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Pathomorphological features of lesions of the choroid of the eyeball in COVID-19 associated cavernous sinus thrombosis

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Abstract

Background. Among the most significant ophthalmic diseases, the development, course and outcome of which is directly affected by coronavirus infection, a special place is occupied by COVID-19 associated cavernous sinus thrombosis (CST), a significant increase in the incidence of which is observed in some regions of the world, which requires a comprehensive study of this pathology.

Purpose. To study the pathomorphological features of damage to the choroid of the eyeball in COVID-19 associated CST.

Methods. The tissue of the iris, ciliary body, and choroid obtained after enucleation of the eyeball served as the material. Histological sections were stained with hematoxylin and eosin.

Results. Pathological examination revealed the presence of signs of a specific inflammatory process in the vessels of the choroid in the form of lymphocytic infiltration. In the lumen of the vessels, signs of vasculitis and the formation of mixed-type thrombosis were determined. The lesion mostly affected the interstitium of the vessels.

Conclusion. The established changes may be a sign of a specific viral lesion and indicate that the development of the necrotic process could be mediated by an autoimmune mechanism as a result of exposure to the pathogen.

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INTRODUCTION

Among the most significant ophthalmic diseases, the development, course and outcome of which is directly affected by coronavirus infection, a special place is occupied by COVID-19 associated cavernous sinus thrombosis (CST), a significant increase in the incidence of which is observed in some regions of the world, which requires conducting a comprehensive study of this pathology [1,2,3].

CST is a rather rare pathology and there are no publications in the literature devoted to the analysis of a large sample of cases. Observations of patients showed that CST had a "variegated" clinical picture and a severe course with a high mortality rate, which distinguishes it from the classical forms of this complication. It was revealed that in CST associated with coronavirus infection, a more pronounced purulent-necrotic process develops in the nasal cavity, paranasal sinuses and orbit, which was accom-

panied by a more frequent transition of the inflammatory process to the frontal lobes of the brain with the development of frontal encephalitis or abscess with severe neurological symptoms [4,5].

Observations have shown [1,2,4] that CST associated with COVID-19 is characterized not only by a high incidence of irreversible blindness, but also by the development of severe purulent-necrotic lesions of the structures of the maxillofacial region, orbit, paranasal sinuses and brain, which is the cause of high mortality rate. At the same time, many questions remain unresolved that relate to the pathogenesis of the development of severe purulent-necrotic lesions of the structures of the maxillofacial region, including the orbit, the eyeball and its individual structures as a result of the development of CST.

This article presents the results of a pathomorphological study of the choroid of the eyeball in a patient with COVID-19 associated CST, complicated by the development of a severe purulent-necrotic process in the orbit.

Purpose of the study. To study the pathomorphological features of lesions of choroid of the eyeball in COVID-19 associated cavernous sinus thrombosis.

METHOD OF PATHOMORPHOLOGICAL STUDY

Material for pathomorphological research was taken during operative intervention. The material consists of structures of eyeball – components of vascular layer (iris, ciliary body and choreoid). For morphological research, the material is fixed in a 10% neutral formalin solution for 3 days. After washing in running water, 2 cups of water are washed with alcohol, concentrated in chloroform, then washed with paraffin and wax. Histological sections obtained on a microtome were stained with hematoxylin and eosin after deparaffinization.

RESULTS OF PATHOMORPHOLOGICAL RESEARCH

Microscopic examination of the vascular mesh of the eyeball showed that as a result of the cerebral venous sinus thrombosis of the SARS-CoV-2 disease, discirculatory and inflammatory changes such as thrombosis and necrosis were detected in the tissues of the orbit and eyeball. Initially, the vascular membrane of the eyeball, which is rich in blood vessels, was studied. In this case, it was found that thrombosis has developed in the venous blood vessel in the part of the vascular membrane adjacent to the sclera. It was found that there is a thrombus in the cavity of the vein in a paralytically dilated state and its components are gathered in one place, fibrin fibers covering desquamated endothelial cells, around which lymphoid cells and other disintegrated cell structures are located. The appearance of a lymphocytic thrombus in the vein confirms that the coronavirus disease has developed as a result. As a result, it is observed that dystrophic and necrobiotic changes have developed in the tissue structures of the vascular para. Fibrous structures in the sclera are observed to be hardened due to sharp swelling (fig. 1).

The pigmented epithelium of the choroid at the border adjacent to the retina is dystrophied and disintegrated, the capillaries of the choriocapillary layer

under it are expanded, diapedesic blood is poured around it, the layer of arterial vessels is also slightly expanded, the vessels are irregularly located, filled with blood, the next layer, i.e., the layer where the large veins are located, has strong venous damping, it is determined that some of them are filled with erythrocytes, others with plasma, and blood is poured around them.

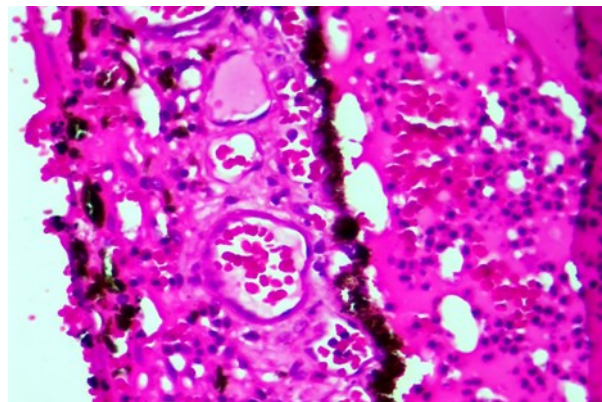


Figure 1. The choreoid of the eyeball, strong discirculatory processes caused swelling of the intermediate tissue, dystrophy and necrobiosis of all tissue structures. Paint: G-E. 10x40.

When the choroid is damaged by a virus, including a coronavirus, an immunopathological lymphoproliferative infiltrate appears due to the development of an acute autoimmune injury in its tissue. Morphologically, almost all layers of the vascular layer are diffusely infiltrated with lymphoid cells, as a result of which some layers, including the pigment epithelium and Bruch's membrane, are separated from the vascular layers. It is determined that the venous vessels in the venous layer are sharply expanded, some of them are ruptured, and blood is poured around them. Necrobiotic dystrophy and necrosis are observed in tissue structures between lymphoid infiltration (fig. 2).

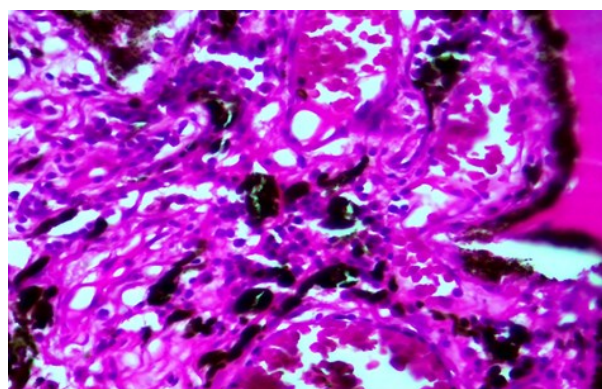


Figure 2. The iris, the vessels are sharply expanded, blood is poured around, the tissue is swollen, lymphoid infiltration has appeared in the interstitial tissue. Paint: G-E.10x40.

Since the pigmented membrane is a part of the vascular membrane, microscopic examination of it revealed the following conditions, the most prominent condition being the sharp expansion of the blood vessels, their filling with blood, and diapedesis blood pouring around them. Another important

change is that the entire area of the tissue is severely swollen, as a result of which the tissue structures are shriveled and disintegrated, some areas are necrobiosis. It is observed that the pigmented cells of the pigmented membrane are shriveled and dislocated, and some of them disintegrate and undergo necrobiosis. Mucoid and fibrinoid staining of stromal vascular protein dystrophy is observed in the anterior border layer with anterior connective tissue of the pigmented membrane under the influence of coronavirus. In the middle mesodermal layer, which is rich in vessels, strong discirculatory changes reveal venous congestion and bleeding. In the back pigment-muscle layer, it is determined that the pigment cells are torn, fragmented, and the muscle cells have contracted randomly. In some cases, development of lymphoproliferative immunopathological inflammation is observed in the pigmented membrane. In this case, it is determined that dense lymphoid infiltration appeared in the anterior connective tissue layer of the pigmented membrane around the interstitial tissue and vessels. It is found that lymphoid infiltration has appeared mainly around the blood vessels, and lymphocytic thrombi have appeared in some veins.

When studying the part of the ciliary body of the choroid, it was found that discirculatory, edematous and destructive-necrotic changes are strongly developed and they are located in the layer of the vascular network of the ciliary body. It was found that the discirculatory processes were manifested by paralytic expansion of blood vessels, rupture of some of them, hemorrhages around them. As a result, it was observed that the muscle fibers in the ciliary body were displaced and deformed, some of them underwent dystrophic and necrotic changes. It is determined that the ciliated growths of the ciliary body are enlarged and deformed due to swelling, mucoid swelling and fibrinoid necrosis have developed in the stroma of some of them. In this case, it is found that the basement membrane of the ciliary body is separated from the sclera and becomes inflamed due to swelling, fibrinoid swelling and fibrinoid necrosis. In some cases, lymphoid infiltration is observed mainly around blood vessels in the mesodermal part of the ciliary body. As a result, it is determined that the pigmented cells in the ciliary body have undergone dystrophy and destruction.

DISCUSSION

S-protein of 2-angiotensin converting enzyme (APF2-enzyme of SARS-CoV-2) has a selective effect on the receptor of respiratory epithelium, alveolocytes, alveolar monocyte, vascular endothelium, gastrointestinal epithelium, urinary tract epithelium, macrophages and even other cells, that is, it has polytropism. SARS-CoV-2 is characterized by active replication in the epithelium of the upper respiratory tract. Therefore, the course and outbreak of COVID-19 causes severe acute respiratory syndrome (SARS) and SARS, the strong replication of which causes viremia, immune disorders, hypoxia, and damages a number of organs, namely the heart, kidneys, gastrointestinal tract, brain, and lungs. venous sinus system, venous vessels and other organs, the receptor for APF2-enzyme is expressed in the cells of these organs and causes clinical severity

in the 2nd week after infection. The main pathogenic essence of this disease is destructive-productive thrombovasculitis and hypercoagulable syndrome, microangiopathy and paralysis of the immune system. In response to SARS-CoV-2, a hyperergic immune reaction in the patient's body causes a strong systemic inflammatory syndrome, severe alteration of lung alveolar tissue and other organs, and development of septic shock [5,6,7].

In addition to the above, many aspects of the pathogenesis and morphogenesis of COVID-19 are still unclear and undefined, including thrombovasculitis and hypercoagulation syndrome in the endothelium of the venous vessels in the tissues of the face-jaw, nose and its sinuses, and the tissues of the eye orbit, which have venous networks of the cerebral venous sinus, as a result, these areas mechanisms of development of inflammatory and necrotic processes in soft tissues have not been studied [8,9,10].

The choroid, in turn, consists of 5 layers: 1) outer layer - connective tissue attached to the sclera, 2) layer of large vessels - Galler's layer, this layer is rich in venous vessels, 3) layer of arterial vessels - Zattler's layer, 4) choriocapillary layer rich in capillaries, 5) vitreous plastic or Brukha's membrane - 2-3 μm thick, separates the vascular network from the retina [7,9].

Due to the large number of columnar barriers in the alveolar venous space of the brain, as a result of damage to the endothelium of the cavity by the COVID-19 virus, a primary thrombocytic thrombus is formed from the adhesion and aggregation of platelets. Due to the large number of columnar barriers in the alveolar venous space, the thrombosis process spreads to the intracerebral veins. The initial symptoms are headache, nausea and vomiting. Ophthalmologically, swelling, redness and pain of the eyeball develop. Chemosis, bilateral exophthalmos, visual impairment appear. A characteristic sign is a mammary tumor. Later hemi- and monoparalysis. Complications: cerebral infarction and bleeding. Thrombosis of the cavernous sinus is a thrombus blockage of the cavernous venous cavity of the brain [11,12,13].

The vitreous membrane of the eyeball occupies a large area and includes the ciliary body and the pigmented membrane. They are supplied with blood from the posterior short ciliary artery, but the venous blood flow is limited by the specific number of varicose veins, and the blood flows slowly through the varicose veins. This condition causes the development of infectious inflammation due to the presence of disease-causing microorganisms in the venous blood. Around the capillaries in the choroid, there is Bruch's membrane, which separates each other from the retina, and pigment epithelium located in a row. The choroid, including its choroidal part, is easily and quickly separated from the sclera, blood is often poured in between [11,14].

CONCLUSION

The development of a necrotic process in the structures of the eyeball with COVID-19 associated cavernous sinus thrombosis is characterized by a heterogeneous pathomorphological picture in the form of areas of a chronic inflammatory process with

lymphocytic infiltration, areas with a proliferative component and the formation of mixed-type thrombosis in the vessels, which may be a sign of a specific viral lesion and indicates that the development of necrosis could be mediated by an autoimmune mechanism as a result of exposure to the pathogen.

Ethics approval and consent to participate - All patients gave written informed consent to participate in the study.

Consent for publication - The study is valid, and recognition by the organization is not required. The author agrees to open publication

Availability of data and material - Available

Competing interests - No

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ПАТОМОРФОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ПОРАЖЕНИЯ СОСУДИСТОЙ ОБОЛОЧКИ ГЛАЗНОГО ЯБЛОКА ПРИ COVID-19 АССОЦИИРОВАННОМ ТРОМБОЗЕ КАВЕРНОЗНОГО СИНУСА

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Абстракт

Введение. Среди наиболее значимых офтальмологических заболеваний, на развитие, течение и исход которых напрямую влияет коронавирусная инфекция, особое место занимает COVID-19 ассоциированный тромбоз кавернозного синуса (ТКС), значительный рост заболеваемости которого наблюдается в некоторых регионах мира, что требует проведения комплексного исследования данной патологии.

Цель. Изучить патоморфологические особенности поражения сосудистой оболочки глазного яблока при COVID-19 ассоциированном ТКС.

Методы. Материалом служили ткани радужки, цилиарного тела и хориоидеи, полученные после энуклеации глазного яблока. Гистологические срезы окрашивались гематоксилином и эозином.

Результаты. Патоморфологическое исследование выявило наличие признаков специфического воспалительного процесса в сосудах хориоидеи в виде лимфоцитарной инфильтрации. В просвете сосудов определялись признаки васкулита и образования тромбов смешанного типа. Поражением в большей степени затрагивало интерстиций сосудов.

Вывод. Установленные изменения могут являться признаком специфического вирусного поражения и свидетельствует о том, что развитие некротического процесса могло быть опосредовано аутоиммунным механизмом в результате воздействия возбудителя.

Ключевые слова. COVID-19; тромбоз кавернозного синуса; хориоидея; патоморфологическое исследование.

COVID-19 BILAN BOG'LIQ KAVERNOZ SINUS TROMBOZIDAGI KO'Z OLMASINING TOMIR PARDASINING PATOMORFOLOGIK XUSUSIYATLARI

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Toshkent tibbiyot akademiyasi

Abstract

Kirish. Rivojlanishi, kechishi va natijalari bevosita koronavirus infeksiyasi bilan bog'liq bo'lgan eng muhim oftalmologik kasalliklar orasida COVID-19 bilan bog'liq bo'lgan kavernoza sinus trombozi (KST) alohida o'rin egallaydi, bu kasallik bilan kasallanishning sezilarli o'sishi dunyoning ba'zi mamlakatlarda kuzatilmoqda va bu patologiyani har tomonlama o'rganishni talab qiladi.

Tadqiqot maqsadi. COVID-19 bilan bog'liq KSTda ko'z olmasining tomir pardasining shikastlanishining patomorfologik xususiyatlarini o'rganish.

Tadqiqot usuli. Ko'z olmasining enukleatsiyasidan so'ng olingan rangdor parda, kipriksimon tana va xoroideya to'qimalari material bo'lib xizmat qildi. Gistologik kesmalar gematoksilin va eozin bilan bo'yalgan.

Natijalar. Patomorfologik tekshiruv chorioideya tomirlarida limfotsitar infiltratsiya shaklida o'ziga xos yallig'lanish jarayonining belgilari mavjudligini aniqladi. Tomirlarda vaskulit belgilari va aralash turdagi tromblarning shakllanishi aniqlandi. Patologik jarayon asosan tomirlarning interstitsiyasiga ta'sir qiladi.

Xulosa. Belgilangan o'zgarishlar o'ziga xos virusli patologik jarayon belgisi bo'lishi mumkin va nekrotik jarayonning rivojlanishi patogenning ta'siri natijasida autoimmun mexanizm orqali amalga oshirilishi mumkinligini ko'rsatadi.

Kalit sozlar. COVID-19; kavernoza sinus trombozi; tomir parda; patomorfologik tadqiqot.