Case report

Bilateral uveitis following intravenous immunoglobulin administration

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ARTICLE INFO

Article history:
Received 11 July 2016
Received in revised form 9 January 2017
Accepted 1 March 2017
Available online 19 March 2017

Keywords:
Uveitis
Drug-induced uveitis
Adverse drug reaction
Intravenous immunoglobulin

ABSTRACT

Purpose: To report a case of bilateral acute anterior uveitis in an adult female occurring following the administration of intravenous immunoglobulin (IVIG).

Observations: A 44-year-old female patient was commenced on IVIG following presentation to hospital with upper limb neuropathic pain. Within two days, she developed bilateral red, painful photophobic eyes. Examination revealed bilateral acute anterior uveitis and IVIG was ceased. Investigations for autoimmune or infective causes for the uveitis were unremarkable. Complete resolution of the uveitis was achieved with topical corticosteroids and cessation of IVIG.

Conclusions and importance: Clinicians should be aware of the possibility of uveitis as an adverse effect of IVIG. Early identification of the offending medication and its cessation in this case were associated with a good visual prognosis.

1. Introduction

Drug-induced uveitis is a rare cause of ocular inflammation that is often overlooked. It is generally recognised as causing 0.5% of all uveitis cases, although an increasing number of medications have been associated with the induction of uveitis. Early diagnosis can avoid the need for an exhaustive workup and prompt withdrawal of the offending medication often results in resolution of the uveitis.

Intravenous immunoglobulin (IVIG) is made from the pooled plasma of donors. Originally used to treat primary immunodeficiency diseases, clinical use of IVIG has expanded into a range of autoimmune and inflammatory conditions. It is an established therapy for Kawasaki disease, idiopathic thrombocytopenic purpura, myasthenia gravis, and demyelinating peripheral neuropathies including Guillain-Barré syndrome. In addition, there are a number of emerging indications for IVIG despite the mechanism for its anti-inflammatory and immunomodulatory properties remaining unclear.

Adverse events are common following IVIG infusion, with systemic reactions reported in 20%–50% of patients. The majority of these are mild and include headache, myalgia, nausea, chills, and low-grade fever. Here, we report a case of bilateral uveitis occurring following intravenous immunoglobulin (IVIG) administration for brachial plexus neuritis.

1.1. Case report

A 44-year-old Caucasian woman was admitted to a tertiary metropolitan hospital with worsening left brachial plexus neuritis in the setting of Charcot-Marie-Tooth type 1 disease. She had been experiencing one month of worsening left upper limb pain associated with weakness. Her medical history was also significant for type 2 diabetes mellitus but she was otherwise systemically well. In particular, there was no underlying disease known to be associated with uveitis. She had no prior ocular history including no previous uveitis, no ophthalmic surgery and no trauma. In the preceding 8 weeks, she had no viral or infective symptoms and did not describe any symptoms consistent with gastrointestinal dysfunction.

She was commenced on human normal IVIG (Privigen, CSL Behring) 30 g per day, with 5 doses planned. Following the second dose of IVIG, she developed bilateral red, painful eyes associated with photophobia. The IVIG infusion was ceased and she was reviewed by an ophthalmologist. She did not report any systemic or constitutional symptoms on review. No new medications apart

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from IVIG were commenced during her admission or in the preceding 8 weeks.

On examination, visual acuity was 6/12 bilaterally and intraocular pressure was 16 mmHg in the right eye and 10 mmHg in the left eye. Slit lamp examination revealed diffuse conjunctival injection bilaterally and grade 2 + anterior chamber cell activity with no posterior synechiae (according to the Standardization of Uveitis Nomenclature Working Group). No vitritis, retinitis or vasculitis was seen on dilated fundus examination. General physical examination did not reveal any rash, lymphadenopathy, or abnormalities of the oral mucosa.

Bilateral acute anterior uveitis (BAAU) was diagnosed and presumed to be an adverse reaction to the IVIG infusion. Topical therapy with phenylephrine 0.12%/prednisolone 1% (Prednefrin Forte, Allergan) hourly and homatropine 0.1% (Isopto Homatropine, Alcon) three times daily was commenced.

In view of the episode of BAAU, basic screening investigations for uveitis were performed. Human leukocyte antigen B27 (HLA-B27) tissue typing, serum treponemal antibodies, serum antinuclear antibodies (ANA), and serum antineutrophil cytoplasmic antibody (ANCa) were all negative. Angiotensin-converting enzyme (ACE) was 25.7 units/L, erythrocyte sedimentation rate (ESR) was 9 mm/h and C-reactive protein (CRP) was 5 mg/L; all these investigations were within normal reported ranges. Full blood count did not show anemia or eosinophilia and liver enzymes were not elevated. Renal function was normal throughout admission with an estimated glomerular filtration rate of >90 ml/min/1.73 m². Urinalysis did not reveal proteinuria or hematuria, the urinary albumin-to-creatinine ratio was 1.1, and beta-2 microglobulin was not elevated. A recent chest radiograph was unremarkable.

On review two days later, visual acuity had improved to 6/9 bilaterally. There was no conjunctival injection present and only trace anterior chamber activity was evident. Following weaning of the topical prednisolone over the next three weeks, complete resolution of the BAAU was achieved at the one-month follow-up. Her upper limb pain was successfully managed with gabapentin.

2. Discussion

The use of IVIG in a variety of autoimmune and inflammatory conditions has grown over the past few decades. IVIG has been trialed with some success in refractory uveitis and birdshot retinochoroidopathy. Increased IVIG use for both on- and off-label indications has highlighted the high incidence of adverse effects associated with its use.

Unilateral uveitis with retinal vasculitis following IVIG administration has been reported twice in the literature. In both cases, underlying systemic vasculitis was thought to account for the presentation. Neutrophil cytoplasmic antibody (ANCA) contamination of IVIG was suggested as a potential mechanism but has not been reliably demonstrated.

We describe a unique case of bilateral anterior uveitis following IVIG. Unlike previously reported cases, the presentation here was that of an isolated anterior uveitis with no posterior segment involvement. There was no posterior uveitis or retinal vasculitis and no evidence of underlying inflammatory disease known to be associated with uveitis. In contrast to previously reported cases detailing unilateral uveitis, the uveitis in this case was bilateral as in most cases of drug-induced uveitis.

Although drug-induced uveitis is a common cause of simultaneous-onset BAAU, other potential causes must be ruled out before confirming the diagnosis. In our case, no evidence was found on history and examination for a post-infectious cause of the uveitis. The patient had no history of preceding infective illness or systematic symptoms such as rash, back pain, arthritis or joint pain other than focal pain associated with Charcot-Marie-Tooth type 1 disease.

A vasculitic screen was negative. Sarcoidosis was unlikely to have caused the uveitis with no systemic symptoms, and a normal ACE, ESR, and chest radiograph. Genotyping confirmed the uveitis was not associated with HLA-B27. Along with the absence of gastrointestinal symptoms, this supports the likelihood that inflammatory bowel disease did not underlie the presentation.

Tubulointerstitial nephritis and uveitis syndrome (TINU) is a common cause of bilateral AAU with a female preponderance. In our case, normal renal function and urinalysis combined with the absence of constitutional symptoms or laboratory abnormalities make TINU unlikely. Finally, Kawasaki disease was ruled out based on the absence of typical signs (fever, lymphadenopathy, and oral mucositis) coupled with a normal ESR and CRP level.

The rapid onset of BAAU following administration, the rapid improvement following cessation of the IVIG infusion, and the exclusion of underlying disease and other potential causes together suggest the uveitis was an adverse effect of IVIG. In this case, early referral to an ophthalmologist enabled rapid diagnosis and initiation of topical corticosteroid treatment.

3. Conclusions

The prevalence of drug-induced uveitis is increasing with the development of novel therapeutics. This case illustrates that clinicians should be aware of the possibility of uveitis as an adverse effect of IVIG given its growing use. Early identification of a potential offending drug and its cessation are crucial to achieve a good visual outcome. We recommend timely ophthalmology referral when patients complain of symptoms suggestive of uveitis when being treated with a newly commenced medication, including IVIG.

4. Patient consent

Written informed consent was obtained from the patient for the publication of personal information including case details.

Funding

No funding or grant support.

Conflict of interest

The following authors have no financial disclosures: EDK, BZW, AJH.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Acknowledgements

None.

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