Clinical features of infectious posterior segment uveitis

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ABSTRACT • RÉSUMÉ

Objective: To assess the clinical findings and microbiology investigations in patients with suspected infectious posterior segment uveitis (PSU).

Design: Retrospective case study.

Methods: Between January and December 2014, medical records of 270 patients with PSU were reviewed. Baseline ocular examination, presumed and final diagnoses, microbiology investigations from aqueous or vitreous fluid, and peripheral blood were reviewed.

Results: Infectious PSU was suspected in 28 patients among 270 PSU cases (10.4%, 28/270), and 11 cases were of infectious origin (4.1%, 11/270). Six patients were immunocompromised: 5 patients in the confirmed infectious PSU group (45.5%, 5/11) and 1 in the confirmed noninfectious group (5.9%, 1/17; $p = 0.002$). Initial visual acuity was 1.8 ± 0.35 logMAR and 0.9 ± 0.23 logMAR for patients with confirmed infectious and noninfectious PSU, respectively ($p = 0.04$). Anterior chamber reaction was worse in patients with confirmed infectious PSU (1.8 ± 0.49) than confirmed noninfectious cases (0.5 ± 0.1; $p = 0.003$). The frequency of chorioretinitis among patients with confirmed infectious and noninfectious PSU is 54.5% (6/11) and 11.8% (2/17; $p = 0.03$), respectively. Onset of confirmed infectious uveitis was more acute (≤6 weeks in duration) than noninfectious cases ($p = 0.0015$). Among the 11 patients with positive blood culture or serology, 6 had anterior and vitreous chamber fluid analysis. The rate of positive cultures and PCR is 16.7% (1/6) for aqueous humour and 50% (3/6) for vitreous samples.

Conclusions: Clinical features more suggestive of infectious PSU include immunosuppression, worse initial visual acuity, acute onset, worse anterior chamber reaction, and chorioretinitis. Further studies are needed to enhance the diagnostic yields of aqueous and vitreous fluid analyses.

Objectif: Évaluer les résultats cliniques et microbiologiques en cas de suspicion d'uvéite postérieure (UP) infectieuse.

Nature: Étude de cas rétrospective.

Méthodes: De janvier à décembre 2014, les dossiers médicaux de 270 patients présentant une UP ont été examinés. L'examen oculaire de départ, les diagnostics présumé et définitif, les examens microbiologiques de l'humeur aqueuse ou vitrée et ceux du sang périphérique ont été passés en revue.

Résultats: On soupçonnait la présence d'une UP infectieuse chez 28 patients sur les 270 cas d'UP (10,4 %; 28/270), et 11 cas étaient effectivement d'origine infectieuse (4,1 %; 11/270). Six patients présentaient une immunodéficience: 5 dans le groupe UP infectieuse confirmée (45,5 %; 5/11) et 1 dans le groupe UP non infectieuse confirmée (5,9 %; 1/17; $p = 0,002$). L'acuité visuelle initiale se chiffrait à 1,8 ± 0,35 logMAR et à 0,9 ± 0,23 logMAR dans l'UP infectieuse et non infectieuse confirmée, respectivement ($p = 0,04$). La réaction inflammatoire de la chambre antérieure était plus prononcée dans le groupe UP infectieuse confirmée (1,8 ± 0,49) que dans le groupe UP non infectieuse confirmée (0,5 ± 0,1; $p = 0,003$). La fréquence de choriorétinite dans le groupe UP infectieuse et non infectieuse confirmée était de 54,5 % (6/11) et de 11,8 % (2/17; $p = 0,03$), respectivement. L'apparition de l'uvéite infectieuse confirmée était plus aigue (durée de ≤ 6 semaines) que celle de l'uvéite non infectieuse ($p = 0,0015$). Chez les 11 patients dont la culture sanguine ou sérologique donnait des résultats positifs, 6 ont subi une analyse de l'humeur aqueuse et vitrée. Le taux de cultures et de réactions en chaîne par polymérase (PCR) positif s'élevait à 16,7 % (1/6) dans le cas de l'humeur aqueuse et à 50 % (3/6) dans le cas de l'humeur vitrée.

Conclusions: Les caractéristiques cliniques évocatrices d'une UP infectieuse sont l'immunosuppression, une moins bonne acuité visuelle initiale, une présentation plus aigue, une réaction inflammatoire de la chambre antérieure plus prononcée et la choriorétinite. D'autres études devront être réalisées pour améliorer le rendement diagnostique des analyses des humeurs aqueuse et vitrée.

Uveitis is one of the leading causes of ocular morbidity in the working age population and accounts for 10%–15% of vision loss in the Western countries.[1,2] Prompt differentiation of infectious from noninfectious posterior segment uveitis is of major significance as these 2 disease entities have vastly different treatment and prognosis. However, posterior uveitis of infectious and noninfectious etiology may have similar clinical signs and symptoms at initial presentation.[3,4] Although aqueous and vitreous fluid analyses are useful adjuvants to confirming the

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etiology, such microbiology investigations are limited to larger centres, and the diagnostic yields of cultures and polymerase chain reaction (PCR) vary greatly in the literature, from 27% to 100%.[5] The objective of this case series is to assess the clinical findings and microbiology testing used in suspected infectious posterior uveitis.

Materials and Methods

Between January 1, 2014, and December 31, 2014, in total 270 consecutive patients were diagnosed with intermediate uveitis, posterior uveitis, or panuveitis (defined as "posterior segment uveitis or PSU" in this study) at the Department of Ophthalmology at St. Michaels Hospital. Toronto, Ont. This study was approved by Research Ethics Board for this retrospective single-centred study. The ocular diagnostic features are helpful but highly variable with overlap between both noninfectious and infectious PSU. For the purpose of this study, "suspected infectious PSU" is defined as PSU where clinical suspicion for infectious etiology is high based on a combination of initial history, disease onset especially if acute, immune status, exposure and travel history, presence of retinitis, vasculitis, chorioretinal lesions, optic nerve swelling, any panuveitis or endophthalmitis, dense vitirits on ultrasonography findings, or delayed resolution to empirical therapy. "Confirmed infectious PSU" refers to suspected infectious PSU cases with the infectious etiology identified by blood culture, serology, or PCR. "Confirmed noninfectious PSU" cases had negative microbiology and inflammatory investigations. Cases were described as idiopathic when no identifiable cause was found following from inflammatory and microbiology investigations. Exclusion criteria were (*i*) presence of anterior uveitis alone, (*ii*) isolated episcleritis or scleritis, (*iii*) isolated optic neuritis, (*iv*) presumed noninfectious uveitis, (*v*) postoperative uveitis, and (*vi*) traumatic uveitis.

Complete history and ophthalmological assessment was performed. Patients were analyzed for sex, age of onset, systemic diseases, immune status including human immunodeficiency virus (HIV), and use of immunosuppressive therapy. Visual acuity, intraocular pressures, laterality, uveitis grading and course based on SUN criteria, and dilated fundus findings were obtained for the initial and final visits during the study period.[4] Systemic work-up including both microbiology and radiologic investigations, and ocular fluid analyses were performed when clinically indicated. Initial clinical diagnoses and confirmatory etiology of uveitis were evaluated.

Diagnostic anterior chamber paracentesis was performed at the slit lamp in outpatient settings, after topical proparacaine hydrochloride, disinfection of ocular surface with povidone-iodine, and placement of sterile lid speculum. A 30-gauge needle on a 1 mL syringe was used to aspirate approximately 0.1–0.2 mL of aqueous humour.

Vitreous specimen was obtained during either tap-and-inject procedures or 23-gauge pars plana vitrectomies (PPV). Vitreous chamber paracentesis was performed at the slit lamp in outpatient settings, after topical anaesthesia and povidone iodine, and placement of sterile lid speculum. A 25- to 27-gauge needle attached to a 1 mL syringe was used to aspirate approximately 0.1–0.2 mL of vitreous at 3.5–4 mm from limbus. In cases were vitreous sample was obtained using 23-gauge transconjunctival sutureless PPV, a standard 3-port setup approach was used in the operating room. Vitreous sample of approximately 0.2–0.3 mL was first obtained without infusion using gentle manual aspiration into a syringe. Thereby undiluted vitreous was retrieved for analysis. Owing to the retrospective nature of this study, the quantity of aqueous or vitreous fluid aspirated was not consistently documented.

Due to the small quantities obtained in aqueous chamber paracentesis and vitreous tap, the physicians need to be selective in the microbiology analysis performed. For suspected bacterial or fungal infectious PSU, gram stains and cultures were performed on the aqueous or vitreous fluid. For patients with suspected ocular toxoplasmosis or viral retinitis, PCR was preferentially performed. If the initial microbiology results were negative and clinical suspicion remain high for infectious etiologies, or there was delayed resolution of PSU with initial therapy, vitreous samples were obtained for additional analysis.

Nuclei acid from 200 μL of aqueous or vitreous fluid was extracted manually using QIAamp DNA (Qiagen, Mississauga, Ont.) and eluted in 200 μL of molecular-grade water according to manufacturer's instructions. Multiplex real-time PCR (RealStar® *alpha* Herpes PCR; Altona Diagnostics, Hamburg, Germany) was performed for herpes simplex virus 1 and 2 (HSV1/2) and varicella zoster virus (VZV) according to manufacturer's instructions. PCR utilizing primers common to herpes virus family members, followed by restriction enzyme digestion, was performed for the detection of Epstein-Barr virus (EBV) and CMV.[6] For molecular detection of toxoplasmosis, samples were sent to the National Parasitology Laboratory, Montreal, Canada.

Commercial software (SPSS version 21.0 for Windows; SPSS, Inc, Chicago, IL) was used for all statistical analyses. Descriptive statistics was reported as means and standard deviation for continuous variables. The χ^2 test was used to compare proportion of categorical variables. A p-value <0.05 was considered statistically significant.

Results

A total of 270 patients with intermediate uveitis, posterior uveitis, and panuveitis were identified between January 2014 and December 2014. The mean age of presentation was 53.3 ± 17.1 years. Twenty-eight of the 270 patients (10.4%) had suspected infectious PSU. Ocular findings of suspected PSU include presence of retinitis, vasculitis, chorioretinal lesions, optic nerve swelling, any panuveitis or endophthalmitis, dense vitritis on ultrasonography findings, or delayed resolution to empirical therapy. Microbiology investigations confirmed an infectious origin in 11 patients