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Confirmation of etiology in fetal hydrops by sonographic evaluation of fluid allocation patterns

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ABSTRACT

Objective: To evaluate patterns of fluid allocations in different etiologies of hydrops fetalis.
Study design: This report is a retrospective cohort study on 20,395 fetal sonographic evaluations in a single tertiary center from 2000 to 2014. Special emphasis was placed on the exact description of the distinct fluid allocation sites in each fetus. Postmortem/postnatal records were evaluated additionally. Mean follow up of the surviving neonates was 34 days (10–60 days).
Results: There seem to be distinctive patterns of fluid allocation in some etiologies leading to fetal hydrops including aneuploidies and Parvovirus B19 related infections.
Conclusion: Due to the allocation patterns of fluid filled sites in fetuses with hydrops fetalis the spectrum of possible etiologies may be narrowed already during initial ultrasound scan. It can contribute substantially to diagnostic accuracy as well as to parental counseling. This knowledge may also help to omit delay in diagnostic routines.

Introduction

Hydrops fetalis (Latin = edema of the fetus) is defined as at least two morbidly increased fluid accumulations in the serous fetal compartments (1) subcutaneous space, (2) pericardial space, (3) pleural space and (4) abdominal cavity [1,2]. An edematous placenta (exceeding a thickness of a minimum of 50 mm), polyhydramnious and reduced fetal movements are often a concomitant feature in fetal hydrops but are not a required attribute in the definition [3].

The incidence of fetal hydrops is 1.34–3/1000 live births [4,5].

There are about 150 different underlying causes known today potentially leading to this fetal alteration [6]. The etiology of this condition is of no importance to the definition as the term "fetal hydrops" is only a description of a symptom. To achieve a reliable diagnosis in fetal hydrops many and often invasive procedures are necessary.

As hydrops fetalis is an end-stage finding it represents a poor prognostic factor for any fetal pathology: perinatal mortality is still high and is reported to be 48–67% [5–7], whereas mortality in prenatally detected hydrops is generally even higher with 58–90% due to higher percentage of aneuploidy, intrauterine fetal death and the option of termination of pregnancy [8,9].

The present report focuses on the possible patterns of distribution of fluid in fetal hydrops in relation to the etiology and as well on the outcome of affected fetuses.

The question was if the presentation of hydrops fetalis is specific for different etiologies and if it is possible to diagnose the specific etiology by the sonographic evaluation of the distinct pattern of fluid accumulation in fetal hydrops?

Materials and methods

A retrospective cohort study including all prenatally detected cases of hydrops fetalis from January 2000 until December 2014 was conducted at a single tertiary referral center for prenatal medicine. We included all vital singleton pregnancies who had at least one fetal sonographic evaluation conducted by a physician with special expertise in fetal ultrasound at our center and where outcome was available. For this purpose 20,395 pregnancies were reviewed. Where applicable obstetrical, neonatal and pathological records were included in the analysis. Mean follow-up of live-borns was 34 days (10–60 days).

All sonographic examinations were performed by using the following high-end ultrasound machines only: ATL HDI 5000 (until 2004) and IU 22 (Philips), Voluson 730 Expert Pro and Voluson E8

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(GE Healthcare) equipped with 5 MHz, 7.5 MHz or 9 MHz sector or curved array probes.

Hydrops fetalis was defined as at least two excessive fluid accumulations in serous cavities as described above.

Diagnosis of underlying etiology was confirmed in all cases with aneuploidy by either prenatal chorionic villus sampling or amniocenteses or postnatal/postmortem evaluation, in all cases with congenital heart defect by postnatal echocardiogram or postmortem evaluation respectively, in all cases with skeletal dysplasias via postnatal or postmortem genetic evaluation, in all cases with maternal Parvovirus B19 infection via diagnosis of maternal seroconversion during pregnancy, in all cases with immunological fetal hydrops via diagnosis of maternal antibody boost during pregnancy and history of alloimmunization. Other origins were also confirmed in all cases if none of the above etiologies could be verified and postnatal or postmortem evaluation confirmed prenatal diagnosis individually. Fetal hydrops was defined as idiopathic if no anatomic alteration could be detected, neither prenatally nor postnatlly, and if no maternal antibodies were present and fetal peak systolic velocity measured in the middle cerebral artery was below 1.5 MoM, if maternal infection screening (including Cytomegalovirus, Toxoplasmosis, Syphilis, Herpes Simplex type 1, Rubella, Parvovirus B19, Adenovirus, Hepatitis A, B, C, Human-immune-deficiency-Virus) remained negative and if fetal karyotype was euploid.

Fetal hydrops first described in missed abortions or intrauterine fetal death was excluded from final analysis as this condition could have evolved postmortem.

Correlation between each subgroup was analyzed via IBM SPSS Statistics 22 using Pearson's correlation coefficient. Significant positive correlation was defined with $p < 0.05$.

Results

In 220/20,395 (1.08%) pregnancies fetal hydrops was detected prenatally. Outcome was available for 220/220 pregnancies. There was neither a false positive nor false negative diagnosis during the study period. Etiology of the fetal hydrops could be ascertained in 166/220 (74.5%) of all cases and comprised aneuploidies (85/220 (38.6%)), congenital heart defects (32/220 (14.5%)), skeletal dysplasias (13/220 (5.9%)), Parvovirus B19 (9/220 (4.1%)), immunologic hydrops fetalis (2/220 (0.9%)), idiopathic conduct (54/220 (24.5%)) and other reasons for hydrops fetalis including mucopolysaccharidosis, meconiumperitonitis, chylothorax/-pericardium, urinary tract obstruction Akinesia-Syndrome (25/220 (11.4%)). For complete spectrum please see Table 4.

Fetal karyotype was available in 133/220 of the cases (60.5%) with an aneuploidy rate of 85/133 (63.9%).

Cystic hygroma as a distinct subgroup of skin edema was analyzed separately.

There were no significant differences in terms of maternal age (mean 31.3 years ranging from 18.2 to 43.4 years), maternal medical history, medication, smoking habits, alcohol intake during pregnancy and parity between the specific groups of etiology.

Mirror syndrome (also known as Ballantyne's syndrome) defined as maternal edema in pregnancies aggravated by hydrops fetalis was present in 15 cases (6 in idiopathic, 4 in PV B19 infection, 5 in cases with other etiology). In ten of those pregnancies missed abortion/IUFT occurred.

Overall survival rate in this survey was 42/220 (19.1%).

Detailed analysis of the distribution of fluid collections in each subgroup, outcome of the fetuses with prenatally detected hydrops fetalis, time of diagnosis and spectrum of other conditions leading to fetal hydrops in this study see Tables 1–4.

Pearson's correlation coefficient showed significant positive correlation between the subgroups CHD and skeletal dysplasias ($r = 0.921$; $p = 0.027$), CHD and idiopathic fetal hydrops ($r = 0.961$; $p = 0.009$), skeletal dysplasias and immunological hydrops fetalis ($r = 0.975$; $p = 0.005$), and idiopathic fetal hydrops and other etiologies ($r = 0.916$; $p = 0.029$). Consequently CHD and immunological hydrops fetalis showed also good positive correlation but did not reach significant values ($r = 0.829$; $p = 0.083$) (Table 5).

Comment

The majority of our cases with substantiated state of etiology (164/166 (98.8%)) had a non-immunologic background of hydrops fetalis (NIHF). After the advent of rhesus prophylaxis in the rhesus-negative gravida this percentage is in concordance with recent data regarding this topic [3,10].

Mean time of detection during sonographic fetal interrogation is the second trimester anomaly scan (102/220 (46.4%)) where nearly half of the fetuses with hydrops fetalis were detected. The reason behind this phenomenon may be seen in the fact, that some

Table 1
Distribution of fluid collection in prenatally detected hydrops fetalis.

Etiology ($n = 220$)	Ascites	Pleural effusions	Pericardial effusions	Skin edema	Cystic hygroma
Aneuploidy ($n = 85$)	34 (40.0%)	30 (35.3)%	8 (9.4%)	59 (69.4%)	44 (51.8%)
CHD ($n = 32$)	22 (68.8%)	10 (31.3%)	4 (12.5%)	25 (78.1%)	4 (12.5%)
Skeletal dysplasias ($n = 13$)	9 (69.2%)	2 (15.4%)	4 (30.8%)	10 (76.9%)	2 (15.4%)
PV B19 ($n = 9$)	6 (66.7%)	4 (44.5%)	6 (66.7%)	5 (55.6%)	1 (11.2%)
Idiopathic ($n = 54$)	35 (64.8%)	26 (48.1%)	5 (9.3%)	44 (81.5%)	4 (7.4%)
IHF ($n = 2$)	2	0	1	2	0
Other ($n = 25$)	14 (56.0%)	16 (64.0%)	9 (36.0%)	17 (68.0%)	6 (24.0%)

CHD, congenital heart defect; IHF, immunologic hydrops fetalis; PV B19, Parvovirus B19.

Table 2
Outcome of fetuses with prenatally detected hydrops fetalis.

Etiology ($n = 220$)	Termination of pregnancy	IUFT	Miscarriage	Neonatal death	Survival
Aneuploidy ($n = 85$)	65	8	3	3	6
CHD ($n = 32$)	24	5	0	2	1
Skeletal dysplasias ($n = 13$)	12	0	0	1	0
PV B19 ($n = 9$)	0	4	1	3	1
Idiopathic ($n = 54$)	20	6	3	1	24 (14 completely healthy)
IHF ($n = 2$)	0	0	0	0	2
Other ($n = 25$)	15	1		1	8

CHD, congenital heart defect; IHF, immunologic hydrops fetalis; PV B19, Parvovirus B19.