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Contribution of fetal brain MRI in management of severe fetal anemia

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ABSTRACT

Introduction: Intrauterine transfusion (IUT) has changed fetal anemia prognosis. However, long-term neurodevelopmental outcome is altered in 5% of children. Our objective was to study the contribution of fetal MRI to diagnosis brain lesions in case of fetal anemia.
Material and Methods: Retrospective monocentric descriptive study from 2005 to 2016, including all patients followed for fetal anemia requiring IUT. The indications for MRI were: hydrops fetalis and / or hemoglobin <5 g / dL and / or more than 3 IUTs and / or acute severe anemia and / or ultrasound abnormality. Fetal and neonatal outcome and pediatric neurological monitoring were studied.
Results: 89 patients were followed for fetal anemia with IUT and 28 (29.1%) had fetal MRI, 12 of which were abnormal. Two out of twelve had abnormal ultrasound. Seven out of twelve had poor neurological prognosis: 2 medical terminations of pregnancy were performed; 2 children had severe developmental delay and 3 children had schooling difficulties. Five out of twelve children had favorable neurological prognosis.
Conclusion: MRI of the fetal brain makes it possible to better detect brain lesions than ultrasound does in the management of severe fetal anemia and seems particularly appropriate in cases of acute anemia.

Introduction

Fetal anemia is a rare condition of pregnancy that is considered to be severe due its potential to result in hydrops fetalis, fetal hypoxic neurological lesions, and intrauterine fetal death [1]. Although fetal anemia has many causes, the most frequent is the alloimmunization (AI) of fetal-maternal erythrocytes, in particular anti-RH1 (700 cases/year in France), followed by infection, in particular parvovirus B19 and cytomegalovirus (CMV) infections [2]. Other less common causes include fetal-maternal hemorrhages and some fetal hemoglobinopathies. In some cases, the anemia is of undetermined etiology [2].

The prognosis of fetal anemia, whatever the etiology, has thoroughly changed since 1980, thanks to intrauterine transfusion (IUT). The effectiveness and safety of this procedure are well established [3–5]. The current survival rate of anemic fetuses requiring IUTs is approximately 90%, in cases without hydrops fetalis [3]. Among the surviving fetuses, the major complication is the occurrence of neurodevelopmental sequelae, particularly in cases of hydrops fetalis [6–9]. The LOTUS study (LOng-Term follow-up after intra-Uterine transfusionS), which prospectively included 291 children, showed a 4.8% risk of sequelae in severe anemia related to AI treated with IUT during pregnancy [9]. The main prenatal risk factors were anemia with hemoglobin < 5 g/dL, hydrops fetalis, and more than three IUTs. Simonazzi et al showed too in a case report study that a severely anemic fetus (haemoglobin mean 2,1 g/dL) may be at increased risk of brain damage, in particular hemorrhage and/or hypoplasia of cerebellum [10].

At present, the follow-up of fetuses with severe fetal anemia requiring IUT is based on ultrasound, which is performed to detect signs of recurrent anemia as well as ischemic or hemorrhagic brain damage. Ultrasound allows for good detection of these abnormalities, however, the relationship between the visualized abnormalities and the child's outcome is not always correlated [11,12] with normal neurological development. In other pathologies, such as twin-twin transfusion syndrome (TTTS), fetal brain MRI is proposed to refine both the diagnosis and the prognosis of brain lesions [12–14] and therefore may be relevant if one of the unfavorable characteristics of neurological development described

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by the LOTUS study is found during a prenatal follow-up of fetal anemia. In 2017, the magnetic resonance imaging to enhance the diagnosis of fetal developmental brain abnormalities in utero (MERIDIAN) study found that adding MRI at ultrasound with brain abnormalities to the diagnostic pathway increased the diagnostic accuracy [15], even if the diagnostic capacities of ultrasound were probably underestimated in this study.

The aim of this study was to investigate the contribution of fetal brain MRI to the diagnosis of cerebral abnormalities in cases of fetal anemia requiring IUT.

Material and methods

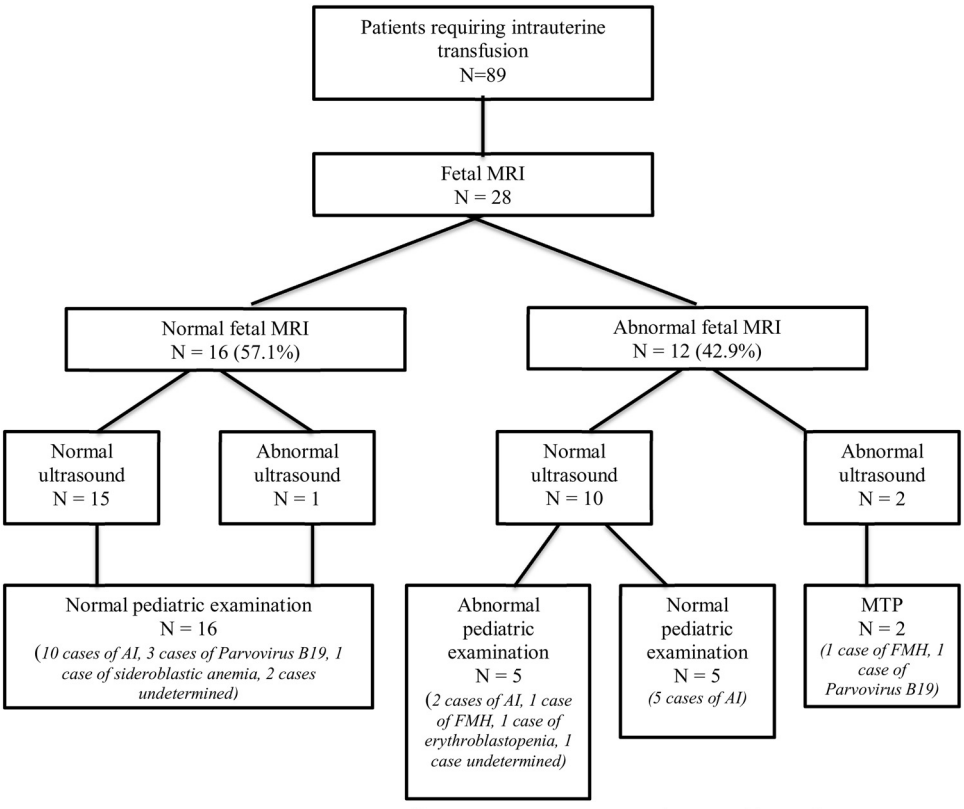
This monocentric, descriptive, retrospective study included all patients followed or referred to our center (Jeanne de Flandre Hospital, Lille, France) for fetal anemia, considering all etiologies that underwent at least one IUT and fetal brain MRI between 2005–2016. Ethics approval was granted by the French Ethics Committee of Research in Gynecology and Obstetrics (CEROG OBS 2012-02-04).

Severe fetal anemia was suspected when the peak systolic velocity at the middle cerebral artery (PSV-MCA) was over 1.50–1.55 MoM and indicated the achievement of the first IUT [16–18]. The IUTs were performed according to the technique we described previously [5,19]. The severity of the anemias was assessed based on the initial hemoglobin levels and the thresholds defined by Mari et al. [16]. The IUTs were performed up to the 34th week of gestation. Beyond this term, fetal extraction was discussed during a perinatology staff meeting [20].

Since 2012, indications for fetal brain MRI have comprised the following: the presence of hydrops fetalis during the diagnosis of fetal anemia and/or observing severe anemia < 5 g/dL during IUT and/or acute severe anemia and/or ultrasound abnormality and/or more than three IUTs being performed. These criteria were defined during a multidisciplinary staff meeting and were confirmed following the publication of the LOTUS study [9]. Before 2012, fetal brain MRI was performed as advised by the Multidisciplinary Center of Prenatal Diagnosis, based on the patient's clinical history and ultrasound findings. It was ideally performed between 30 and 32 weeks of gestation (WG) and within a minimum of 3 weeks after the first IUT. It could be carried out more quickly in an emergency situation (e.g., induced preterm birth) or later, if the discovery of anemia occurred after 30–32 WG. If the first MRI showed abnormalities, a second MRI could be performed in order to clarify the evolution of lesions and, in particular, to determine if ischemic infarction was present in cases of hemorrhagic lesions that were initially observed and to assess cerebral biometry. The MRI was conducted with PHILIPS Achieva® 1.5 T and PHILIPS Achieva® 3 T (beginning in December 2011). The protocol consisted of making 3-plane (axial, coronal, and sagittal) sections at the cerebral level in T2-weighted sequences in single-shot fast-spin echo (SSFSE) imaging, in gradient-echo T1-weighted sequences, and in gradient-echo T2*-weighted sequences and single shot.

In the week before MRI was performed, ultrasound examinations were conducted by a maternal fetal medicine sonographer via the use of a Voluson® E8 or E10 ultrasound system from GE Healthcare France. In cases of cephalic presentation, vaginal ultrasound imaging helped to refine the examination of the cerebral parenchyma.

For each case, we collected the obstetric history, the characteristics of the patient, the etiology of fetal anemia (allo immunization, Parvovirus B19 discovered secondary to hydrops or clinical



MRI = magnetic resonance imaging, AI = alloimmunization, FMH = Fetal-maternal hemorrhage, MTP = Medical termination of pregnancy

Fig. 1. Flow chart.
MRI = magnetic resonance imaging, AI = alloimmunization, FMH = Fetal-maternal hemorrhage, MTP = Medical termination of pregnancy.