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CURRENT APPROACHES TO THE DIAGNOSIS AND TREATMENT OF UVEITIS

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ABSTRACT Uveitis represents a spectrum of ocular inflammatory disorders, differentiated by anatomical location into anterior, intermediate, posterior, and panuveitis. Each type presents distinct clinical manifestations: anterior uveitis features redness, photophobia, and pain; intermediate involves floaters and blurred vision; posterior uveitis threatens significant vision loss, characterized by visual disturbances without redness or pain; and panuveitis combines symptoms of all types with severe outcomes. This article reviews the diagnostic methodologies and treatment modalities for uveitis. Diagnosis primarily relies on detailed patient history, clinical examination, and specialized imaging techniques such as fluorescein angiography and optical coherence tomography (OCT). Management strategies differ based on the etiology: infectious uveitis requires pathogen-specific antimicrobials, whereas non-infectious uveitis is treated with corticosteroids, immunosuppressants, and, in severe cases, biologics or surgical interventions.

KEYWORDS : Uveitis, Anterior Uveitis, Posterior Uveitis, Choroiditis, Fluorescein Angiography.

INTRODUCTION

Uveitis, characterized by intraocular inflammation, remains a challenging and multifaceted condition in ophthalmology, necessitating an intricate approach to its diagnosis and management. This article aims to synthesize the latest insights and strategies in addressing uveitis, highlighting both etiological complexities and the nuanced therapeutic interventions required. The differential diagnosis of uveitis is extensive, reflecting a spectrum of infectious, autoimmune, and idiopathic origins, which necessitates a tailored diagnostic strategy to identify underlying causes effectively. This review not only explores established diagnostic and therapeutic paradigms but also integrates emerging research and clinical pathways, aiming to provide a comprehensive resource for clinicians navigating the complexities of uveitis management (1).

Methods

Searches were conducted across four major databases: PubMed, EMBASE, Cochrane Library, and Web of Science, using a combination of specific keywords and MeSH terms. Keywords included "uveitis," "diagnosis," "treatment," "clinical management," and "therapy," applied in various configurations to maximize the retrieval of relevant articles. Clear inclusion criteria were established to select studies that provided up-to-date and pertinent evidence on diagnostic modalities and treatment options for uveitis. All articles were assessed for relevance and methodological quality by two independent reviewers. At the end of the process, a total of 15 references were selected and analyzed, forming the basis of the narrative review presented in this article.

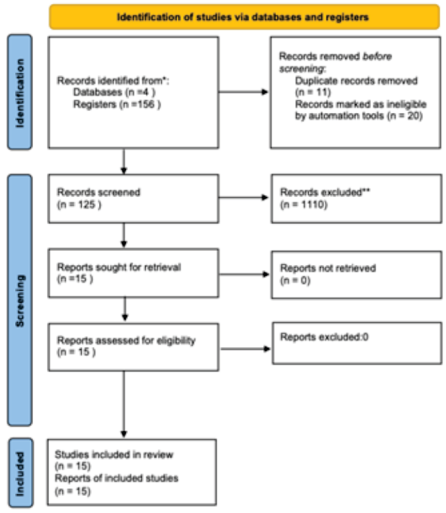

Figure 1. PRISMA.

Etiology

The etiology of uveitis encompasses a broad spectrum of infectious, autoimmune, and idiopathic factors, each contributing to the complex pathophysiology of intraocular inflammation. Infectious causes are identified through the detection of specific pathogens that can incite uveitis, including bacteria such as Mycobacterium tuberculosis, viruses like herpes simplex, and parasites such as Toxoplasma gondii. These infections trigger an immune response within the uveal tract, leading to inflammation that can vary in intensity and duration (1,2).

Autoimmune mechanisms play a critical role in a significant subset of uveitis cases, where the immune system aberrantly targets uveal tissue, resulting in conditions such as Behçet's disease and sarcoidosis. These diseases are often characterized by a systemic immune dysregulation that manifests in the eyes but is not limited to ocular structures, indicating a complex interplay between systemic immunity and local ocular immune responses (3).

Idiopathic uveitis, where the cause remains undefined, represents a diagnostic challenge and comprises a considerable proportion of cases. This category necessitates a thorough exclusion of infectious and known autoimmune causes, relying heavily on clinical judgment and comprehensive diagnostic approaches to manage the disease effectively while avoiding unnecessary immunosuppression in cases where an underlying pathogen may still be unidentified (4).

Clinical Manifestations

Uveitis, a term that encompasses a diverse group of disorders characterized by intraocular inflammation, manifests through a variety of clinical signs and symptoms, which can be highly variable depending on the specific part of the uveal tract affected. The uveal tract includes the iris, ciliary body, and choroid, and inflammation in these areas can be classified as anterior, intermediate, posterior, or panuveitis, each with distinct clinical features (5).

Anterior uveitis, the most common form, primarily involves the iris and ciliary body. Patients typically present with redness, photophobia, blurred vision, and ocular pain. Slit-lamp examination may reveal keratic precipitates, iris atrophy, and cells and flare in the anterior chamber, indicating active inflammation. Complications can include synechiae, where the iris adheres to the lens or cornea, potentially leading to irregular pupil shape and secondary glaucoma (6).

Intermediate uveitis targets the vitreous and peripheral retina.

It is often characterized by floaters and blurred vision, with minimal pain or redness. Examination usually shows vitreous cells and haze, and peripheral vascular sheathing. It is particularly associated with systemic diseases like sarcoidosis and multiple sclerosis (6,7).

Posterior uveitis affects the choroid and retina and can be the most vision-threatening form. Symptoms include visual disturbances such as floaters and decreased visual acuity but typically lack the pain or redness associated with anterior uveitis. Fundoscopic examination is crucial and may reveal retinal lesions, choroidal neovascularization, or retinal detachment(6,7).

Panuveitis involves inflammation of all segments of the uveal tract and presents with a combination of the symptoms of anterior, intermediate, and posterior uveitis. It is often severe, with rapid progression and significant risk of permanent vision loss if not promptly and effectively treated(6,7).

Diagnosis

Diagnosing uveitis involves a multifaceted approach that combines clinical examination, laboratory investigations, and imaging studies to identify the underlying cause and assess the extent of intraocular inflammation. The initial step in diagnosing uveitis is a detailed patient history and comprehensive eye examination. The history should focus on the onset, duration, and characteristics of symptoms, along with any associated systemic symptoms or known autoimmune disorders (7).

The eye examination includes visual acuity testing, slit-lamp examination, and fundoscopy. Slit-lamp examination is crucial for assessing anterior chamber inflammation, detecting keratic precipitates, and observing any iris or angle neovascularization that might indicate chronic inflammation or ischemic processes. Intraocular pressure should also be measured as uveitis can lead to secondary glaucoma. Fundoscopy is essential for evaluating the vitreous and retina, helping to identify posterior uveitis through findings such as retinal vasculitis, choroidal neovascularization, or retinal detachment (8).

Imaging techniques play a critical role in the diagnosis and management of uveitis. Fluorescein angiography can detect leakage from inflamed blood vessels, non-perfusion areas, and neovascularization. Optical coherence tomography (OCT) is invaluable for assessing macular edema and epiretinal membrane formation. Ultrasound may be necessary in cases where media opacity precludes a clear view of the posterior segment (8,9).

Laboratory tests are tailored based on the suspected underlying etiology. These might include complete blood count, serum angiotensin-converting enzyme level, syphilis serology, and tests for specific pathogens or autoimmune markers. In selected cases, aqueous or vitreous samples may be analyzed to identify infectious agents or malignant cells (9).

Treatment

Infectious Uveitis Treatment

The treatment of infectious uveitis aims to eradicate the pathogen while controlling the inflammatory response to prevent tissue damage. The specific antimicrobial therapy depends on the identified or suspected infectious agent (10).

Bacterial Uveitis: Treatment typically involves specific antibiotics. For example, uveitis caused by Mycobacterium tuberculosis requires a combination of anti-tubercular medications over an extended period. In cases of syphilitic uveitis, intravenous penicillin G is the treatment of choice. Broad-spectrum antibiotics are used empirically until culture results specify a pathogen (11).

Viral Uveitis: Herpes simplex virus (HSV) or varicella-zoster virus (VZV) infections are treated with systemic antiviral agents such as acyclovir, valacyclovir, or famciclovir. For cytomegalovirus (CMV) retinitis, ganciclovir or foscarnet are used. The use of topical antivirals may also be necessary depending on the site of infection (12).

Fungal Uveitis: Antifungal treatments such as fluconazole or voriconazole are administered for fungal infections, with the choice of agent guided by species identification and sensitivity patterns (12,13).

Parasitic Uveitis: Anti-parasitic agents are used for conditions like toxoplasmosis, commonly treated with a combination of pyrimethamine, sulfadiazine, and folinic acid to reduce the risk of hematologic toxicity(12,13).

In addition to antimicrobial therapy, corticosteroids may be used to control the inflammatory response once the infection is adequately treated or concurrently with antimicrobials under careful observation to prevent exacerbation of the infection(12,13).

Non-Infectious Uveitis Treatment

Non-infectious uveitis treatment focuses on controlling inflammation and managing symptoms, often requiring immunosuppressive and immunomodulatory therapies.

Corticosteroids: These are the cornerstone for acute management, available in topical, periocular, intraocular, and systemic forms. Topical steroids are used primarily for anterior uveitis. Periocular or intraocular injections of steroids may be employed for intermediate and posterior uveitis. Systemic steroids are reserved for severe or panuveitis and cases where other therapies have failed (12,13).

Immunosuppressants: For patients who cannot tolerate steroids, who require long-term steroid use, or who have steroid-resistant uveitis, immunosuppressive agents such as methotrexate, azathioprine, or mycophenolate mofetil are used. These agents help in reducing the dose of steroids needed and control inflammation by modulating the immune response (14,15).

Biologic Agents: Biologics such as tumor necrosis factor (TNF) inhibitors (e.g., infliximab, adalimumab) are used in cases resistant to traditional immunosuppressives or when rapid control of inflammation is necessary. Interleukin inhibitors (e.g., tocilizumab) and other newer agents provide alternatives for patients who do not respond to TNF inhibitors (14,15).

Other Therapies: Additional treatments may include the use of local ocular hypotensive agents to manage secondary glaucoma or the use of cycloplegic agents to relieve pain from ciliary spasm in acute anterior uveitis (15).

Surgical Intervention: In cases where medical therapy fails to control the inflammation or to manage complications such as cataract or glaucoma, surgical intervention may be required. Vitrectomy may be performed for persistent vitreous opacities or to manage retinal complications (15).

CONCLUSION

Effective management of uveitis hinges on accurately distinguishing between infectious and non-infectious etiologies, as this guides targeted therapeutic strategies. Both scenarios necessitate a coordinated approach involving tailored pharmacological interventions and vigilant monitoring to mitigate complications, preserve vision, and enhance quality of life for affected individuals.

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