JUVENILE XANTHOGRANULOMA IN AN ATYPICAL LOCATION IN A NEWBORN AND MATERNAL SARS-COV-2 INFECTION DURING PREGNANCY

JUVENILE XANTHOGRANULOMA O NIETYPOWEJ LOKALIZACJI U NOWORODKA, A INFEKCJA SARS-COV2 MATKI W TRAKCIE CIĄŻY

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ABSTRACT

Juvenile Xanthogranuloma (JXG) is a rare condition that belongs to the group of histiocytoses from cells other than Langerhans cells. It most commonly manifests as single or multiple skin lesions in the form of yellow-brown nodules or papules. Skin lesions typically do not require treatment and resolve spontaneously. Involvement of other areas and internal organs is rare. Skin lesions typically do not require treatment and resolve spontaneously. Systemic JXG is associated with numerous complications, increased mortality and requires intensive treatment. The pathogenesis of JXG has not been clearly explained. There is a suspicion of a connection between the development of JXG and viral infection. This paper presents the case of a child with abnormalities detected during the fetal period. The fetal pathology appeared at the time of the mother's infection with the SARS-COV2 virus. The cause of the abnormalities in the child was systemic JXG. The aim of this work is to analyze and discuss the potential correlation between the occurrence of JXG in the fetus and the maternal infection.

KEY WORDS: Juvenile Xanthogranuloma, maternal SARS-CoV-2 infection, fetal abnormalities, neonatal care

STRESZCZENIE

Juvenile Xanthogranuloma (JXG) to rzadkie zmiany wywodzące się z grupy histiocytoz z komórek innych niż Langerhansa. Najczęściej objawiają się jako pojedyncze lub mnogie zmiany skórne w postaci żółto-brązowych guzków lub grudek. Zmiany skórne zwykle nie wymagają leczenia i ustępują samoistnie. Zajęcie innych obszarów i narządów wewnętrznych jest rzadkie. Ogólnoustrojowy JXG wiąże się z licznymi powikłaniami oraz zwiększeniem śmiertelności i wymaga intensywnego leczenia. Patogeneza JXG nie została jednoznacznie wyjaśniona. Podejrzewa się związek pomiędzy powstaniem JXG, a infekcją wirusową. W pracy przedstawiono przypadek dziecka, u którego stwierdzono nieprawidłowości już w okresie płodowym. Patologie płodu pojawiły się w trakcie zakażenia matki wirusem SARS-COV2. Przyczyną wystąpienia nieprawidłowości u dziecka był ogólnoustrojowy JXG. Celem niniejszej pracy jest analiza i poddanie pod dyskusję potencjalnej korelacji pomiędzy wystąpieniem JXG u płodu a przebytą infekcją u matki.

SŁOWA KLUCZOWE: Juvenile Xanthogranuloma, infekcja SARC-CoV-2 ciężarnej, nieprawidłowości płodu, opieka neonatologiczna

INTRODUCTION

JXG is a benign condition which originate from histiocytoses of cell lines other than Langerhans cells. The disease usually presents as single or multiple skin lesions in the form of yellow-brown nodules or papules, primarily found on the face, neck, and trunk [1]. Skin lesions typically resolve spontaneously within 1–5 years and usually do not require treatment. The involvement of internal organs such as the viscera, eyes, lungs, or the central nervous system is less common, however, it can lead to numerous complications requiring intensive therapy. Particularly poor prognosis is associated with cases involving liver or central nervous system infiltration, which significantly increases mortality.

Histopathologically, JXG is characterized by the presence of Touton giant cells. However, their absence does not exclude the diagnosis. In immunohistochemical studies, the lesions show expression of CD68, anti-FXIIIa, and vimentin markers, but do not express S100 and CD1a proteins - with CD1a being a marker characteristic of Langerhans cells [2]. The pathogenesis of JXG has not yet been fully explained. It is considered a non-neoplastic process, potentially induced by nonspecific tissue damage or viral infection [3].

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CASE HISTORY

The authors present a case of a male newborn born at 36 weeks of gestation via C-section due to signs of intrauterine asphyxia. Until the 33rd week the course of pregnancy had been uncomplicated. At the beginning of the 34th week of pregnancy, the mother contracted COVID-19, and due to feeling unwell, she sought consultation with a gynaecologist. A follow-up ultrasound was performed, which revealed ascites and fetal hepatosplenomegaly. In the subsequent ultrasound performed at 36 weeks, the fetus's condition worsened – there was centralization of circulation and tachycardia. A C-section was performed. During the physical examination of the newborn, significant ascites was observed with visible vessels on the abdomen, hydrocele of both testes, and tachypnoea. The baby's respiratory condition was stabilized, and he was transferred to the neonatal intensive care unit.

The repeated abdominal ultrasound revealed significant amounts of fluid in the abdominal cavity (photo 1, photo 2) and soft tissue swelling. It was decided to perform drainage to relieve the abdominal cavity. 112 ml of clear fluid was obtained. The peritoneal fluid culture was sterile. After drainage, there was an improvement in respiratory function. The baby was administered a diuretic - furosemide.

Photo 1. 6 mm of fluid around the liver (red arrow).

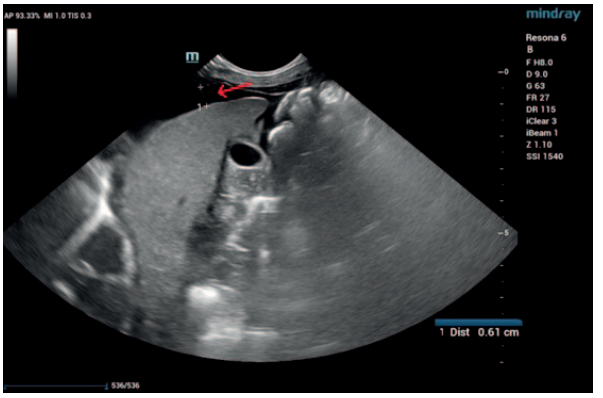
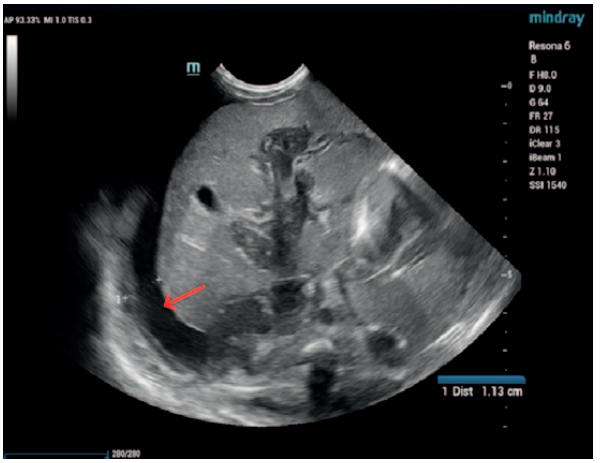


Photo 2. 11 mm of fluid around the liver (red arrow).



Subsequent ultrasound examinations showed significant narrowing of the Inferior Vena Cava (IVC) in the hepatic segment. Due to suspected IVC thrombosis, heparin was administered, until thrombosis was ruled out in laboratory and imaging tests. The newborn was also consulted with haematologist.

Despite the administration of furosemide, the fluid in the abdominal cavity continued to accumulate. Another drainage was performed and a permanent drain was left in place.

An abdominal CT with contrast revealed changes in the peritoneum and swelling with abnormalities in the region of the pancreas. The tail of the pancreas did not contract and fused with the surrounding tissues.

An exploratory laparotomy was performed. After visualizing the inside of the abdomen, it turned out that the entire peritoneum was inflamed and covered with calcified nodules. A whitish raid was observed on the intestines as well as increased cohesiveness of most organs. Behind the stomach, at the location of the pancreas, the surgical team observed a hard, non-uniform nodule. During surgery, samples were taken for histopathological tests. The results made it possible to get a final diagnosis - the immunophenotype of the lesions indicated an infiltration of histiocytic cells with a phenotype resembling JXG.

The boy was transferred to a referral centre, where he received several courses of chemotherapy.

The child is now just over 3 years old and his intellectual development remains normal. He remains under the care of a neurologist due to motor aphasia. A residual lesion remains in the abdomen, which is described by oncologists as scar tissue. The boy has a regular ultrasound examination of the abdomen. A PET examination is also repeated. So far, no recurrence of JXG has been observed.

DISCUSSION

The abnormalities in the fetus were directly preceded by a COVID-19 infection in the mother. The question was raised whether these two conditions could be related Could the COVID infection have influenced the development of JXG in the fetus?

Analysing the described disease from the histological and cytological perspective, it can be stated that histiocytoses are rare proliferative disorders in which there is excessive synthesis of histiocytes. They can be divided into Langerhans cell histiocytoses (LCH) and those that do not phenotypically match them (non-LCH).

All histiocytes originate in bone marrow from precursor cells expressing the CD34 antigen. Under the influence of cytokines, subsequent proteins, including CD14 and factor XIIIa, are expressed on the surface of the progeny cells. Cells lacking both CD14 and factor XIIIa differentiate into Langerhans cells, those with only CD14 differentiate into macrophages, and cells with both proteins differentiate into dendrocytes, which are considered the starting point for JXG. This process

is complex, but particular attention should be given to the role of cytokines GM-CSF and TNF-α, whose expression increases during a COVID-19 infection [4, 5]. Studies have shown that in COVID-19 patients, the virus leads to the development of a cytokine storm. Another effect of the pathogen is the disregulation of interferon synthesis and activity, which mobilizes immune cells, including macrophages, to fight viruses [5]. This entire process may predispose to the development of JXG.

Several cases have been described so far indicating a possible link between a COVID-19 infection and the development of non-LCH [6, 7]. A link between the CMV virus and JXG is also suspected [8, 9].

Although the development of JXG in this patient may have been spontaneous, we consider the possibility that the SARS-CoV-2 virus, after crossing the placenta, triggered an inflammatory response in the fetus and induced uncontrolled histiocyte proliferation. This is supported by the fact that, for the majority of the pregnancy, the fetus developed normally. Serious complications such as fetal ascites and hepatosplenomegaly appeared after the mother's COVID-19 infection. Although there is no conclusive evidence that the virus crossed the blood-placental barrier, this cannot be excluded. There have been documented cases confirming the possibility of SARS-CoV-2 crossing into the amniotic fluid [7, 8]. Therefore, attention should be drawn to the necessity of conducting studies that would provide information on how contact with the SARS-CoV-2 virus affects fetal development and what pathologies might potentially be expected in newborns. Such data, along with guidelines based on them, would undoubtedly positively influence the diagnostic process.

The consent was obtained from the patient's legal guardian for the use of the child's data for scientific purposes.

The authors have no conflicts of interest to declare.

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