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DIAGNOSIS AND TREATMENT OF OPTIC NERVE VASCULITIS: PATHOGENESIS, CLINICAL FEATURES, AND MODERN APPROACHES

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ABSTRACT

Optic nerve vasculitis represents a rare but clinically significant group of diseases characterized by inflammatory damage to the vessels supplying the optic nerve. These conditions can lead to significant visual impairment, including complete blindness.

KEYWORDS: *optic nerve vasculitis, systemic vasculitis, optic disc edema.*

INTRODUCTION

Optic nerve vasculitis (ONV) is considered a rare disease; however, it is known to occur at any age and affect both men and women. In the literature, ONV has been referred to by various terms such as papillophlebitis, angiitis, phlebitis, and others. It is often underdiagnosed or misdiagnosed as central retinal vein occlusion (CRVO), optic neuritis, or anterior ischemic optic neuropathy (AION). It is crucial to note that the etiology and pathogenesis of these conditions differ, as do their treatment approaches. Consequently, a differential approach to the diagnosis, management, and treatment of ONV is one of the key challenges in modern ophthalmology.

In 1972, S.S. Hayreh described a distinct form of vascular pathology of the optic nerve resembling venous circulation disorders, which he termed optic nerve vasculitis. The disease typically occurs in young individuals, is unilateral in nature, and manifests clinically in two forms: edematous and diffuse-hemorrhagic. According to contemporary data, ONV is an immunopathological condition characterized by the accumulation of immune complexes in the walls of microvessels or the development of cell-mediated hypersensitivity. This process involves perivascular accumulation of lymphocytes, macrophages, neutrophils, and plasma cells, leading to localized inflammation, endothelial damage, and disruption of intravascular hemostasis.

Epidemiology

Systemic vasculitides, such as granulomatosis with polyangiitis (GPA), polyarteritis nodosa, and giant cell arteritis (GCA), affect the optic nerve in 10-20% of patients with these conditions. GCA, the most common form of vasculitis in patients over 50 years old, is characterized by acute impairment of blood supply to the anterior segment of the optic nerve, potentially leading to irreversible ischemic optic neuropathy. The prevalence of GCA in Europe is 15-25 cases per 100,000 people annually. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides, including microscopic polyangiitis and GPA, occur with a frequency of 3-12 cases per million people annually. Neurological complications, including optic nerve involvement, are observed in 30-50% of patients with these forms of vasculitis.

Localized forms of ONV are significantly rarer and often diagnosed as isolated cases. Their prevalence is challenging to estimate due to the limited number of reported cases. These localized vasculitides are most commonly associated with idiopathic inflammatory processes or infectious agents (e.g., syphilis or tuberculosis). The prognosis for such patients varies depending on the timeliness of diagnosis and initiation of treatment.

Cases of optic nerve vasculitis combined with central retinal artery occlusion in one eye and an episode of amaurosis fugax in the other eye have been described in a patient with Crohn's disease. [16] According to Andrew Go Lee et al., optic nerve vasculitis most commonly occurs in young women aged 20 to 35 years. [12] Based on the literature, the disease is considered idiopathic; however, there is a tendency for symptoms to manifest following infectious diseases due to changes in the blood coagulation system. Additionally, cases of optic nerve vasculitis have been reported during pregnancy, after the use of oral contraceptives, following gastrointestinal infections, psoriasis, and after COVID-19, which are also associated with alterations in the blood coagulation system. [19-20]

Pathogenesis of Optic Nerve Vasculitis

ONV may be primary, associated with autoimmune processes, or secondary, arising against the background of systemic diseases, infections, or exposure to toxic factors. The pathogenesis involves complex immunological and vascular mechanisms. T-cell and B-cell activation plays a significant role, leading to the production of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α),

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and interferon-γ (IFN-γ). These mediators exacerbate inflammation and damage to vascular walls.

The formation of immune complexes and their deposition in vessel walls activates the complement system, triggering neutrophil and macrophage chemotaxis. Inflammation in the microvessel walls causes endothelial damage, increased vascular permeability, and exudation. Endothelial cell activation promotes adhesion molecule expression, intensifying the influx of inflammatory cells to the affected area. Microthrombus formation resulting from endothelial damage disrupts microcirculation and induces ischemia in optic nerve tissues. Hypoxic changes compromise axonal blood supply, a critical factor in visual function loss.

Clinical Manifestations

The clinical symptoms of optic nerve vasculitis depend on the location of the lesion, the type of vasculitis, and the extent of vascular involvement in the optic nerve's blood supply. These symptoms are primarily driven by inflammatory and ischemic processes that result in optic nerve dysfunction. The main symptoms include a reduction in visual acuity, often with an acute onset, associated with ischemic damage to the optic nerve. Visual acuity may range from moderate to significant impairment. Orbital pain or pain during eye movement is characteristic of inflammatory processes involving the vessels surrounding the optic nerve. Pain may precede or accompany visual disturbances. Visual field defects may include peripheral scotomas or central field defects, as well as an enlargement of the blind spot, caused by localized ischemia of optic nerve axons. Optic disc edema is detected during ophthalmoscopy or optical coherence tomography (OCT). The edema can be pronounced and accompanied by retinal hemorrhages, exudates, or vascular sheathing. [7-9] In later stages, optic disc pallor and atrophy become apparent. Optic neuropathy is often associated with giant cell arteritis or polyarteritis nodosa. Systemic vasculitis may present with fever, general weakness, weight loss, myalgia, and arthralgia. ANCA-associated vasculitides (e.g., granulomatosis with polyangiitis) are often accompanied by involvement of the respiratory system and kidneys. Ophthalmoplegia and ptosis may occur when the vasculature supplying the orbital muscles is affected, which is seen in some forms of systemic vasculitis. [10]

The diagnosis of optic nerve vasculitis requires consideration of the clinical picture, ophthalmological and neurological findings, and laboratory test results. Investigations such as ANCA testing, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and other inflammatory markers play a crucial role in establishing the diagnosis.

Diagnosis of Optic Nerve Vasculitis

The diagnosis of optic nerve vasculitis includes, in addition to standard ophthalmological examination methods, specialized techniques such as optical coherence tomography (OCT), OCT angiography, computer perimetry, electroretinography (ERG), color fundus photography, magnetic resonance imaging (MRI) of the head and orbit, blood tests, immunogram, coagulation profile, and rheumatoid factor analysis. Differential diagnosis of optic nerve vasculitis presents significant challenges due to the similarity of its clinical manifestations with other neurological and ophthalmological conditions [7-9].

The key diagnostic steps include medical history and clinical examination focused on visual acuity reduction, pain during eye movement, and peripheral scotomas. Optical coherence tomography (OCT) demonstrates optic nerve edema and retinal layer changes. Magnetic resonance imaging (MRI): visualization of inflammatory changes and exclusion of compressive lesions. Blood analysis: elevated C-reactive protein (CRP) levels and accelerated erythrocyte sedimentation rate (ESR). Immunological testing: identification of antineutrophil cytoplasmic antibodies (ANCA) and antinuclear antibodies (ANA).

Classification of Optic Nerve Vasculitis

Optic nerve vasculitis is classified into primary (isolated or systemic) and secondary types, which occur in the context of other diseases. This classification is based on the recommendations of the International Consensus Conference in Chapel Hill and modern clinical studies (Jennette et al., 2013). Primary optic nerve vasculitis may affect only the optic nerve or be accompanied by systemic vascular inflammation. The main forms include: a) ANCA-associated vasculitides Granulomatosis with polyangiitis (GPA): Characterized by necrotizing inflammation of small and medium-sized vessels with granuloma formation. It frequently affects the respiratory tract, kidneys, and optic nerve. Microscopic polyangiitis (MPA): Predominantly a necrotizing vasculitis without granulomas, associated with a high risk of optic nerve involvement. Eosinophilic granulomatosis with polyangiitis (EGPA) accompanied by eosinophilia and asthma, it can cause orbital vasculitis. b) Giant cell arteritis (GCA): Most commonly seen in patients over 50 years of age, it is characterized by inflammation of large vessels, including the temporal artery. It is a leading cause of ischemic optic neuropathy [2-3]. The classification of optic nerve vasculitis can also be structured based on the size of the affected vessels. This approach divides vasculitides into the following categories:

-Large-vessel vasculitis, such as giant cell arteritis.
- Medium-vessel vasculitis, including polyarteritis nodosa.
-Small-vessel vasculitis, encompassing ANCA-associated vasculitides and secondary vasculitis observed in the context of autoimmune and infectious diseases

Treatment of Optic Nerve Vasculitis

Effective treatment of optic nerve vasculitis (ONV) requires a multidisciplinary approach, including timely immunosuppressive therapy, targeted biological agents, and supportive care. The main goals of treatment are to suppress inflammation, prevent further vascular damage, and restore or preserve vision. The primary aspects of treatment include: Immunosuppressive Therapy Glucocorticoids: High-dose glucocorticoids are the first-line therapy for most forms of ONV. Intravenous methylprednisolone (1 g/day for 3-5 days) is often used in acute cases, followed by oral prednisolone (1 mg/kg/day) with gradual dose tapering based on the clinical response [17-18]. Antithrombotic therapy includes aspirin or anticoagulants in confirmed thrombosis cases. Supportive therapy plasmapheresis or intravenous immunoglobulin in

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refractory cases. Secondary vasculitis requires specific antimicrobial or systemic autoimmune disease treatment. Cytotoxic agents cyclophosphamide is used in severe or refractory cases, especially in ANCA-associated vasculitis. Azathioprine or mycophenolate mofetil is utilized for maintenance therapy to reduce steroid doses. Tocilizumab has demonstrated efficacy in giant cell arteritis (GCA) by inhibiting the IL-6 pathway and reducing the risk of relapse. Anti-TNF therapy with infliximab or adalimumab may be employed in uncomplicated cases of systemic autoimmune vasculitis. Antiplatelet agents, such as aspirin, may be prescribed in GCA to lower the risk of ischemic complications. Anticoagulants are considered in cases with confirmed thrombosis. Plasmapheresis is beneficial in severe ANCA-associated vasculitis with renal involvement or pulmonary hemorrhage, though its role in isolated ONV is less well-studied. Intravenous immunoglobulin may be considered in refractory or recurrent cases where standard therapy proves ineffective. Management of infectious vasculitis involves targeted antimicrobial therapy based on the causative agent. Specific treatment for conditions such as systemic lupus erythematosus or sarcoidosis includes drugs like hydroxychloroquine or methotrexate, along with long-term management as needed [19]. Patients with ONV require long-term monitoring to assess disease activity, adjust therapy, and manage complications. Modern imaging techniques, such as optical coherence tomography (OCT) and magnetic resonance imaging (MRI), are valuable for tracking structural and functional recovery of the optic nerve.

CONCLUSION

ONV is a vascular pathology of the optic nerve that can arise from systemic, infectious, or autoimmune conditions or isolated ocular pathologies. Accurate and individualized diagnostic approaches are essential for successful treatment. Advanced imaging and laboratory techniques are pivotal in monitoring disease progression and therapeutic efficacy.

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