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Case Report

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Neonatal Alloimmune Thrombocytopenia with Intracranial Porencephalic Cysts: A Case Report

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Abstract

Neonatal alloimmune thrombocytopenia (NAIT) is a rare yet significant cause of thrombocytopenia in newborns, resulting from the production of maternal antibodies against alloantigens present on fetal platelets, namely HPA-1a, and often leading to severe intracranial hemorrhage. We present a case of a newborn with NAIT who exhibited multiple intracranial cyst-like lesions on neuroimaging. MRI revealed distinctive cystic lesions, hyperintense on T2 and FLAIR imaging, hypointense on T1 imaging, and rimmed with dark internal lining on susceptibility-weighted imaging (SWI). These lesions exhibited mass effects and shifts, consistent with porencephalic cysts. The diagnosis of NAIT was confirmed through clinical presentation and serological studies, revealing maternal antibodies targeting fetal platelet alloantigens, specifically HPA-1a. We propose that fetal intracranial hemorrhage due to NAIT initiated the development of porencephalic cysts in utero. The unique presence of multiple cysts, their varying sizes, and shared neuroimaging characteristics distinguish this case. Additionally, the presence of tiny calcifications on the inner lining of the largest cystic lesion is a unique and uncommon presentation. This case underscores the significance of NAIT as a cause of fetal intracranial hemorrhage and the subsequent development of porencephalic cysts.

Keywords: *Neonatal alloimmune thrombocytopenia (NAIT), HPA-1a, porencephaly, intracranial cysts, intracranial hemorrhage, intracranial calcifications.*

Case Summary

A newborn presented at birth with a generalized petechial rash, and multiple intracranial cyst-like lesions seen on neuroimaging. These included an 80 x 60 x 50 mm right frontoparietal cyst with mass effect and midline shift, smaller cysts with similar characteristics in the left temporal and right posterior parietal regions, and a cyst within the right lateral ventricle. These lesions exhibited MR characteristics consistent with porencephalic cysts. Microbleeds were also seen. The diagnosis of neonatal alloimmune thrombocytopenia (NAIT) was confirmed through clinical presentation and serological studies, revealing maternal antibodies targeting fetal platelet alloantigens, specifically HPA-1a. It is proposed that fetal intracranial hemorrhage due to NAIT initiated the development of porencephalic cysts in utero. Additionally, the presence of tiny calcifications within the largest cystic lesion is a unique and uncommon presentation. The patient was born at term (39 weeks) and large for gestational age (5100 grams) following a cesarean delivery due to breech position. The mother received regular prenatal care.

Imaging Findings

MRI showed four distinct cyst-like lesions. The first cyst-like lesion was large (80 x 60 x 50 mm), located in the right frontoparietal region, hyperintense on T2WI and hypointense on T1WI with a dark rimmed internal lining on susceptibility-weighted imaging (SWI) (Figure 1). Coagulated blood was seen along its medial aspect (Figure 2). A small intra-cystic calcification was also noted (Figure 3). This lesion exerted a mass effect and a 5 mm midline shift to the left. A second left temporal cyst-like lesion with similar MR characteristics was noted, measuring 40 x 26 x 24 mm, and exerted mild mass effect. A third ovoid cyst-like lesion was noted at the right posterior parietal region, measuring about 25 x 17 mm. A fourth cyst-like lesion was noted within the posterior aspect of the temporal horn of the right lateral ventricle, measuring about 20 x 10 x 10 mm. Innumerable bilateral cerebral, cerebellar, and brainstem micro bleeds were also seen.

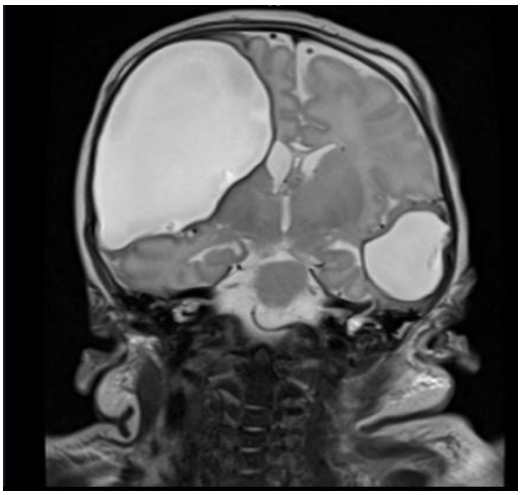
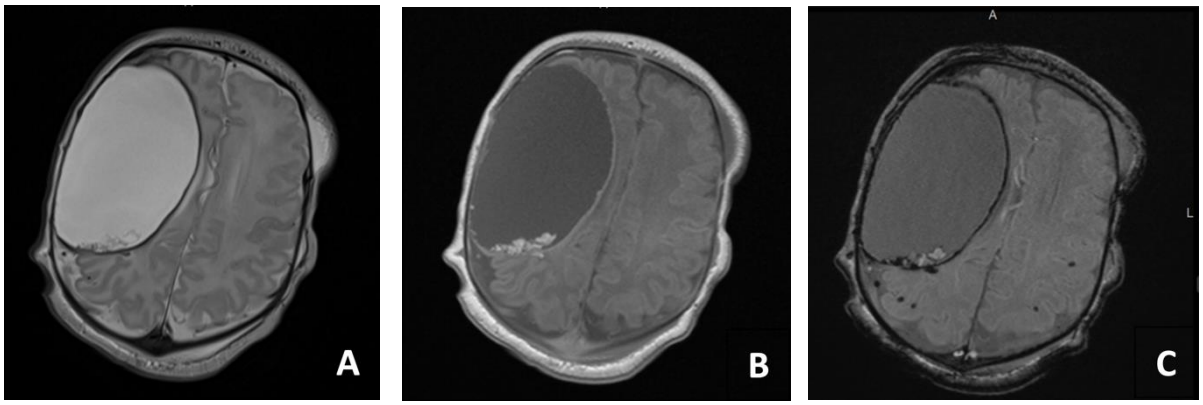


Figure 1: Coronal T2WI. Multiple porencephalic cysts are seen in the patient. Pictured are a right frontoparietal cystic lesion measuring 80 x 60 x 50 mm and a left temporal cystic lesion measuring 40 x 26 x 24 mm.



(A) Axial T2WI (B) FLAIR (C) SWI

Figure 2: Coagulated blood is seen on the medial aspect of the large right frontoparietal porencephalic cyst, suggestive of intracranial hemorrhaging. This are visualized on (A) Axial T2WI, (B) FLAIR, (C) SWI.

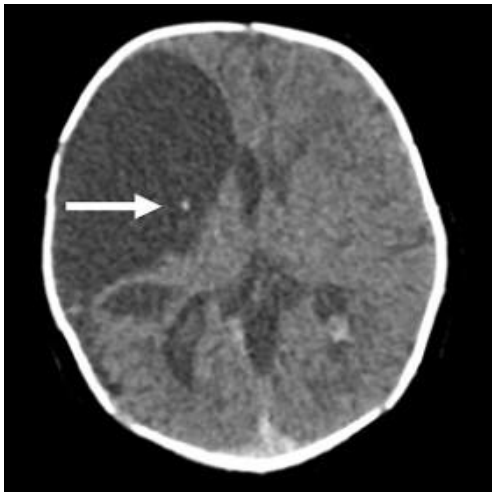


Figure 3: Axial CT. Intra-cystic calcification (arrow) seen within the largest porencephalic cyst, visualized using phase image analysis.

Diagnosis

Porencephalic cysts in a newborn with NAIT. The differential diagnosis of a well-circumscribed cystic lesion includes arachnoid cysts, neuroglial cysts, or schizencephaly.

Discussion

NAIT is an uncommon, yet important cause of thrombocytopenia in newborns [1]. NAIT results from the production of maternal antibodies against alloantigens present on fetal platelets, namely HPA-1a, which is the most common trigger. It is the most common cause of intracranial

hemorrhage in full-term infants. Intracranial hemorrhage is a feared complication that can occur in about 10 to 20% of symptomatic infants [2]. A potential consequence of severe intracranial hemorrhage in NAIT is the development of porencephalic cysts. Past case reports have described the development of porencephalic cysts due to parenchymal damage by the hemorrhage itself. These processes can begin to occur in utero [3]. As a result, infants can be born with characteristic petechial hemorrhages and purpura [2]. Porencephalic cysts can vary in size, location, and symptomatology. They present as well-demarcated cysts containing CSF. On neuroimaging, porencephalic cysts are hyperintense on T2WI. They are also hypointense on T1WI. Some patients can present with hydrocephalus depending on ventricular involvement.

The diagnosis of NAIT was confirmed from both the clinical presentation and the serological studies. Antibodies against HPA-1a platelets were detected in the maternal serum. The platelet typing studies, together with the serologic results support a diagnosis of NAIT. Thrombocytopenia associated with NAIT led to the intracranial hemorrhage seen in this patient. Platelets at birth were measured at $3x10^9$/L and normalized at $260x10^9$/L two days later.

It is postulated that this process began in utero with associated intraparenchymal damage. There have been previous reports of porencephalic cysts believed to have developed secondary to fetal intracranial hemorrhage [3,4,5]. In this patient, we see the development of more than a single porencephalic cyst (Figure 1). They vary in size and location but share similar architecture and neuroimaging characteristics. All four cystic lesions were well delineated and filled with fluid. Differentials include arachnoid cysts, which can present similarly on neuroimaging, but are less commonly associated with a diagnosis of NAIT.

A small intra-cystic calcification was noted within the largest porencephalic cyst (Figure 3). Phase image analysis as described by Berberet and colleagues in 2014 was used to confirm the presence of calcification as opposed to hemorrhage. In the filtered phase image of SWI, calcified parts show opposite signal intensity to the veins along the sulci confirming that the dark areas on the magnitude images are calcifications, not haemorrhage [6]. While not commonly reported in porencephalic cysts, calcifications can occasionally be seen in other types of intracranial cysts [7]. Internal calcifications, more specifically, are usually more commonly seen in fetal intracranial tumors [8]. Intracranial calcifications also raise suspicion for congenital toxoplasma and cytomegalovirus (CMV) infections. These were ruled out following negative polymerase chain reactions (PCR) tests. Past review papers have described the possible association between NAIT and porencephalic cysts in relation to the wide spectrum of COL4A1-related disorders [9,10]. Coagulated blood, probably due to intracranial hemorrhaging can also be seen on the internal aspect of the largest porencephalic cyst (Figure 2).

Fetal imaging plays a crucial role in managing subsequent pregnancies in the case of confirmed NAIT. This includes early and regular monitoring of fetal growth by Ultrasound imaging to detect fetal bleeding or signs of low platelet count, at an early stage. Fetal imaging results can also play a significant role in counseling expectant parents about the risks and potential outcomes of the pregnancy. This information helps parents make informed decisions about their pregnancy and the management of NAIT-related concerns. Screening for NAIT in the first pregnancy can significantly reduce the adverse outcomes related to thrombocytopenia and severe intracranial hemorrhage. A screening program involving 100,448 pregnant women identified 161 affected infants, among whom 3 (6%) experienced adverse events, compared to 10 (20%) of 51 infants born to unscreened mothers [11]. In the case of suspected NAIT in an infant, prompt treatment is imperative. This involves intravenous immunoglobulin (IVIg). Matched platelet transfusions are also indicated for severe thrombocytopenia or bleeding [12] Intracranial hemorrhage in NAIT is associated with mortality rates ranging from 15% to 30%. Survivors often contend with neurological complications such as cerebral palsy, mental retardation, cortical blindness, and seizures [13].

Result

The patient presented with NAIT at birth. Four porencephalic cysts with areas of coagulated blood and a tiny intra-cystic calcification were seen on neuroimaging. IVIG treatment resolved the underlying thrombocytopenia related to NAIT. The intra-cystic calcification is a unique presentation that was not associated to any known congenital infections but may be related to the wide spectrum of COL4A1-related disorders. The neurological sequelae related to the NAIT in conjunction with porencephaly is yet to be completely elucidated.

Conclusion

NAIT resulted in the development of four distinct porencephalic cysts visualized on neuroimaging two days after birth. Porencephalic cysts are well-circumscribed and can exert mass effect on the developing brain. This case underscores the significance of NAIT as a cause of fetal intracranial hemorrhage and its potential sequelae. Early and regular fetal imaging, screening, as well as timely interventions, such as IVIg and matched platelet transfusions, are crucial for treating NAIT-related complications and mitigating the associated neurodevelopmental risks.

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None.

References

1. Burrows RF, Caco CC, Kelton JG. Neonatal alloimmune thrombocytopenia: Spontaneous in utero intracranial hemorrhage. *Am J Haem.* 1988; 28 (2):98-102. doi 10.1002/ajh.2830280207.
2. Peterson JA, McFarland JG, Curtis BR, Aster RH. Neonatal alloimmune thrombocytopenia: pathogenesis, diagnosis and management. *Br J Haem*. 2013; 161 (1):3-14. doi 10.1111/bjh.12235.
3. Pasternak JF, Mantovani JF, Volpe JJ. Porencephaly from periventricular intracerebral hemorrhage in a premature infant. *Am J Dis Child*. 1980; 134 (7):673-5. doi 10.1001/archpedi.1980.02130190041010.
4. Harada T, Uegaki T, Arata K, Tsunetou T, Taniguchi F, Harada T. Schizencephaly and Porencephaly Due to Fetal Intracranial Hemorrhage: A Report of Two Cases. *Yonago Acta Med*. 2018; 60 (4):241-5. doi 10.24563/yam.2017.12.005
9. Huang SJ, Salsbery KT, Steiner RD. Porencephaly and Intracranial Calcifications in a Neonate. *Pediatr Rev.* 2020; 41 (10): 543-545. doi 10.1542/pir.2018-0309.
10. Meuwissen ME, Halley DJ, Smit LS, Lequin MH, Cobben JM, de Coo R, van Harssel J, Sallevelt S, Woldringh G, van der Knaap MS, de Vries LS, Mancini GM. The expanding phenotype of COL4A1 and COL4A2 mutations: clinical data on 13 newly identified families and a review of the literature. *Genet Med.* 2015; 17 (11): 843–853. doi: 10.1038/gim.2014.210.
11. Killie MK, Kjeldsen-Kragh J, Husebekk A, Skogen B, Olsen JA, Kristiansen IS. Cost-effectiveness of antenatal screening for neonatal alloimmune thrombocytopenia. *Br J Obst Gyn*. 2007; 114 (5):588-595. doi 10.1111/j.1471-0528.2007.01289.x.
12. Arnold DM, Smith JW, Kelton JG. Diagnosis and management of neonatal alloimmune thrombocytopenia. *Transfus Med Rev*. 2008; 22 (4):255-267. doi 10.1016/j.tmrv.2008.05.003.
13. Silva F, Morais S, Sevivas T, Veiga R, Salvado R, Taborda A. Severe intracranial haemorrhage in neonatal alloimmune thrombocytopenia. *BMJ Case Rep.* 2011: bcr0720114563. doi 10.1136/bcr.07.2011.4563.
5. Dale ST, Coleman LT. Neonatal Alloimmune Thrombocytopenia: Antenatal and Postnatal Imaging Findings in the Pediatric Brain. *Am J Neuroradiol*. 2002; 23 (9):1457-65.
6. Berberat J, Grobholz R, Boxheimer L, Rogers S, Remonda L, Roelcke U. Differentiation Between Calcification and Hemorrhage in Brain Tumors Using Susceptibility-Weighted Imaging: A Pilot Study. *AJR Am J Roentgenol.* 2014; 202 (4): 847-850. doi 10.2214/AJR.13.10745.
7. Pereira RG, Ribeiro BNF, Hollanda RTL, Almeida LB, Simeao TB, Marchiori E. Non-neoplastic intracranial cystic lesions: not everything is an arachnoid cyst. *Radiol Bras*. 2021; 54 (1):49-55. doi 10.1590/0100-3984.2019.0144.
8. Putbrese B, Kennedy A. Findings and differential diagnosis of fetal intracranial haemorrhage and fetal ischaemic brain injury: what is the role of fetal MRI? *Br J Radiol*. 2017; 90 (1070):20160253. doi 10.1259/bjr.20160253.