Literature Review

https://doi.org/10.31288/oftalmolzh202354652

Disorders of aqueous humor flow in the posterior part of the eye in the mechanisms of optic nerve damage development (literature review)

Nataliya Moyseyenko

Ivano-Frankivsk National Medical University

Ivano-Frankivsk (Ukraine)

The study based on the literature search revealed that the peculiarities of fluid circulation in the posterior part of the eye have been studied insufficiently compared to the anterior part. It is suggested that the retina and optic nerve have their own cleansing system, which functions independently or in interaction with the brain's cleansing system. Of interest is the theory of the glymphatic system of the eye, which probably functions similarly to the glymphatic system of the brain, has four segments and ensures the exchange between intraocular, intracranial and interstitial fluids and the removal of metabolic waste products in the posterior part of the eye.

Purpose. *To determine the disorders of fluid circulation in the posterior part of the eye in the mechanisms of optic nerve damage development according to the literature.*

Methods: *literature search of 48 sources.*

It is important to understand that the optic nerve under normal conditions passes a large amount of fluid from the eye to the brain and vice versa. The balance of perfusion (and, presumably, reperfusion in case of pathology) is ensured by the lamina cribrosa, the location of subarachnoid spaces in different parts of the nerve, and the AQP4 channels that support them.

The question is whether the optic nerve has its own separate glymphatic system, or whether it interacts with the glymphatic system of the brain. It also remains unclear how the circulation of intraocular fluid, interstitial fluid of the retina and brain, and cerebrospinal fluid in the optic nerve is coordinated with blood, as well as with fluctuations in atmospheric pressure.

Although this theory has not yet been recognized, it nevertheless has many supporters who explain optic nerve damage as a result of fluid circulation disturbances.

The slowing of fluid flow, as well as the slowing of axonal transport, can be considered as the moment when neuropathy transforms into optic atrophy.

That is why the study of the peculiarities of fluid flow and exchange in the posterior part of the eye is important when studying diseases of the optic nerve, whereas the correction of such circulation disorders could be used for therapeutic purposes.

Conclusion. *Impaired fluid circulation in the posterior part of the eye can occur in mechanisms of optic nerve damage. Improved diagnostics with the ability to assess hydrodynamics will help to understand the role of individual components, while their correction will likely contribute to the optic nerve recovery.*

Keywords:

optic nerve, acute optic neuropathy, glymphatic system of the eye, translaminar gradient, high myopia, optic disc drusen, inflammatory optic neuropathy

Most research is focused on the functioning of the anterior (so-called conventional) outflow pathway: the trabecular meshwork, the juxtacanalicular connective tissue, Schlemm's canal, and the collecting channels, from which the aqueous humor flows into the episcleral venous system [1, 2]. Unconventional outflow may drain through an uveoscleral pathway [3].

The flow of the fluid (blood, intraocular fluid, interstitial fluid, and metabolic waste products) in the posterior part of the eye has differences compared to the anterior part of the eye. The disorders can be considered in the hypotheses of

developing both acute and chronic diseases of the choroid, retina, and optic nerve.

With regard to the optic nerve, the question arises as to the regularity and interrelation of fluid flow, perfusion and reperfusion, axonal transport in the anti- and retrograde direction, as well as to the understanding that the slowing of such processes underlies the transformation of neuropathy into optic atrophy, and therefore the possibility of restoring structure and function.

That is why studying the peculiarities of fluid flow and exchange in the posterior part of the eye is important when studying diseases of the optic nerve, and correction of such flow disorders could be used for therapeutic purposes.

Fluid flow and exchange in the posterior part of the eye is less well understood than those in the anterior part. Of interest is the theory of the glymphatic system of the eye, which explains the exchange and cleansing of metabolic waste products of the choroid and retina through the system of interaction between intraocular, intracranial, and interstitial fluids.

The authors of this theory borrowed data on the circulation of cerebrospinal fluid (CSF) in the brain [4] and suggest that the retina and optic nerve can be cleared from metabolic waste products by analogous pathways [5, 6].

The glymphatic system of the brain was first described in 2012 (Fig. 1) [4].

The authors showed in the experiment on mice that CSF enters the brain through a para-arterial influx route for exchange with the interstitial fluid (ISF) while ISF is cleared from the brain through a paravenous ISF clearance route, from where it flows to the lymphatic vessels of the neck and, ultimately, to the systemic circulation [4]. It is suggested that the perivascular spaces of the retina may provide a similar function in the eye as in the brain [7].

Proponents, based on experimental studies, argue that the ocular glymphatic system in the posterior part of the eye operates through four functional segments [8]. Aqueous humor is produced by the ciliary body (first segment) and enters the retina through the vitreous body (second segment).

In the third segment, aqueous humor mixes with the interstitial fluid of the retina, and excess fluid is transported along the axons of ganglion cells through the lamina cribrosa, from where the fluid flows into the perivenous spaces and through aquaporin-4 (AQP4) water channel.

An important factor in ensuring the fluid flow through the lamina cribrosa is the difference between intraocular and intracranial pressure (translaminar gradient). Light-induced pupil constriction accelerates the flow of intraocular indicators into the optic nerve, which is supported by smooth muscle pressure contractions, and also promotes fluid migration to the posterior eye.

In the fourth segment, intraocular removal indicators, i.e. β-amyloid (Aβ) are cleared from the eye along the axons of the retinal ganglion cells and then enter the perivenous space and subsequently drained to lymphatic vessels in cervical lymph nodes.

The optic nerve also has a system that ensures the circulation of SCF in its various parts along the central retinal artery [9], and therefore, presumably, this is where the glymphatic system of the eye (the third and fourth

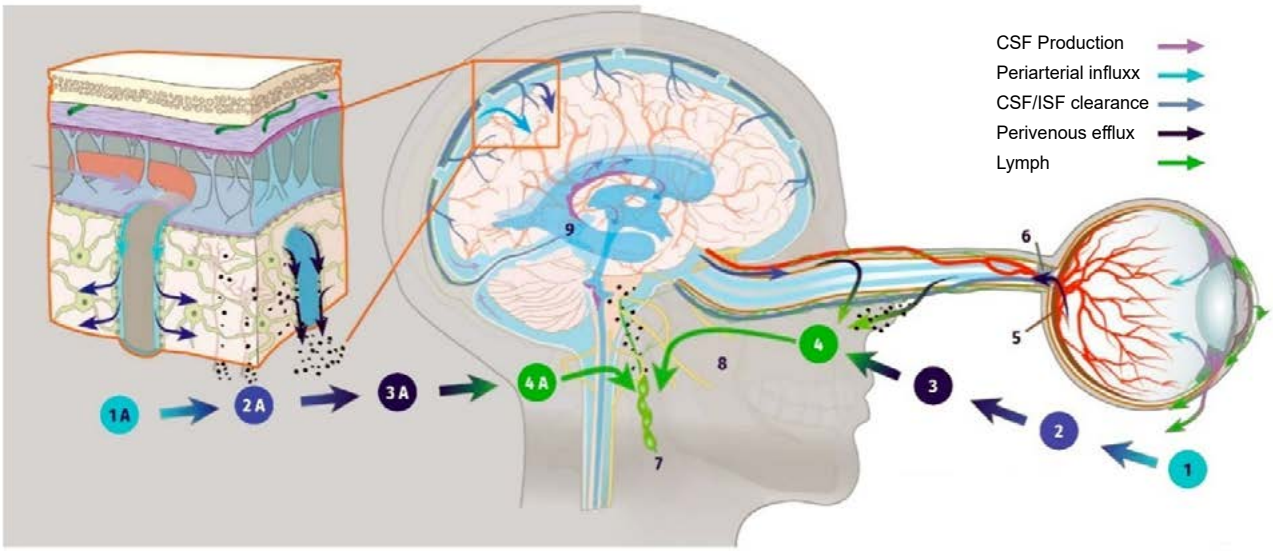

Fig. 1. Glymphatic system of the braine and the eye

Notes: 1A – in the brain, cerebrospinal fluid (CSF) is produced and transported to the subarachnoid space, periarterial influx, 2A – CSF and intracellular fluid (ICF) exchange in the brain; 3A –perivenous efflux; 1 – Aqueous humor is produced in the eye, 2 – ICF-CSF exchange in the retina; 3 – perivenous efflux; 4A, 4 – lymph nodes; 5 – retina, 6 – lamina cribrosa, 7 – lymphatic drainage, 8 – cranial nerves, 9 – choroid plexus [48].

components) and the brain mix or interact. In particular, it is known that intraocular fluid, interstitisl fluid of the retina and brain, and cerebrospinal fluid circulate in the optic nerve, and therefore it is important to understand the mechanisms that ensure the balance between them in order to enable the nerve to function.

The question arises as to whether the optic nerve has its own separate glymphatic system or whether it interacts with the glymphatic system of the brain [8].

It is known that the fluid in the optic nerve spreads due to the structure of the nerve itself and the position of the subarachnoid space, which in the bulbar segment consists of trabeculae (similar to trabeculae in the anterior segment of the eye), in the middle orbital segment - of septa and columns, and in the tubular part contains both trabeculae and columns (Fig. 2) [11].

It also remains unclear how the circulation of intraocular fluid, interstitial fluid of the retina and brain, and cerebrospinal fluid in the optic nerve is coordinated with blood and also changes with fluctuations in atmospheric pressure.

The expression of aquaporin-4, which belongs to the third segment of the glymphatic system of the eye, is found in the retina and optic nerve [12] and is also interesting in the context of studying the possibility of developing optic nerve damage.

Thus, it can be assumed that disturbances in the circulation of fluids in the posterior eye may be a part of the hypotheses related to optic nerve damage. Similar processes are being studied in the pathogenesis of Alzheimer's disease, glaucoma [13], and age-related maculopathy [14].

We propose to consider the possibility of a similar mechanism in the development of acute optic neuropathies, which will make it possible to correct them in the future.

The aim is to determine the disorders of fluid circulation in the posterior part of the eye in the mechanisms of optic nerve damage development according to the literature.

Methods: literature search of 48 sources.

Results

Possible hypotheses about the factors which lead to impaired circulation of fluids in the posterior eye

1. Translaminar circulation.

A. Lamina cribrosa displacement, when it is unable to maintain a balance between intraocular pressure and CSF pressure [15].

The ability to tolerate pressure differences depends on many factors such as the elasticity, stiffness, and geometry (thickness, shape, or curvature) of the lamina cribrosa and connective tissue around the optic disc, which is determined by genetic predisposition, race, or age [16].

Eyes with a stiffer lamina cribrosa may be more resistant to deformation. Eyes with a thinner lamina cribrosa are more susceptible to its deformation. Regardless of its susceptibility to deformation, a thinner lamina cribrosa also contributes to increased translaminar pressure resulting from the reduced distance between the intraocular space and the retrolaminar space, which may interrupt both orthograde and retrograde axoplasmic transport [17].

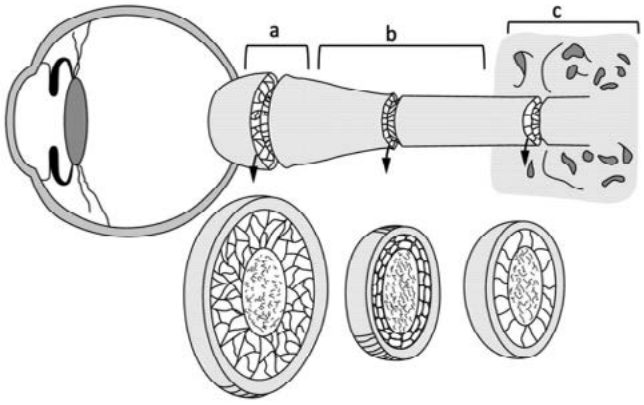

Fig. 2. Distribution of subarachnoid spaces in the intraocular (a), intraorbital (b) part and in the canal (c) of the optic nerve

B. High myopia with an increased size of the eyeball leads to deformation and thickening of lamina cribrosa. At the same time, there is a hypothesis that myopia complications are likely to some extent due to inflammation. The authors claim that multiple autoimmune foci of inflammation occur between the layers of the choroid [18].

In high myopia, according to the author, the likelihood of multiple evanescent white dots syndrome and acute idiopathic blind spot enlargement syndrome increases. This is explained by blocking the exchange between intraocular and interstitial fluids and impaired cleansing of the posterior part of the eye.

C. Multiple evanescent white dots syndrome is of autoimmune origin and includes unilateral yellowish-white foci on the fundus, slight swelling of the optic disc, visual impairment and visual field alterations [19].

D. Acute idiopathic blind spot enlargement syndrome is characterized by normal visual acuity, fundus and pupillary response. It causes scotomas in the projection of the optic disc. In such cases, electrical retinography reveals a decrease in the activity of the peripapillary retina. This condition is also explained by inflammation and possible occlusion of the choroidal capillaries around the optic disc, which probably leads to impaired fluid flow and exchange in the posterior eye caused by secondary ischemia of the outer retina [20].

Under unfavorable conditions, ischemia becomes more pronounced, provoking compensatory non-expansion of the internal retinal vessels and neovascularization.

In severe cases, there is acute onset of myopic optic neuropathy [23]. In this case, the pressure of the episcleral veins (through which the intraocular fluid flows) increases in an enlarged eyeball with a dense sclera as well as the optic nerve is damaged [24].

E. Mechanical optic neuropathy occurs as a result of critical atmospheric pressure fluctuations associated with airplane flights or deep diving on the background of deformed lamina cribrosa. Symptoms are explained by the action of gravitational forces or acceleration/ deceleration forces that occur during the airplane landing [25]. Such forces can cause mechanical stretching of the already deformed and enlarged optic nerve and eyeball, which can occur in case of high myopia. In addition, high-acceleration force may induce transient visual acuity reduction associated with changes in the outflow of aqueous humor [26].

It is believed that high acceleration during airplane landing can cause a critical increase in venous pressure. Herewith, blood will accumulate in the lower extremities, which will lead to ischemia and hypoxia of the brain and eyes with temporary loss of central or peripheral vision and loss of consciousness [27].

It is believed that lamina cribrosa, which is supposed to balance intrathoracic, abdominal and cranial hydrostatic pressures, is stretched and thinned due to myopic morphological changes, and therefore loses its ability to tolerate. That is why the pressure gradient exerted on the deformed optic nerve leads to even more severe damage after an increase in CSF pressure caused by free fall during an airplane landing or diving to depths [28].

In the progression of myopia, the aperture of the scleral flange around the optic disc increases, but the size of the nerve itself does not change. This increases exposure of peripheral posterior lamina cribrosa surface. Lamina cribrosa loses its damping properties towards the optic nerve head, which is exposed to orbital CSF, leading to acute optic neuropathy under conditions of critical fluctuations in hydrostatic pressure [29].

F. Optic disc drusen are often an incidental finding during fundus examination. They can be located superficially or in deep structures, even between the cells of the lamina cribrosa, limiting its damping properties and impeding the flow of fluids in the optic nerve.

Rarely, druses can be combined and thereby worsen the situation in the case of anterior ischemic neuropathy [30]. Moreover, the tortuosity of the disc venules and capillary hemorrhages associated with stagnation will help to diagnose optic nerve edema. It is this edema of the nerve fibers that serves as an additional factor in limiting the fluid circulation in the posterior optic nerve segment of the eye. The exchange of intraocular and interstitial fluids, as well as their transportation to the venous collectors of the brain, is impaired [31, 32]. Fibers are compressed, axial transportation in both anti- and retrograde directions is impaired [33].

Moreover, it is believed that drusen may be a factor in the occurrence of ischemic eye damage, such as central vein occlusion and neovascularization, which also occur under the influence of impaired fluid perfusion and the posterior segment cleansing system [34].

It is noted that ischemic optic neuropathy occurs in younger patients and is less favorable in the setting of optic nerve head drusen [36].

2. Orbitopathy.

Orbital inflammation, which includes both idiopathic diseases and the consequences of systemic or local inflammatory conditions, is often the result of neoplasms, infectious lesions, congenital malformations or trauma, are often combined with systemic thyroid inflammation, sarcoidosis, Wegener's granulomatosis, Crohn's disease, systemic lupus erythematosus, Churg-Strauss, Erdheim-Chester syndrome, histiocytosis X and giant cell arteritis [37].

3. Paranasal sinuses.

A. Sinusitis. Paranasal sinus disease can cause a condition that mimics demyelinating optic neuritis, with acute optic neuropathy and pain on eye movements, or can cause a progressive optic neuropathy resulting from compression [38].

B. Polyps. Compressive optic neuropathy can be caused by mucocele or mucopyoceles of the ethmoid and/ or sphenoid sinus and/or edema and thickening of the sinus walls associated with them. Polyps involving the mucous membrane of the sphenoid sinus also cause nerve compression.

By causing optic nerve edema, paranasal sinuses [39] can also cause impaired fluid circulation in the posterior eye.

C. The local anatomy of the venous circulation in the orbital-apical region may also play a role in the pathogenesis of optic neuropathy associated with sinus disease. Optic neuropathy can be related to the spread of cytokines and/or immune mediators from the sinuses to the orbital apical portion of the optic nerve through the local venous circulation with vasomotor changes. Secondary inflammatory occlusive vasculitis can also cause optic neuritis [40].

4. AQP4

AQP4 plays a role in the fluid circulation of the posterior part of the eye, as it facilitates the influx of fluid from nerve cells into the interstitial space and into the intermembrane spaces (Fig. 3).

Devic's neuromyelitis optica is a type of autoimmune disease of the central nervous system that damages the optic nerve and spinal cord [41]. In this case, astrocyte destruction causes a significant edema of axons, which may be the cause of myelin loss [42].

The role of the glymphatic system of the brain or eye in the development of optic neuromyelitis is not yet clear. However, it is known that in this case the immune system produces antibodies to AQP4 channels along with optic nerve edema, which suppresses the glymphatic system of the eyes and brain [43].

The study based on the literature search revealed that the peculiarities of fluid circulation in the posterior part

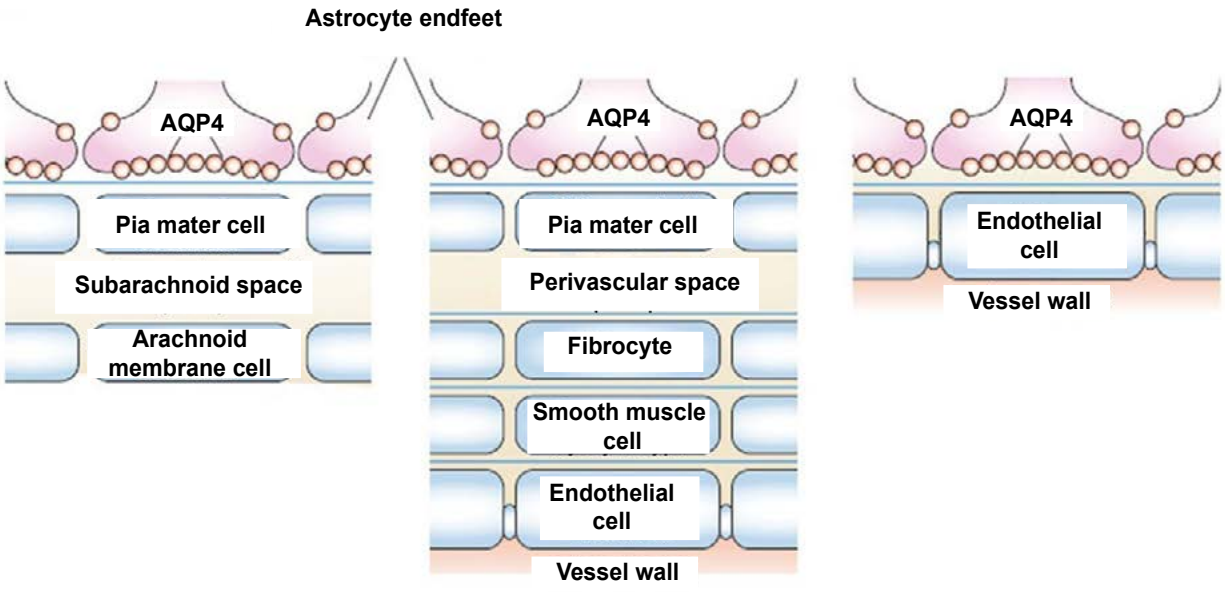

Fig. 3. The role of AQP4 in fluid circulation in brain spaces

of the eye have been studied much less than those in the anterior eye.

It is assumed that the retina and optic nerve have their own cleansing systems that function independently or in interaction with the brain's cleansing system.

Of interest is the theory of the glymphatic system of the eye, which probably functions similarly to the glymphatic system of the brain. It has four segments and ensures the exchange between intraocular, intracranial and interstitial fluids and the removal of metabolic waste products in the posterior part of the eye.

It is important to understand that the optic nerve under normal conditions passes a large amount of fluid from the eye to the brain and vice versa. The balance of perfusion (and presumably reperfusion in case of pathology) is ensured by the lamina cribrosa, the location of subarachnoid spaces in different parts of the nerve, and the AQP4 channels that support them.

The question is whether the optic nerve has its own separate glymphatic system, or whether it interacts with the glymphatic system of the brain. It also remains unclear how the circulation of intraocular fluid, interstitial fluid of the retina and brain, and cerebrospinal fluid in the optic nerve is coordinated with blood and how it changes with fluctuations in atmospheric pressure.

Although this theory has not yet been recognized, it nevertheless has many supporters who explain the damage to the optic nerve precisely because of impaired fluid circulation. The slowing of fluid movement, as well as the slowing of axonal transport, can be considered as the moment when neuropathy transforms into optic atrophy.

Although the hypothesis of impaired fluid circulation in the posterior eye is still experimental, the α-2-antagonist brimonidine is included in the treatment protocols of many countries as a treatment for ischemic optic neuropathy precisely because of its properties to affect eye pressure [44] and thereby improves blood supply to the nerve [45].

Also, endothelin receptor antagonists are used for therapeutic purposes, improving the circulation of both blood and intraocular fluid in the posterior segment in case of ischemic neuropathy [46, 47].

That is why the study on the fluid flow and exchange in the posterior part of the eye is important when studying diseases of the optic nerve, while the correction of such circulation disorders could be used for therapeutic purposes.

Conclusion

Impaired fluid circulation in the posterior segment of the eye can occur in case of damage to the optic nerve. Improved diagnostics with the ability to assess hydrodynamics will help to understand the role of individual components, while their correction will likely contribute to the optic nerve recovery.

References:

1. Tamm ER. The trabecular meshwork outflow pathways: Structural and functional aspects. Exp. Eye Res. 2009;88:648-55.
2. Braunger BM, Fuchshofer R, Tamm ER. The aqueous humor outflow pathways in glaucoma: A unifying concept of disease mechanisms and causative treatment. Eur. J. Pharm. Biopharm. 2015;95:173-81.
3. Johnson M, McLaren JW, Overby DR. Unconventional Aqueous Humor Outflow: A Review. Exp Eye Res. 2017 May;158:94-111.
4. Iliff JJ, Wang M, Liao Y, Plogg BA, Peng W, et al. A paravascular pathway facilitates CSF flow through the brain

parenchyma and the clearance of interstitial solutes, including amyloid β. Sci Transl Med. 2012 Aug 15;4(147):147ra111.
5. Wostyn P, De Groot V, Van Dam D, Audenaert K, De Deyn PP, Killer HE. The Glymphatic System: A New Player in Ocular Diseases? IOVS. 2016;57:5426-27.
6. Denniston AK, Keane PA. Paravascular pathways in the eye: Is there an 'ocular glymphatic system? IOVS. 2015;56:3955-56.
7. Errera M-H, Coisy S, Fardeau C, et al. Retinal vasculitis imaging by adaptive optics. Ophthalmology. 2014;121:1311-12, e2.
8. Wang X, Lou N, Eberhardt A, Yang Y, Kusk P, et al. An ocular glymphatic clearance system removes amyloid from the rodent eye. Sci. Transl. Med. 2020;12, eaaw 3210.
9. Mathieu E, Gupta N, Paczka-Giorgi LA, Zhou X, Ahari A, et al. Reduced Cerebrospinal Fluid Inflow to the Optic Nerve in Glaucoma. Investig. Ophthalmol. Vis. Sci. 2018;59:5876-84.
10. Killer HE, Laeng HR, Flammer J, Groscurth P. Architecture of arachnoid trabeculae, pillars, and septa in the subarachnoid space of the human optic nerve: anatomy and clinical considerations. Br. J. Ophthalmol. 2003;87:777-81.
11. Wostyn P, Van Dam D, Audenaert K, Killer HE, De Deyn PP, De Groot V. A new glaucoma hypothesis: a role of glymphatic system dysfunction. Fluids Barriers CNS. 2015 Jun;29;12:16.
12. Schey KL, Wang ZL, Wenke JQiY. Aquaporins in the eye: expression, function, and roles in ocular disease. Biochim. Biophys. Acta. 2014;1840:1513-23.
13. Wostyn P. Do normal-tension and high-tension glaucoma result from brain and ocular glymphatic system disturbances, respectively? Eye (Lond). 2021;35(10):2905-06.
14. Wostyn P, De Groot V, Van Dam D, Audenaert K, Killer HE, De Deyn PP. Age-related macular degeneration, glaucoma and Alzheimer's disease: amyloidogenic diseases with the same glymphatic background? Cell Mol Life Sci. 2016;73:4299-301.
15. Morgan WH, Chauhan BC, Yu D-Y, et al.Optic disc movement with variations in intraocular and cerebrospinal fluid pressure. IOVS. 2002;43:3236-42.
16. Rhodes LA, Huisingh C, Johnstone J, et al. Variation of laminar depth in normal eyes with age and race. IOVS. 2014;55:8123-33.
17. Lee DS, Lee EJ, Kim T-W, et al. Influence of translaminar pressure dynamics on the position of the anterior lamina cribrosa surface. Invest Ophthalmol Vis Sci. 2015;56:2833-41.
18. Herbort CP, Papadia M, Neri P. Myopia and Inflammation. Journal Of Ophthalmic And Vision Research. 2011;6(4):270-83.
19. Herbort CP. Multiple Evanescent White Dot Syndrome (MEWDS) and Acute Idiopathic Blind Spot Enlargement (AIBSE). In: Gupta A, Gupta V, Herbort CP, Khairallah M (eds). Uveitis, Text and. Imaging. 1st ed. New Delhi: Jaypee; 2009:441-46.
20. Pece A, Sadun F, Trabucchi G, Brancato R. Indocyanine green angiography in enlarged blind spot syndrome. Am. J. Ophthalmolю 1998;126:604-7.
21. Machida S, Fujiwara T, Murai K, Kubo M, Kurosaka D. Idiopathic choroidal neovascularization as an early manifestation of inflammatory chorioretinal diseases. Retina. 2008;28:703-10.
22. Papadia M, Herbort CP. Idiopathic choroidal neovascularization as the inaugural sign of multiple evanescent white dot syndromes. Middle East. Afr. J. Ophthalmol. 2010;17:270-4.
23. Liao L, Fang R, Fang F, Zhu XH. Clinical observations of acute onset of myopic optic neuropathy in a real-world setting. Int. J. Ophthalmol. 2021;14(3):461-7.
24. Park HYL, Paik JS, Cho WK, Park CK, Yang SW. Tight orbit syndrome resulting from large globe with high myopia: intractable glaucoma treated by orbital decompression. Clin. Exp. Ophthalmol. 2012;40(2):214-6.
25. Bontzos G, Plainis S, Papadaki E, Giannakopoulou T, Detorakis E. Mechanical optic neuropathy in high myopia. Clin. Exp. Optom. 2018;101(4):613-5.
26. Tsai ML, Liu CC, Wu YC. et al. Ocular responsesand visual performance after high-acceleration force exposure. IOVS. 2009;50:4836-9.
27. Fitt AD, Gonzalez G. Fluid mechanics of the human eye: aqueous humor flow in the anterior chamber. Bull. Math. Biol. 2006;68:53-71.
28. Jonas JB, Berenshtein E, Holbach L. Anatomic relationship between lamina cribrosa, intraocular space and cerebrospinal fluid space. IOVS. 2003;44:5189-95.
29. Jonas JB, Xu L. Histological changes of high axialmyopia. Eye (Lond). 2014;28:113-7.
30. Purvin V, King R, Kawasaki A, Yee R. Anterior ischemic optic neuropathy in eyes with optic disc drusen. Arch. Ophthalmol. 2004;122:48-53.
31. Storoni M, Chan CKM, Cheng ACO, Chan NCY, Leung CKS. The pathogenesis of nonarteritic anterior ischemic optic neuropathy. Asia Pac. J. Ophthalmol (Phila). 2013;2:132-5.
32. Berry S, Lin W, Sadaka A, Lee A. Nonarteritic anterior ischemic optic neuropathy: cause, effect, and management. Eye Brain. 2017;9:23-8.
33. Rueløkke Lea L, Malmqvist Lasse, Wegener Marianne, Hamann Steffen. Optic Disc Drusen Associated Anterior Ischemic Optic Neuropathy: Prevalence of Comorbidities and Vascular Risk Factors. Journal of Neuro-Ophthalmology. 2020;40(3):356-61.
34. Yan Y, Zhou X, Chu Z, et al. Vision loss in optic disc drusen correlates with increased macular vessel diameter and flux and reduced peripapillary vascular density. Am. J. Ophthalmol. 2020;218:214–24.
35. Ruelokke LL, Malmqvist L, Wegener M, et al. Optic disc drusen associated anterior ischemic optic neuropathy: prevalence of comorbidities and vascular risk factors. J. Neuroophthalmol. 2020;40:356-61.
36. Bradley D, Baughman RP, Raymond L, Kaufman AH. Ocular manifestations of sarcoidosis. Semin. Respir. Crit. Care. Med 2002;23:543-8.
37. Siemerink MJ, Freling NJM, Saeed P. Chronic orbital inflammatory disease and optic neuropathy associated with long-term intranasal cocaine abuse: 2 cases and literature review. Orbit. 2017; Oct;36(5):350-5.
38. Balcer LJ, Prasad S. Abnormalities of optic nerve and retina; in Daroff RB, Fenichel GM, Jancovic J, Mazziotta JC. (eds): Bradley's Neurology in Clinical Practice, ed 6. Philadelphia, Elsevier Saunders. 2012:172-5.
39. Del Noce et al. Swollen Optic Disc and Sinusitis. Case Rep Ophthalmol. 2017;8:421-4.
40. Gallagher D, Quigley C, Lyons C, Mcelnea E, Fulcher T. Optic Neuropathy and Sinus Disease. Journal of Medical Cases, North America. January 2018;9(1):11-5.
41. Paul F, Jarius S, Aktas O, Bluthner M, Bauer O, Appelhans H, et al. Palace Antibody to aquaporin 4 in the diagnosis of neuromyelitis optica. J. PLoS Med. 2007;4:e133.

42. Bennett JL, Owens GP. Neuromyelitis Optica: Deciphering a Complex Immune-Mediated Astrocytopathy. J. Neuroophthalmol. 2017;37:291-9.
43. Mestre H, Hablitz LM, Xavier ALR, Feng W, Zou W, et al. Aquaporin-4-dependent glymphatic solute transport in the rodent brain. Elife. 2018;7:1-31.
44. Fazzone HE, Kupersmith MJ, Leibmann J. Doest opical brimonidinetartrate help NAION? Br J Ophthalmol. 2003;87(9):1193-4.
45. Wilhelm B, Lüdtke H, Wilhelm H. BRAION Study Group. Efficacy and tolerability of 0.2% brimonidine tartrate for the treatment of acute non-arteritic anterior ischemic optic neuropathy (NAION): a 3-month, double-masked, randomised, placebo-controlled trial. Graefes Arch Clin Exp Ophthalmol. 2006;244(5): 551-8.
46. Chiquet C, Vignal C, Gohier P, Heron E, Thuret G, at al. ENDOTHELION group. Treatment of nonarteritic anterior ischemic optic neuropathy with an endothelin antagonist: ENDOTHELION (ENDOTHEL in antagonist receptor in Ischemic Optic Neuropathy) – a multicenter randomized controlled trial protocol. Trials. 2022;23(1):916.
47. Lantos K, Dömötör ZR, Farkas N, Kiss S, Szakács Z, at al. Efficacy of Treatments in Nonarteritic Ischemic Optic Neuropathy: A Systematic Review and Meta-Analysis. Int. J. Environ. Res. Public. Health. 2022;19(5):2718.
48. Frida Lind-Holm Mogensen, Christine Delle, Maiken Nedergaard. The Glymphatic System (En)during Inflammation. Int. J. Mol. Sci. 2021;22(14):7491.

Disclosures

Received 12.01.2023

Accepted 08.06.2023

Corresponding author: *Natalia Moiseenko, E-mail: natalymoyseenko@gmail.com*

Conflict of interest. *The author has no actual or potential conflicts of interest that could influence the opinion on the subject matter or materials presented and discussed in this manuscript.*

Sources of support. *None.*

Disclaimer. *The opinions expressed in this article are those of the authors and do not represent the official position of the institution.*