Case report

Delayed bilateral fibrinous anterior chamber reaction following autologous bone marrow transplant and cataract surgery

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Purpose: Immune reconstitution uveitis (IRU) is a well-described phenomenon that by definition occurs in patients with AIDS who undergo highly active antiretroviral therapy resulting in a rebound inflammatory response to the presence of clinically latent cytomegalovirus (CMV). We hypothesize that similar phenomena may exist in other cohorts who undergo transient immunosuppression with rapid white blood cell count recovery.

Observations: A patient developed rebound inflammation a few months after cataract surgery with intraocular lens placement characterized by photophobia, significant anterior chamber cell and fibrinous deposits. She had a history of multiple myeloma treated with chemotherapy and a recovery of white blood cell counts following autologous bone marrow transplant. She underwent a thorough work-up for infectious etiologies, as well as the presence of intraocular CMV, which were negative. Her vision and symptoms improved to baseline with the use of topical steroids and at one year her exam remained stable.

Conclusions and Importance: With a negative work-up for infectious etiologies, and the timing and clinical presentation, the patient’s inflammation was likely the result of rapid white blood cell count recovery following iatrogenic immunosuppression similar to the mechanism described for IRU. © 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Immune system reconstitution following either infectious, neoplastic, or iatrogenic immunosuppression is associated with a systemic process known as immune reconstitution inflammatory syndrome. In this process, there is a paradoxical worsening of inflammatory signs and symptoms associated with a pre-existent infection acquired during the period of immunosuppression. Within the realm of ophthalmology, immune reconstitution uveitis (IRU) is a well-described phenomenon that by definition occurs in patients with AIDS placed on highly active antiretroviral therapy which results in a rebound inflammatory response to the presence of clinically latent cytomegalovirus (CMV). We hypothesize that similar phenomena may exist in other cohorts who undergo transient immunosuppression with rapid white blood cell count recovery.

2. Case report

A 65-year-old woman with a history of multiple myeloma and diabetes without retinopathy was seen in consultation by the retina service for a week of worsening bilateral light sensitivity and progressive decrease in vision despite being re-started on topical steroids. She had uncomplicated bilateral cataract surgery a few months earlier (92 days prior in the right eye and 71 days prior in the left eye). Her last post-operative cataract check showed no signs of intraocular inflammation. Seventeen days before presentation, she had received an autologous bone marrow transplant in the setting of melphalan chemotherapy for multiple myeloma. Her worsening symptoms correlated with a rebound in her blood counts (Fig. 1).

Best-corrected visual acuity (BCVA) was 20/200 in the right eye and 20/60 in the left eye. Intraocular pressures were unremarkable. There was bilateral mild conjunctival injection, corneas were clear without keratic precipitates, and anterior chambers were notable for 4+ cell in the right eye and 2+ cell in the left eye. Posterior synechiae were present in the right eye and a flat, dense, pale-gray, fibrotic membrane with an irregular texture covered the anterior
surface of a one-piece acrylic posterior chamber intraocular lens (IOL). The left one-piece acrylic IOL had numerous pale fibrotic deposits on the anterior surface. Dilated fundus exam was normal in both eyes with a hazy view, and B-scan ultrasonography was notable for mild anterior vitritis in the right eye.

The differential diagnosis included late infectious endophthalmitis, non-infectious bilateral anterior uveitis, rebound inflammation after cataract surgery, immune reconstitution uveitis following autologous stem cell rescue, and ocular involvement of multiple myeloma. Anterior chamber paracentesis and vitreous tap and injection of intravitreal antibiotics were performed for the right eye. Work up for infectious, uveitic, and malignant causes were unremarkable (Table 1). The patient’s medications at the time of admission included: ciprofloxacin, fluconazole, hydrocodone-acetaminophen, lorazepam, losartan, ondansetron, oxybutynin, prochlorperazine, sitagliptin-metformin, zoledronic acid injections three weeks prior, and valacyclovir.

The patient’s topical prednisolone acetate was increased to every 2 h and later increased again to every hour. Eight days after increased topical steroid treatment, BCVA improved to 20/30 OD and 20/25 OS with reduction in anterior chamber cell to 2 + OD and 1 + OS and persistent fibrinous deposits on the IOLs (Fig. 2). Systemic steroids were not used due to diabetes control and the patient deferred local steroid injections. By 1.5 months, BCVA was stable and all anterior chamber cell had resolved. At 2 months, all steroids had been discontinued. By 3 months, all fibrin membranes resolved, with mild residual posterior synechiae. At 6 months and again at 1 year, her exam remained stable.

3. Discussion

With negative ocular and systemic work-up, an immune reconstitution phenomenon is the proposed mechanism of her bilateral anterior uveitis one week following autologous stem cell rescue and recent bilateral cataract extraction. A similar entity, immune reconstitution uveitis (IRU), was first described as a new

| Table 1 |
|----------------------------------|----------------------------------|
| Specimen (timepoint) | Test |
| Vitreous Tap OD (Day 92) | Gram Stain |
| | Bacterial and fungal culture |
| | Cytology  Inflammatory cells |
| Serum (Day 92) | Toxoplasma gondii Ab IgG |
| | Toxoplasma gondii Ab IgM |
| | Toxoplasma gondii PCR |
| | Quantiferon gold |
| | VDRL |
| | ANA |
| | ANCA screen |
| | HLA B27 |
| Aqueous Tap OD (Day 94) | Angiotensin converting enzyme |
| | VZV PCR |
| | HSV PCR |
| | EBV PCR |
| | CMV PCR |
| Serum (Day 94) | Adenovirus PCR |
| | Blood Culture |

Fig. 1. Timing and severity of patient’s immune reconstitution uveitis correlated with rebound in serum WBC (white blood cell) count, ANC (absolute neutrophil count) and ALC (absolute lymphocyte count). CE/IOL (Cataract extraction, placement of intraocular lens); HSCT (hematopoietic stem cell transplant).

Fig. 2. Day 100; anterior segment photo of the right eye shows residual fibrin membrane, posterior synechiae. 2 + cell, vision improved to 20/30.
intraocular inflammatory syndrome developing in AIDS patients with inactive CMV retinitis: HAART initiation results in CD4+ T-lymphocyte activation and subsequent intraocular inflammation [1]. Cytokine profiles clearly distinguish the inflammation of IRU from that associated with active CMV retinitis [2]. While still a matter of investigation, the primary mechanism of IRU likely involves either primary CMV fragments or a CMV-specific antigen delivered to lymphoid tissue, triggering a T-cell response [1]. IRU is typically a posterior entity, but anterior segment involvement has been shown to follow the recent introduction of foreign material (intraocular surgery or injection) [3].

Besides IRU and the listed work-up, a number of other etiologies deserve specific mention. Though this patient was not HIV positive and CMV was not identified in her ocular samples, she did have positive CMV serology prior to transplant however this in and of itself is common and CMV re-activation following autologous transplant is exceedingly rare. Similarly, HSV serology is not routinely sent prior to bone marrow transplant, but prophylactic treatment with valacyclovir (as this patient underwent) is thought to generally eliminate HSV as a causative pathogen during the short period of immunosuppression following transplant. There are a few alternative etiologies in immunocompromised patients which were not tested during the patient’s initial work-up, including HHV-6 and torque teno virus. Valacyclovir is typically effective in preventing HHV-6 reactivation (though not as treatment for a primary infection), and our patient was already being treated prophylactically prior to onset of her symptoms [4]. Torque teno virus has been shown to be related to culture negative endophthalmitis (though unclear if as a causative pathogen), but though not tested specifically in our patient the lack of posterior segment involvement and would make this less likely to be a primary etiology in our patient [5]. Multiple myeloma can often masquerade as refractory anterior uveitis if there is invasion of the iris, however the patient’s cytology from her vitreous and aqueous taps were negative and the inflammation would have been unlikely to respond to steroid therapy. There were no signs of posterior segment inflammation or any evidence of occult diabetic retinopathy on examination (patient’s last hemoglobin A1c 7.8%), which could have exacerbated post-operative inflammation. Finally, the patient was on no medications that are known to cause intraocular inflammation.

4. Conclusions

With a negative work-up for infectious etiologies, and the timing and clinical presentation, the patient’s inflammation is believed to be the result of rapid white blood cell count recovery following iatrogenic immunosuppression similar to the mechanism described for IRU.

Authors’ contributions

All authors contributed significantly to the creation of this manuscript, each fulfilled criteria as established by the ICMJE.

Consent to publish

Informed consent was obtained in writing from the patient for the use of their information and external photograph for the purpose of this report.

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