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Chorioretinitis in infants

Zapalenie tylnego odcinka błony naczyniowej w okresie niemowlęcym

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Summary: Purpose: The aim of this review is to present cases of chorioretinitis in infants caused by viral and parasitic infections.
Material and methods: Four infants with viral chorioretinitis were identified in a routine ophthalmological examination. Laboratory tests towards bacterial, viral and parasitic diseases were performed.
Results: Toxoplasmosis, rubella, and CMV infections were diagnosed in clinical and laboratory tests. After a wide spectrum of therapy a total remission of inflammatory process in all the discussed children was observed.
Conclusions: Posterior uveitis is an ocular complication which can be connected with viral or parasitic infections in postnatal period. Prematurity, normal delivery, intrauterine transmission, breast feeding, comorbid diseases might be associated with chorioretinitis in infants.

Key words: infants, chorioretinitis, viral and parasitic infections.

Streszczenie: Cel: celem pracy jest przedstawienie objawów klinicznych zapaleń błony naczyniowej o etiologii wirusowej i pasożytniczej oraz przebiegu tej choroby, a także współistniejących zmian siatkówkowych w okresie niemowlęcym.
Pacjent i metody: zapalenie błony naczyniowej i siatkówki rozpoznano u czworga niemowląt w okresowym, rutynowym badaniu okulistycznym. W celu ustalenia diagnozy u chorych w obserwowanej grupie wykonano badania laboratoryjne w kierunku schorzeń bakteryjnych, wirusowych i pasożytniczych. Obrazy z dna oka archiwizowano za pomocą aparatu Ret-Cam II. W omawianych przypadkach w leczeniu stosowano celowaną antybiotykoterapię oraz leki przeciwwirusowe. W przypadku współwystępowania odczynu szklistkowego z zapaleniem błony naczyniowej leczenie wspomagano steroidoterapią.
Wyniki: u niemowląt na podstawie badania okulistycznego potwierdzonego testami laboratoryjnymi rozpoznano infekcję wirusową. U dwojga z omawianych dzieci zakażenie spowodowane było infekcją cytomegalowirusem (CMV) w przebiegu transferu wewnątrzmacicznego od matki chorego dziecka, zakażenia okołoporodowego lub podczas karmienia piersią. W dwóch pozostałych przypadkach infekcja miała charakter mieszany, pasożytniczo-wirusowy, spowodowany jednocześnie toksoplazmozą, różyczką i cytomegalią. Zastosowanie terapii o szerokim spektrum działania doprowadziło do całkowitego wyleczenia zmian zapalnych siatkówkowo-naczyniówkowych u wszystkich omawianych dzieci.
Wnioski: zapalenie tylnego odcinka błony naczyniowej w okresie noworodkowym lub niemowlęcym może być powikłaniem związanym z infekcją wirusową lub pasożytniczą. Obecność okulistycznych objawów zapalenia w błonie naczyniowej i siatkówce może być wskazaniem do wykonania badań serologicznych w celu potwierdzenia infekcyjnej etiologii zapalenia. Wcześniactwo, karmienie piersią, poród siłami natury i schorzenia współistniejące mogą być czynnikami sprzyjającymi występowaniu chorioretinitis w okresie niemowlęcym.

Słowa kluczowe: zapalenie błony naczyniowej, infekcje wirusowe i pasożytnicze, okres niemowlęcy.

Introduction

The etiology of chorioretinitis still remains unclear and although it is thought that most cases of the disease, particularly in infancy, is caused by immunological reaction there are forms of chorioretinitis due to infectious factors. The course of the disease can take a latent, smoldering or chronic form (1). Both retina and choroid are highly vascularized structures of the eye. The disease can create favorable conditions for bacterial colonizations through hematogenic route during the course of generalized infectious diseases. The etiological factors for chorioretinitis can be fungi, bacteria, parasites and viruses. Chorioretinitis in infancy is mostly caused by both herpes viruses (HSV, VZV) and CMV viruses. Advanced ocular symptoms, such as acute retinal necrosis syndrome, are particularly observed in children with decreased immunological resistance. Literature findings seem to suggest that viral uveitis is most common in immunosuppressed patients, in AIDS, lymphoma and during immunomodulatory therapy (2).

Although the most common cause of chorioretinitis in the neonatal and early infancy period is a viral infection and symptoms are quite characteristic, it is necessary to confirm this etiology in laboratory and imaging examinations to be able to set correct diagnosis and implement appropriate treatment. Because there are only few findings in the literature on viral

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and parasitic ocular complications in newborns and infants the authors of the present paper decided to present ophthalmological changes with this etiology in the youngest group of patients.

Experimental procedures

Out of a group of 984 children (2006-2009) born until 39-th week of gestation with birth weight up to 3270 g, a group of infants (n = 4, i.e. 0.08%) with chorioretinitis was selected. Children with suspected viral infection were born between 27-th and 35-th week of gestation (mean 34.25 Hbd, SD 5.12), with the birth weight between 1200 and 3270 g (mean 2607.5 g, SD 956.12). Out of the four children one was born at term and three were born before term. The latter children were ophthalmologically examined in the first, second and third month of life due to preterm birth and the indications included perinatal history and comorbidity. In the investigated group three children were male and one child was female. They were physiologically born and breast fed on demand. The ophthalmological examinations were performed according to the standards. The eye fundus was assessed after mydriasis (Tropicamidum 0.5% and Neosynephrin 2.5%) using a retina camera system RetCam II. While assessing factors affecting the development of the infection, the authors also collected clinical data concerning the course of gestation and delivery, infectious risk factors from both mother and child, degree of prematurity of the infant, comorbid diseases and treatment to date. The laboratory and imaging tests results were also analyzed.

Results

The ophthalmological examination conducted in the investigated group of infants revealed various lesions in the posterior parts of their eyes. In the retina of two infants some signs of perivascular infection as well as white, fluffy lesions with intra- and preretinal hemorrhage were found. The inflammatory process observed in the successive ophthalmological examinations developed along vessels like "burning grass" finally reaching the optic nerve disc. In all the infants the disease affected the posterior vitreous body in its peripheral parts starting with massive, occasionally "cloudy" hemorrhages with inflammatory reaction in the vitreous body, which while withdrawing revealed white, fluffy foci of infection (Fig. 1-4).

Fig. 1. Hemorrhages and white inflammatory foci visible under the hemorrhages during the course of CMV infection.
Ryc. 1. Wylewy krwotoczne i białe ogniska zapalne widoczne pod wylewami w przebiegu infekcji CMV.

Fig. 2. Lesions looking like "burning grass" and vascular inflammatory infiltrate in the retina caused by CMV infection.
Ryc. 2. Zmiany chorobowe w postaci palących się traw i okołonaczyniowe nacieki zapalne w siatkówce spowodowane zakażeniem CMV.

Fig. 3. Numerous circular preretinal hemorrhages affecting the posterior pole during the course of CMV infection.
Ryc. 3. Liczne okrągłe wylewy przedsiatkówkowe obejmujące biegun tylny w przebiegu infekcji CMV.

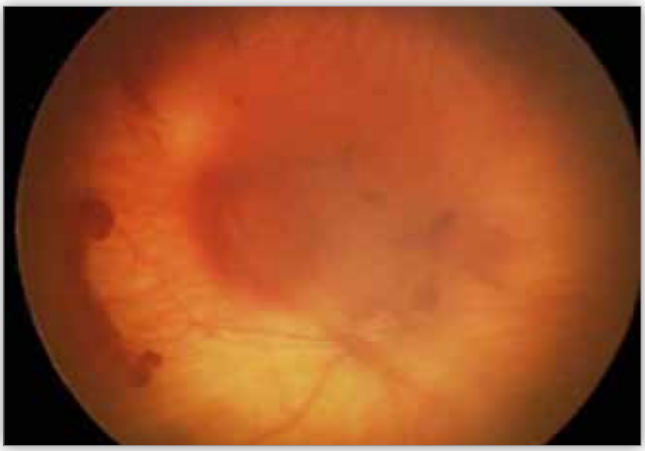

Fig. 4. Subretinal hemorrhage and hemorrhage to the vitreous body caused by mixed infection (rubella, toxoplasmosis and CMV).
Ryc. 4. Wylewy podsiatkówkowe i do komory ciała szklistego spowodowane infekcją mieszaną (różyczką, toksoplazmozą, cytomegalowirusem).

During the regression of the inflammatory process the blood and infection absorption was accompanied by vast transfers

of pigment which left scars in these places of the retina. In the remaining group of two children in the far periphery of the fundus pre-retinal hemorrhages were observed below which yellow inflammatory spots were found. Vitreous and retinal changes were seen in the spots as well as discreet exudate in the vitreous body. Quite large (approximately three times larger than the optic nerve disc), subretinal hemorrhage accompanied by vascular inflammation was observed close to the retinal macula (Fig. 5-8).

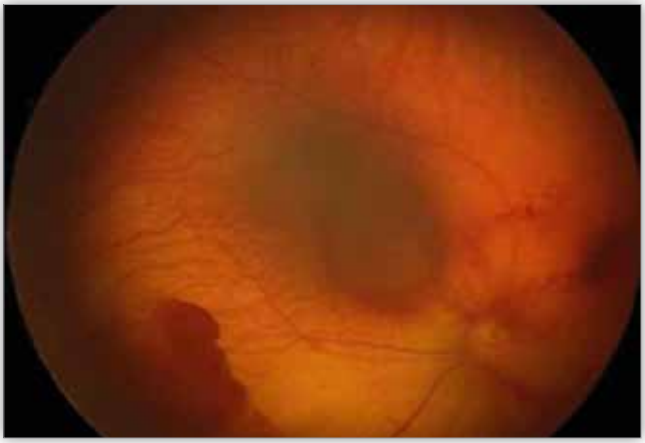

Fig. 5. Remnant hemorrhage in the periphery in close to the retinal macula with three yellow inflammatory foci in mixed infection (CMV, toxoplasmosis, rubella).
Ryc. 5. Resztkowy wylew na obwodzie i w okolicy plamki z trzema żółtymi ogniskami zapalnymi w przebiegu infekcji mieszanej (CMV, toksoplazmozy, różyczki).

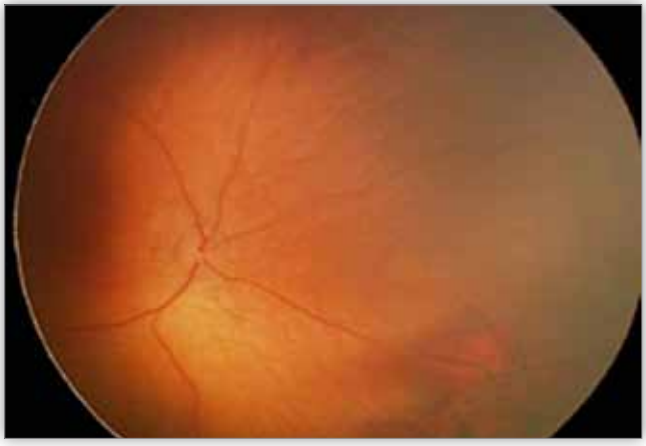

Fig. 6. Subretinal hemorrhage foci and white infiltrate in the periphery and proliferation sequence in mixed infection (rubella, toxoplasmosis, CMV).
Ryc. 6. Ogniska wylewów podsiatkówkowych i białe nacieki na obwodzie oraz ciąg proliferacyjny w przebiegu infekcji mieszanej (różyczki, toksoplazmozy, cytomegalowirusa).

In all the above described cases chorioretinitis was suggested after conducting ophthalmological examination. Laboratory tests excluded bacterial or mycotic infection, sarcoidosis and viral tests performed using Elis, Western Blott and Meia techniques revealed the following results: HBs Ag (-), p-c anti HCV (-), anti Borrelia IgM (-) IgG (-), in two cases anti Toxo IgG (+) IgM (-), anti Toxocara canis IgG (-), HIV Ab/Ag (-), in four cases anti CMV IgG (+), in one case anti HSV 1/HSV 2 IgM (-)

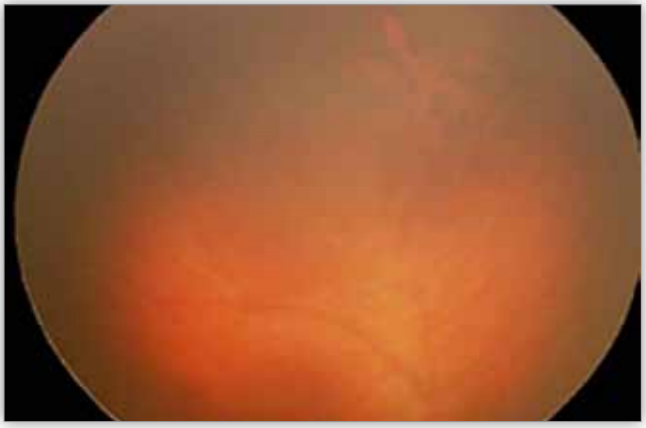

Fig. 7. Vitreous – retinal changes caused by mixed infection (rubella, toxoplasmosis, CMV).
Ryc. 7. Zmiany szklistkowo-siatkówkowe spowodowane infekcją mieszaną (różyczką, toksoplazmozą, cytomegalowirusem).

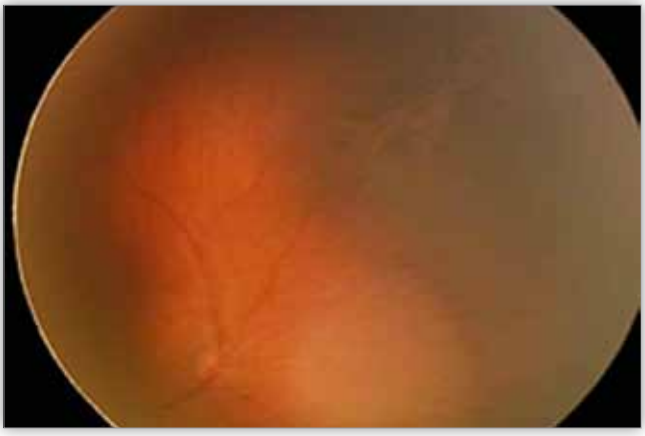

Fig. 8. Regression of inflammatory changes caused by mixed infection (rubella, toxoplasmosis, CMV).
Ryc. 8. Regresja zmian zapalnych, które są spowodowane infekcją mieszaną (różyczką, toksoplazmozą, cytomegalowirusem).

IgG (+), in two cases anti Rubella IgG (+) IgM (-). In two cases the diagnostics also included HIV tests and in one case syphilis test. The results were negative. In two infants the infection was also diagnosed in their pregnant mothers. The results of serological testing were as follows: CMV IgM (-) and CMV IgG (+) 73.0 AU/ml; for Toxo IgG (+) 103.0 IU/ml. In one infant the case history confirmed that its pregnant mother had contact with Herpes simplex virus (HSV) (Tab. I). On the basis of subjective, objective and additionally performed tests a diagnosis of chorioretinitis was made. In the first two cases the disease was caused by CMV infection whereas in the remaining two cases the infection was mixed (toxoplasmosis, rubella, CMV). The treatment included generally and locally administered antibiotics, steroids, and antiviral medication. Owing to the treatment an improvement in both eyes and remission of symptoms was achieved.

Discussion

The available literature knows the risk of intrauterine transmission of viral or parasitic infection from HIV positive mother, as well as cases of infecting a new born during natural delivery, breast feeding (3) or during red cells concentrate transfusion (4). Newborns and infants with low birth weight are particularly

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Number of children n = 4/ Liczba dzieci n = 4	Child 1/ Dziecko 1.	Child 2/ Dziecko 2.	Child 3/ Dziecko 3.	Child 4/ Dziecko 4.
Birth/ Poród	Natural/ Naturalny	Natural/ Naturalny	Natural/ Naturalny	Natural/ Naturalny
Hbd/ Tydzień ciąży	35	36	27	39
Mean birth of weight (g)/ Waga urodzeniowa (g)	2830	3130	1200	3270
Feeding/ Karmienie	Breast/ Piersią	Breast/ Piersią	Breast/ Piersią	Breast/ Piersią
Pathogen found in chorioretinitis/ Patogen wykryty w zapaleniu naczyniówki i siatkówki				
Anti Toxo	IgG (+) IgM (-)	IgG (+) 45,8 IU/ml IgM (-)	IgG (-) IgM (-)	IgG (-) IgM (-)
Anti Rubella	IgG (+) IgM (-)	IgG (+) 31,8 nIU/ml IgM (-)	IgG (-) IgM (-)	IgG (-) IgM (-)
Anti CMV	IgG (+) IgM (-)	IgG (+) 6 AU/ml IgM (-)	IgG (+) 187,3 AU/ml IgM (-)	IgM (+) IgG (+)
Anti HSV1/2	IgG (+) IgM (-)	IgG (-) IgM (-)	IgG (-) IgM (-)	IgG (-) IgM (-)
Anti Borrelia	IgG (-) IgM (-)	IgG (-) IgM (-)	IgG (-) IgM (-)	IgG (-) IgM (-)
Anti Toxocara	IgE (-) IgG (-)	IgE(-) IgM(-)	IgE (-) IgG (-)	IgG (-) IgM (-)
HIV Ab/Ag	(-)	(-)	(-)	(-)
VDRL	(-)	(-)	(-)	(-)
HbsAg	(-)	(-)	(-)	(-)
Anti HCV	(-)	(-)	(-)	(-)
Applied treatment/ Zastosowane leczenie	Antibiotic intravenously and orally, steroids administered generally and locally, antiviral medication, medication to seal vessels	Antibiotic intravenously and orally, steroids administered generally and locally, medication to seal vessels	Antibiotic intravenously and orally, steroids administered generally and locally, antiviral medication, medication to seal vessels	Antibiotic intravenously and orally, medication to seal vessels
Comorbid disease in the infant/ Współistniejące choroby u dzieci	Preterm birth, anemia, respiratory tract infections	Preterm birth, encephalopathy IV H I/II degree on the right side, jaundice, anemia, metabolic acidosis, disorders of coagulation system (p. IX by 36.4%)	Extreme preterm birth, perinatal asphyxia, RDS, dyspnoea, bronchopulmonary dysplasia, jaundice, anemia, metabolic acidosis	Birth at term, congenital CMV, thrombocytopenia
Comorbid disease in the mother/ Współistniejące choroby u matki	Infection with Herpes simplex virus in patient's sister	anti Toxo IgG (+) 103.0 IU/ml	Anti CMV IgG (-)	anti CMV IgM (-) IgG (+) 73.0 AU/ml high avidity

Tab. I. Characteristic of group of infants with chorioretinitis.
Tab. I. Charakterystyka dzieci z zapaleniem siatkówkowo-naczyniówkowym.

susceptible to infection (5,6). In the group of infants with viral (CMV, rubella and Herpes virus) and parasitic (toxoplasmosis) infection investigated by the authors of the present paper the clinical pictures of both the anterior and posterior eye were similar and the differential diagnosis took into account the clinical picture of other bacterial, fungoid or parasitic inflammations (2,7-9). CMV infections in the retina are accompanied by numerous, granular hemorrhagic foci or white inflammatory spots with clear boundaries, vascular infections in the form of white small sacks along a blood vessel and comorbid inflammation of the vitreous body. The inflammation process can spread along vessels like " burning grass" reaching the optic nerve disc. Absorption of blood hemorrhage and inflammation spots leading to widespread scars in the retina or secondary retinal detachment can accompany the process of lesions regression (7). The differentiation process during CMC inflammation should include chorioretinitis caused by HIV which is characterized by irregular grey-white or yellow changes found in medium or far periphery. Microangiopathy and small hemorrhages can accompany the above mentioned symptoms (2).

The distinctive features of congenital rubella are: anterior uveitis with iris atrophy and salt-and-pepper retinopathy in the rear pole and in the far periphery of the retina. The above mentioned diseases can be comorbid with microphthalmia, cataract, glaucoma, keratitis and eye refraction disorders. Ocular infection due to varicella and zoster (VZV) is initially one sided and reveals itself as vascular membrane inflammation in the form of multiple foci of white-yellow infiltrations of the retina, which can be accompanied by the inflammation of the vitreous body and the vicinity of the retinal macula. HSV virus usually causes one-sided acute

retinal necrosis. Granulomatous anterior uveitis with the inflammation of the vitreous body and peripheral periarterial inflammation, white-yellow infiltration multiple foci can accompany this kind of infection (2,8). Clinical symptoms of chorioretinitis in toxoplasmosis include anterior uveitis and inflammatory foci at the fundus adjacent to old colored scars. Sometimes this condition can be comorbid to the inflammation of the vitreous body with "headlights in the fog" (2,8,9). Toxocariasis infection manifests itself with the peripheral and intermediate part of the retina covered with thick grey-white exudates similar to "a bank of snow" (2). Chorioretinitis in Lyme disease can be manifested as severe anterior uveitis of the intermediate part of the vascular membrane as well as multiple foci, peripheral inflammations of the choroid and symptoms of neuroretinitis (2,9). Ocular candidiasis is characterized by fluffy, white inflammatory lesions in the retina and in the vitreous body resembling "cotton wool swabs" or "string of pearls" (2). Ocular form of syphilis is rare and has no pathognomonic signs. The anterior part of the eye is affected, usually in the form of iris gumma or multiple foci chorioretinitis or neuroretinitis. Cured lesions leave areas of retinal atrophy with reshuffled pigment (8,9). There are no specific symptoms of chorioretinitis in TB and the clinical picture is pleomorphic. Iris and choroid granuloma as well as retinal vascular inflammation are most common (9).

Recent findings suggest that it is possible to implement new diagnostic methods in fundus inflammation diseases, including viral infections. These include analysis of watery liquid using PCR method in order to find specific antibodies towards HSV virus, varicella, VZV, CMV and toxoplasmosis. Owing to these it is possible to determine the etiological factor in approximately 30% of patients (10). Additionally, studies on the presence of specific anti CMV antibodies in tears are being carried out (11). The latest research suggest that β2-macroglobulin (β2M) can indicate viral infection and the level of the substance is significantly increased in congenital toxoplasmosis and CMV in the first weeks of life (12).

Antiviral therapy is a treatment of choice in viral uveitis. In treatment and prevention the following are used: ganciclovir, valganciclovir, foscarnet, cidofovir first intravenously and later orally. Injections directly into the vitreous body or retarded release vitreous body implants containing ganciclovir are also used (13). Similar treatment to the one described in the literature was used by the authors of reports. Additionally, given retinal complications including retinal macula, good therapeutic results are achieved after glicocortycosteroids being administered intravenously which was exemplified in the remission of symptoms in the fundus in the cases described by the authors (1).

Conclusions

1. Such ocular complications as posterior uveitis with vitreous reaction and preretinal hemorrhages in newborns and infants require conducting laboratory tests towards viral infections.
2. Preterm birth, natural birth, breast feeding with other comorbid diseases can be considered as risk factors for chorioretinitis with viral etiology in the first months of the infant's life.

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