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Features of Visual Pathology in Patients with Chronic Liver Disorders

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Abstract Great attention in the literature is given to eye pathology in viral hepatitis. Currently, diseases of chronic hepatitis of various etiologies occupy a significant place among the causes of disability and mortality in the adult population throughout the world. About 1 million people die each year from hepatitis B virus (HBV)-related liver disease, and among all causes of death, the consequences of HBV infection rank 10th in the world. According to the World Health Organization, 3% of the world's population (about 170 million people) are infected with hepatitis C virus (HCV), while the disease in 85% of cases becomes a chronic process, ending in 15-25 years with cirrhosis or primary liver cancer. Due to the fact that the liver is the leading organ that provides a dynamic balance of proteins, lipids, carbohydrates, enzymes, biologically active substances. The eye symptoms occur at 80% of patients. In this case, the incidence of this pathology, directly related to the hepatitis virus, ranges from 4% - 5% to 10% -20%.

Keywords Eye pathology, Chronic liver disorders, Organ of vision, Pathogenetic mechanisms

1. Introduction

The difficulty of chronic liver diseases occupies a leading place in the general human pathology. Over the past few years, there has been an increase in the number of patients with liver pathology among childhood. Etiological polymorphism, difficulties in differential diagnosis and prognosis of the course of chronic liver diseases in children, and severe outcomes make this problem extremely relevant for pediatrics [9]. It has been established that 84-100% of adult patients with chronic liver diseases have eye symptoms. They include impaired microcirculation of the conjunctiva, iris, clouding of the cornea and lens, as well as vascular and degenerative changes in the fundus [16,20,22,23,24,28]. The connection of liver diseases with eye pathology was noticed as early as the end of the 19th century [1,7,8], however, a targeted study of the condition of the eyes in chronic liver diseases of hereditary, viral, and unidentified etiology began to be actively carried out only in recent years.

Many pathological changes in the organ of vision are reversed against the background of pathogenetically substantiated therapy, but at the same time, the presence of chronic liver diseases is an aggravating factor in various eye diseases, contributes to the earlier development of age-related cataracts, aggravates the course of inflammatory processes, and leads to a significant impairment of visual functions [6].

Great attention in the literature is given to eye pathology in viral hepatitis. Currently, diseases of chronic hepatitis of various etiologies occupy a significant place among the causes of disability and mortality in the adult population throughout the world. About 1 million people die each year from hepatitis B virus (HBV)-related liver disease, and among all causes of death, the consequences of HBV infection rank 10th in the world. According to the World Health Organization, 3% of the world's population (about 170 million people) are infected with hepatitis C virus (HCV), while the disease in 85% of cases becomes a chronic process, ending in 15-25 years with cirrhosis or primary liver cancer. Due to the fact that the liver is the leading organ that provides a dynamic balance of proteins, lipids, carbohydrates, enzymes, biologically active substances. The eye symptoms occur at 80% of patients. In this case, the incidence of this pathology, directly related to the hepatitis virus, ranges from 4% - 5% to 10% -20%. According to Kushnir V.N. [10], significant disturbances of blood microcirculation were revealed in various liver injuries that occur with HBV. The most characteristic signs were microaneurysms, aggregation of erythrocytes, slowing of blood flow and the presence of single ischemic zones. As a result of the studies,

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deterioration of perivascular, vascular and rheological changes in patients with chronic liver lesions was revealed. This pathology, according to the author, is the result of pathological processes occurring in the body of patients with liver damage, leading to destructive changes in the walls of microvessels, disruption of their permeability, deterioration of blood circulation, which is lead to hypoxia of the tissues of the eyeball, which is consistent with the data of foreign literature [18,13], attention is paid to a decrease in the overall level of metabolic processes in the retina, resulting from a violation of its trophism. According to the literature, in patients with chronic hepatitis, there is a decrease in the critical flicker fusion number (CFFF) and an increase in the area of the blind spot, indicating atrophic changes in the inner layer of the retina and axons of ganglion cells that form the optic nerve. Among other clinical and morphological features of the course of ocular pathology against the background of chronic hepatitis, in foreign literature, there is a decrease in the sensitivity of the cornea in all quadrants, which occurs, presumably, due to inhibition of the function of the ciliary nerves [13].

2. Materials and Methods

Studies of the anterior segment of the eye in patients with chronic HCV infection included the detection of changes in the state of the cornea, conjunctiva, sclera, iris, lens and vitreous body, as well as the state of the eyelids, mucous membranes and microcirculation of the bulbar conjunctiva. More often, patients' complaints related to manifestations of corneal-conjunctival xerosis (RCC). In patients with chronic HCV infection, microsigns were registered, which were detected in the form of subjective and objective complaints.

Changes in the retina in patients with chronic HCV infection were manifested as angioretinopathy (cotton-like foci). Patients with hepatitis C may develop ischemic retinopathy, a manifestation of systemic vasculitis caused by infection. The pathogenesis of such changes is based on occlusion of retinal vessels by microemboli consisting of immune complexes and complement. Studies show that the prevalence of idiopathic retinopathy in at least one eye is 31.8%. Binocular retinopathy is detected in half of these patients. These symptoms were accompanied more often by a change in the caliber of the vessels. It should be noted that simultaneously with a change in the caliber of the vessels, there were symptoms of damage to the optic nerve head of patients in the form of decoloration of the optic nerve head (along the periphery in the form of a pigmented corolla) and in the form of blurring borders. Alterations in the macular area in patients with chronic HCV infection were found in the form of pigmentation rarefaction (pigment redistribution). A distinctive feature of changes in the macular area in patients with chronic HCV infection was frequent microaneurysms (the frequency ranged from 24.3 to 26.3% in patients who had an infection experience of 5 10 years or more) [1]. The inflammatory reaction of the eye that accompanies viral infections, including hepatitis, includes the release of inflammatory mediators (prostaglandins, substance P), microcirculation disorders, disruption of the hematoophthalmic and hematoretinal barriers, stimulation of pain receptors, and dysfunction of immune defense mechanisms. In this regard, it is advisable to prescribe anti-inflammatory drugs, for example, Indocollyre 0.1% (Bausch + Lomb), which allow counteracting the effects of prostaglandins such as edema, pupillary sphincter contraction, stimulation of painful nerve endings, increased vascular wall permeability, etc. Rare Morena's ulcer is a form of peripheral keratitis, also associated with viral hepatitis. In the early stages, this damage is limited to the periphery of the cornea, but may eventually involve the entire cornea.

In addition, the effect of the hepatitis C virus on the meibomian glands has been established [11]. The studies carried out have shown that In chronic hepatitis C, there is a violation of tear formation. There are reports in the literature about the relationship between Sjogren's syndrome and HCV infection [13]. Sjogren's syndrome is a systemic autoimmune disease characterized by dryness of the mucous membranes of the mouth (xerostomia) and eyes (xerophthalmia). Histological changes characteristic of Sjogren's syndrome were found in the labial salivary glands in 58% of patients infected with HCV. The possibility of a connection between Sjogren's syndrome and chronic viral hepatitis C or the possibility of a combination of individual symptoms that mimic the primary Sjogren's syndrome has been proven. Patients with a combination of HCV infection and Sjogren's syndrome have much stronger neurological symptoms and weaker articular lesions than patients with Sjogren's syndrome without hepatitis C [5]. In another clinical study [4], a large number of clinical and serological differences were noted between primary Sjogren's syndrome and its association with chronic HCV infection. The mechanism of changes in the salivary and lacrimal glands in the combination of chronic viral hepatitis C and Sjogren's syndrome is unclear. The mechanisms of exocrine glandular dysfunction are thought to include direct exposure of the HCV virus to gland cells and molecular mimicry between the gland and the virus, leading to an autoimmune response to the lacrimal gland tissue. Subsequently, the reaction develops through the deposition of immune complexes and/or lymphocytic infiltration [5]. According to some authors [5,15,25,35], 10% of patients infected with HCV infection complained of dry mouth and/or a feeling of dry eyes. Koike K. The level of total tear production during the Schirmer test is 1.82±0.09 mm. Changes in the secretion of lacrimal fluid in the form of its increase and decrease already at an early stage, with an infection duration of up to 3 years - in 46% of cases, and with an infection duration of more than 5 years - in 68.4%. In 18%-50% of cases, it is associated with antiviral therapy and may be accompanied by pathological changes in the retina and optic nerve. As a result, one of the target organs in the event of side effects of interferon therapy for chronic viral hepatitis is the eye. Thus, during antiviral

therapy of chronic viral hepatitis B and C with the use of interferon preparations, pathological changes in the retina, namely cotton-wool foci and hemorrhages, may occur.

Mechanisms of eye damage in chronic HCV infections. One of the important functions of the liver is protein-synthetic, regulating the provision of dynamic balance in the body. It can be assumed that the disorder of these mechanisms together can lead to changes, including in the microcirculatory bed of the liver and the body as a whole, which are factors contributing to the emergence and development of the pathology of the organ of vision. In addition, according to the literature, the persistence of HBV and HCV in the blood is accompanied by their penetration into the structures of the tissues of internal organs, including the eye [12]. In the available literature, there are no clear ideas about the possible mechanisms of eye damage in chronic viral hepatitis C, so we made an attempt to systematize the available literature data in this direction. In the foreign literature, there is information indicating the isolation of the hepatitis C virus in the lacrimal fluid and in the moisture of the anterior chamber in patients with CHC who have a high viral replication (viral load). At the same time, the authors note a higher frequency of detection of viral RNA in the lacrimal fluid compared to the patient's blood serum [21]. In addition, researchers have expressed an opinion about the possible spread of NSU through tear fluid and medical instruments. Cases of detecting anti-HCV in the cornea of anti-HCV seropositive blood donors have also been described [19,25,37]. In connection with the detection of HCV markers in materials obtained from the ocular tissue bank, the risk of infection with viral hepatitis through the donor cornea is discussed. It is stated that storage in a tissue bank for 6 days (under generally accepted conditions) cannot eliminate the virus, as a result, the possibility of its transfer to the recipient during keratoplasty and cataract operations remains [29,32]. 2 cases of acute viral hepatitis were registered after penetrating corneal transplantation; the presence of HBV in the serum of both corneal donors was retrospectively proven. A group of researchers during screening of donor corneas found HBV markers in 0.25%, HCV - in 0.93% of cases [31].

3. Result and Discussion

There are reports of the ability of hepatitis A, B, and C viruses to directly cause damage to the retina and choroid [9,10]. "Molecular" mimicry has been found in the peptides of the retinal S-antigen (S-AG) and hepatitis B DNA virus. The importance of this virus in the etiology of a number of human uveitis has been established. With endogenous uveitis, about half of the patients are infected with the hepatitis B virus. And among them, much more often than in other forms of ophthalmopathology, there are persons suffering from chronic hepatitis (73.5%), including those of unclear etiology (23.4%), and this allows us to say that liver pathology, not necessarily of HBV nature, is in itself a factor predisposing to the development of uveitis and postveal cataracts, which confirms the opinion of a number of researchers about the presence of cross-reacting antigens in the structures of the liver, uveal membrane and lens capsule [14,33]. In addition, hepatitis B virus antigen was found in the corneal stroma. There are known cases of infection of patients with the hepatitis B virus after keratoplasty, where the donor was a carrier of HBsAg. The release of HBsAg in tears, anterior chamber moisture, subretinal fluid in patients after acute hepatitis B has been described [9]. Evidence of the direct involvement of hepatitis B virus in the etiopathogenesis of uveitis, complicated and congenital cataracts, damage and progression of corneal pathology is a very high percentage of detection of markers of active infection or chronic virus carriage not only in the SC and SF, but also in eye tissues, and in some cases (from 11 to 60% among infected individuals) HBV markers are detected only in the structures of the eye, not found in the blood. All this testifies to the undoubted role of hepatitis viruses in the formation of ophthalmopathology.

An indisputable fact is the damage to the organ of vision in a severe hereditary disease - Wilson's disease [2,26,30,34]. It was shown that the severity of eye manifestations in all patients with Wilson's disease depends on the duration of the disease, the nature of pathological changes in the liver, brain, and pathogenetic therapy. In 56.3% of cases, moderate icterus of the sclera is detected, in 43.8% - retraction of the mimic muscles of the face, in adult patients in 90.6% of cases there is a Kaiser-Fleischer ring in both eyes, in 53.1% - "copper" cataract (figure of a sunflower). In 18.7% - signs of bilateral sluggish uveitis and 40.6% - destruction and clouding of the vitreous body. All patients showed changes in the fundus of the eye of varying severity [30]. In patients with damage to the organ of vision in liver pathology, disorders of immune homeostasis develop according to the type of secondary immunological deficiency, mainly the suppressor variant of immunodeficiency, which manifests itself in the form of T-lymphopenia, an imbalance of helper-suppressor subpopulations of T cells with a decrease in the immunoregulatory index, an increase in the level of the CEC, mainly due to the most pathogenic medium and small molecular fractions, and an increase in the sensitization of peripheral blood leukocytes to eye autoantigens (retina, lens, uveal tract). Many authors believe that a characteristic pathogenetic moment in the development of eye diseases in patients with liver pathology of various origins are disorders of immune homeostasis, leading to a decrease in the general and local resistance of the body.

More than 60% of patients with liver cirrhosis have clinical manifestations of portal hypertension (splenomegaly, ascites, etc.). One of the first mentions of condition of eyes in patients with cirrhosis of the liver dates back to 1895. A.V. Natanson describes in patients with liver cirrhosis "pigmented retinal degeneration, vasoconstriction, a kind of atrophy of the optic nerves, narrowing of the visual fields and the presence of hemorrhages in the fundus with interstitial hepatitis" [9]. Ophthalmic pathologies of cirrhosis in the literature include xerophthalmia, vitamin A deficiency,

and color blindness. The xerophthalmia and keratoconjunctivitis seen in Shegren's syndrome may be associated with autoimmune hepatitis and primary biliary cirrhosis. Xerophthalmia is also observed in vitamin A deficiency. It can even progress to the appearance of small grayish lesions, namely Bitot's spots, and blindness. Night blindness may develop. Vitamin A deficiency can be observed in cirrhosis of the liver, since the liver is the organ in which vitamin A is deposited [35,36]. Color blindness can be observed with cirrhosis of the liver, especially the alcoholic type. Exudates and hemorrhages may be observed in the retina. Increased hydrostatic pressure caused by high portal pressure, hypoalbuminemia in cirrhosis, and the associated decrease in oncotic pressure may also contribute to exudate formation by extravasation of plasma contents. A study by Dittmer K. and colleagues confirms this assumption [17]. A study on 17 patients with liver cirrhosis and portal hypertension, largely due to alcohol consumption, who underwent ophthalmological examination before and after transjugular intrahepatic portosystemic shunting, revealed the following: retinopathy was expressed in 11 patients, of which 5 were exudative in nature. Retinopathy significantly regressed or completely disappeared after this procedure, which has a hemodynamic effect on systemic blood flow. These results were associated with the fact that cirrhosis of the liver leads to a decrease in retinal perfusion.

4. Conclusions

Therefore, in diseases of liver are revealed a wide range of ocular symptoms including both anterior (conjunctival xerosis, etc.), and the posterior segment of the eye (angiopathy, retinopathy, etc.), as well as impaired function of the lacrimal gland. The main mechanisms of these pathologies are virological, immunological mechanisms, microcirculatory and metabolic disorders. Given the multiple eye disorders in patients with chronic liver diseases and the pathogenetic mechanisms of the development of these manifestations, it is necessary to conduct a comprehensive analysis of the condition of the eyes in patients with chronic liver diseases for early diagnosis and timely treatment of these ophthalmic pathologies.

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