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Myocarditis as a cause of neonate's circulatory failure during delivery - case study

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Abstract: Myocarditis (MCI) is a heart pathology characterized by its rare occurrence and a possible fatal course. In the natural history of the disease inflammatory cell infiltrates are present. There are subtypes of MCI depending on the predominant cell type in the biopsy sampls. One of them is eosinophilic myocarditis. In eosinophilic myocarditis more that 50%

of the cells are eosinophils. In the later phases of the disease the myocardium is infiltrated by fibrous tissue and the heart vessels are often affected by thrombosis. Cardiomyopathy is a common long-term complication of the MCI.

Reported case presents a death of a male neonate. The neonate was delivered by vaginal delivery. Both prenatal development and all the prenatal tests indicated proper development of the fetus. At the delivery the neonate weight was 3900 grams and was evaluated with only 1 point on the Apgar score. Moreover the neonate presented a complete acute cardiorespiratory failure at birth. Despite the 2 hour-long cardio-pulmonary resuscitation no return of spontaneous circulation was observed. The neonate's remains were pathologically as well as histologically examined. The microscopic examination of the neonate's heart samples contained many inflammatory cell infiltrations. Microabscesses with Charcot-Leyden crystals inside were also observed. Furthermore, the presence of atypical, polynuclear cells was noted. On the basis of the morphological image, it was recognized as an eosinophilic MCI.

Described case is an example that even advanced obstetric diagnosing tools can be insufficient in some cases.

Keywords: myocarditis, eosinophilic myocarditis

Introduction: In literature the MCI is mostly described as a disease affecting adult patients. Since 1996 it is a part of cardiomyopathies classification edited by World Health Organization [1]. MCI remains a common cause of sudden cardiac deaths (SCD). According to autopsy studies it is estimated to be a cause of around 6-10% of all pediatric SCD [2,3]. Most publications differentiate myocarditis into acute and chronic form. The acute form can be diagnosed when clinical symptoms are present not longer than 1 month. When the conditions are present longer than a month, clinicians describe it as a chronic inflammatory cardiomyopathy [4]. There is variety of cardiovascular symptoms that myocarditis can cause, from palpitations, moderate dyspnea or chest discomfort which are often self limiting to

syncope, cardiogenic shock and death [5]. A common first symptom is impaired exercise tolerance [6].

MCI, a condition characterized by inflammation of the heart muscle, can stem from various causes. Generally speaking the causes of MCI can be infectious and non-infectious [7] Viral infections, such as enteroviruses and adenoviruses, often trigger myocarditis as the immune response directed against the virus inadvertently targets the heart tissue. Autoimmune reactions where the immune system attacks the heart muscle cells, can also lead to myocarditis. Most common systemic diseases that can lead to MCI are Churg-Strauss syndrome, sarcoidosis, eosinophilic granulomatosis with polyangiitis and lupus. Other potential factors include bacterial infections, certain medications, environmental toxins [8,9,10]. While the exact causes can be multifaceted, understanding these triggers is crucial for effective prevention and management of myocarditis.

The pathology of myocarditis involves a complex interplay of immune responses and tissue damage within the heart. Inflammatory cells, predominantly lymphocytes, infiltrate the heart muscle tissue, leading to inflammation. This inflammatory process can cause damage to the heart muscle cells (cardiomyocytes) directly, disrupting their function and potentially leading to cell death. The body's immune system, while attempting to clear the infection or respond to an autoimmune trigger, can inadvertently cause collateral damage to the heart tissue. Even though there may not be any early signs of tissue inflammation, inflammatory cells are important participants in the process, and pathologic diagnosis depends heavily on finding and characterizing these cells in cardiac tissue. Myocarditis has a wide range of histopathological subgroups, each with unique patterns that represent the underlying etiology. Main types are lymphocytic, eosinophilic, giant cell, granulomatous and mixed-cell MCI. In most samples various cells can be found. The key to differentiate a subtype is predominant cell type [11,12]. The widely accepted classification of histologic pattern is the Dallas classification [13].

For years the golden standard for MCI diagnosis was a myocardial biopsy. Nowadays with modern, advanced magnetic resonance imaging (MRI) less and less biopsies are being performed. Edema, hyperemia, and fibrosis are examples of tissue damage that MRI may identify. One should remember that in many cases the MRI is not sufficient for a certain diagnosis thus a myocardial biopsy can be necessary [14,15].

The treatment of MCI depends on the underlying cause, severity of symptoms, and complications. It is crucial to perform wide diagnosis, detect the factor causing MCI and treat the factor. Because in many cases the trigger can not be found, treatment typically involves a combination of approaches to manage inflammation and support heart function. For most patients supportive care is sufficient [16,17]. Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids can be used to reduce inflammation process in the heart tissue. However, the use of these medications should be carefully considered in pediatric group of patients due to potential side effects and clinicians need to balance their benefits against risks. Accepted therapy is lowering the heart's preload and afterload by administering angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB) and beta-blockers [18]. A well studied beta-blocker used for MCI treatment is carvedilol. If needed, diuretics can be added. Case studies imply a potential for mechanical circulatory support, such as ventricular assist devices or extracorporeal membrane oxygenation, as a bridge to transplantation in individuals whose status worsens despite the treatment. Therapy for arrhythmias is also beneficial in patients with acute MCI since these arrhythmias are often self-limiting and are gone after the acute phase of the illness. If a viral infection is identified as the cause of MCI, antiviral medications might be prescribed to target the underlying infection and reduce viral load [19]. The use of intravenous immune globulin and immunosuppressive agents remains disputable [20,21]. It's important to note that the treatment approach will vary for each individual, and decisions should be made in consultation with a qualified healthcare professional. Early diagnosis, appropriate management, and addressing the underlying cause play a crucial role in improving outcomes for individuals with myocarditis.

Case report: The neonate's period of fetal development did not arouse any suspicion. The pregnant woman underwent a set of standard tests and screening recommended by the Polish Gynecological Society. These tests included: blood test for TORCH infections, determination of the Rh group, test for the presence of the anti-Rh antibodies, glucose and TSH levels as well as regular ultrasound. Not one test presented alarming results. The neonate delivery was through vaginal birth at 41. week of pregnancy. The whole labour lasted 7 hours. The newborn weighted 3900 grams, length was 60 centimeters, chest circumference was 34 centimeters. The neonate was in a severe condition. Pulse was 30 beats per minute with central cyanosis and lack of muscle tone. The child scored 1 in the Apgar score and neonatologist started immediate cardiopulmonary resuscitation (CPR) in accordance to

European Resuscitation Council. CPR was started with five insufflation breaths. The given drugs were: oxygen, intravenous fluids, adrenalin and sodium bicarbonate. The neonate was intubated at the beginning of the resuscitation. During the resuscitation positive end-expiratory pressure was maintained all the time. Despite two hours of resuscitation, the heart and breathing could not be restored. The newborn was pronounced dead. Autopsy and histopathological examinations were performed. Myocardial sections preserved in paraffin were subjected to a series of stainings. Staining of histological slides included: haematoxylin and eosin, orcein and Masson's trichrome. The slides underwent a thorough evaluation by histologists later. The presence of leukocyte infiltrates with eosinophilic cells predominance was one of the findings (Fig. 1). The studies samples contained several foci of microabscesses as well (Fig. 2). Presence of atypical several nucleated cells with predominance of eosinophils and neutrophils was observed (Fig. 3)

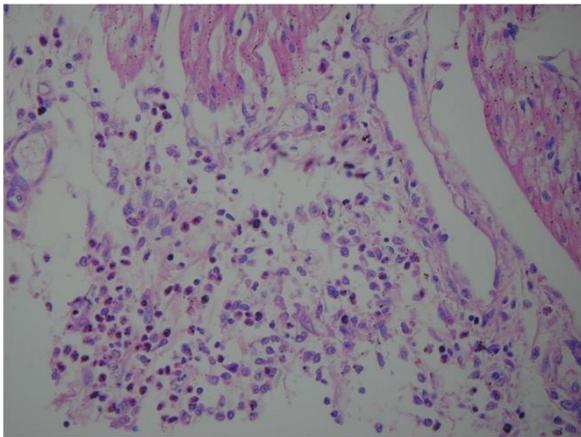


Fig. 1. Lymphocytes and eosinophils infiltrations

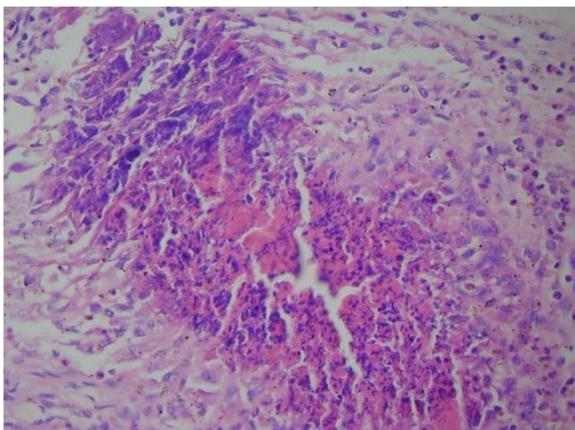


Fig. 2. Microabscess

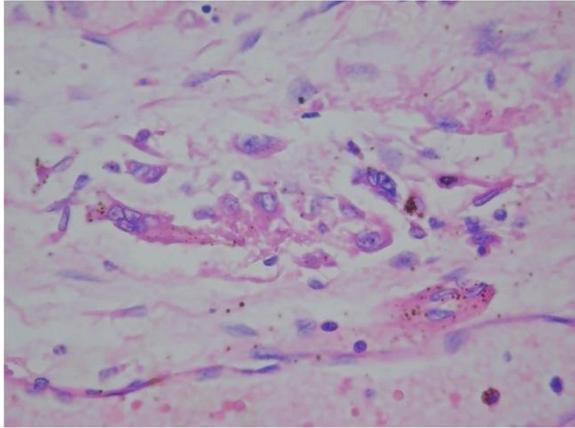


Fig. 3. Polinuclear cells

Increased vascular stasis was observed in coronary microcirculation vessels in the area of cell infiltration. The diagnosis was made: myocarditis with the dominance of the eosinophilic component. This disease entity was most likely the cause of the perinatal severe condition of the newborn. The direct or indirect cause of my inflammation could not be determined.

Discussion: MCI is a seldom occurring heart pathology. Moreover - its occurrence in newborns has been described only in some case reports. What is interesting is the fact that eosinophilic MCI is one of the rarest types of MCI at all. Even among adult patients diseases like MCI do not have to present typical symptoms. Fakadej et al. described a case report of a 70 years old woman who presented only with a febrile temperature [22]. Only after more detailed diagnostics such as magnetic resonance it was possible to diagnose MCI. To make it even more difficult - Fakadej's patient's eosinophils count was only slightly above the norm.

The most common cause of MCI in children seem to be viral infections [23]. There are some rare viruses such as Chikungunya or Zika virus described as potential MCI causing factors [24,25] but also rhinoviruses - a common pathogens in Europe can trigger MCI [26]. One should know, that even after recovery, irreversible changes in heart may be present. These changes can be arrhythmias, ventricular wall aneurysm or heart failure [27]. In a review article by Freund et al. 66% of the MCI survivors developed chronic cardiac dysfunction. After the follow-up only 23% recovered fully [27]. In our case, just before the delivery, the fetus was properly developed. Only if the MCI and circulatory failure wasn't present the newborn would be able to live and probably score 9 or 10 points on the Apgar score. The circulatory insufficiency occurred as a result of the isolated eosinophilic myocarditis. Delivery and squeezing of the neonate through the birth canal is exhausting for the child and this could have exacerbated already occurring myocardium dysfunction.

The course of eosinophilic myocarditis is divided into three phases. Eosinophils infiltration and accumulation during the acute stage cause endocardial damage through cytokines [28]. As a result, the condition progresses to the stage with enhanced thrombosis, when a layered thrombus develops as a result of the eosinophils' activation of tissue factor [29]. Common cause of eosinophilia are allergy reactions, parasite infections, hypereosinophilic syndrome, autoimmune syndromes [30]. These should be always considered when the dominance of eosinophils is present in the examined sample.

In samples studied typical eosinophils with red stained cytoplasmic granules were found. Some focal abscesses with typical Charcot-Leiden crystal comprising of Galactin-10 were also found. These structures are often found in patient's tissues who suffer from allergies, asthma and parasitizes. Histological findings can only indicate the possibility, that the neonate suffered from one of these conditions prenatally.

According to American Heart Association statement, MCI is still very deceptive disease in a pediatric group of patients. It is not only challenging to diagnose but to treat as well [31].

Conclusions: To sum up, despite the availability of advanced prenatal and perinatal diagnostics, many diseases still can cause a serious neonatal medical condition. The full-blown, often dramatic course is usually revealed because of a huge effort for the fetus, which is vaginal delivery. Various, rare diseases are still problematic to diagnose in the 21st century. The described case is a perfect illustration to this fact. The importance of regular prenatal screening should be underlined. Both scientists and clinicians are looking forward to witness what the galloping revolution in ultrasound and MRI use in practice will bring to prevent such tragic situations. As well as neonatologists and anesthesiologists should always be always on full alert during each labour, even if the pregnancy period was uncomplicated.

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- Conceptualization, supervision and project administration: Maciej Pękała, Aleksandra Berner, Katarzyna Stencel
- Methodology: Katarzyna Stencel, Maciej Pękała, Klaudia Marczyk, Anna Olszewska, Karina Stelmaszak, Aleksandra Berner, Karolina Matyja

- Software, validation, formal analysis, investigation, resources, writing original draft preparation: Anna Olszewska, Klaudia Marczyk, Karina Stelmaszak, Monika Polaszek, Marta Bogowska, Paulina Polak, Karolina Matyja
- Writing review, editing and visualization: Katarzyna Stencel, Anna Olszewska, Monika Polaszek, Marta Bogowska

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