPCs were screened and extracted by a second reviewer. Discrepancies were resolved via consensus between the two reviewers.

Results: In total, 39 drugs were included, used across 20 indications: nine conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), six targeted synthetic DMARDs (tsDMARDs; four Janus kinase [JAK] inhibitors, two spondyloinflammatory targets) and 24 biologic DMARDs (17 cytokine-targeted; seven cell-targeted).

The most common sites of infection are listed by drug group in Figure 1. Upper respiratory, ear/nose/throat (including sinusitis) and urinary tract infections were able for most csDMARDs and siponimod, certolizumab pegol and rituximab. The Electronic Medicines Compendium (EMC) was searched for commonly prescribed immune-modulatory drugs used for the above indications. SmPC documents were manually searched for information on infection frequency, extracted from sections 4.4 and 4.8. Infection frequency was recorded as per convention in the SmPC: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/10000); very rare (<1/10000) (1), for each drug. Information was further extracted on infection site (e.g. respiratory, skin etc), type (e.g. bacterial, viral etc) and individual pathogenic organisms.

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Twelve sites of infection were recorded. Minimal or no site information was available for most csDMARDs and siponimod, certolizumab pegol and rituximab. The most common sites of infection are listed by drug group in Figure 1. Upper respiratory tract was the most common site, especially with bDMARDs. Lower respiratory, ear/nose/throat (including sinusitis) and urinary tract infections were moderately common, with clustering within drug groups. No drugs reported risk of cardiac infections; the eye, musculoskeletal, neurological, oral and reproductive sites were the least common with reported sites of infection.

Infection data for 27 distinct pathogens were recorded, the majority viruses, especially with bDMARD use. Herpes simplex and zoster were the most frequently
list of (mainly with bDMARDs and tsDMARDs), followed by influenza. Common non-viral causes of infection were candida and limes species.

Variable or absent reporting was noted for opportunistic infections (e.g. tuberculosis and fungi) and certain high-prevalence viruses e.g. Epstein-Barr.

**Conclusion:** The SmPC literature reports differences in infection risk, by site and pathogen, between immune-modulatory drugs. The findings can be used to visualise differences and aid treatment decisions. However, some of the patterns we have shown lack face-validity to clinicians familiar with real-world safety data. The data fail to capture risk of rare infections, are likely skewed by trial selection criteria, varying number of trials per drug and quirks of individual study-reporting methodologies. The findings highlight the need for robust post-marketing pharmacovigilance studies.

**REFERENCES:**