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Clinical outcomes in chronic intervillositis of unknown etiology

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ABSTRACT

Introduction: Chronic intervillositis of unknown etiology (CIUE) is a histopathological lesion of the placenta that is frequently accompanied by unfavourable pregnancy outcomes, e.g. miscarriage, fetal growth restriction (FGR) and intrauterine fetal death. Earlier described case series and cohorts have been based on diverse diagnostic criteria of CIUE. To improve our understanding of clinical outcomes associated with CIUE, we report the obstetric and perinatal outcomes in a cohort based on the recently described diagnostic criteria.

Methods: CIUE is defined as an infiltrate occupying 5% or more of the intervillous space with approximately 80% of mononuclear cells positive for CD68 in the absence of an infection. Thirty-eight cases were included. Also previous and subsequent pregnancies were described.

Results: Pregnancies accompanied by CIUE frequently resulted in FGR (51.6%) and pre-term birth (55.3%). Twenty-nine out of 38 pregnancies (76.3%) with CIUE resulted in a living baby. Women with CIUE frequently have had a miscarriage (16/38; 42%). Four-teen subsequent pregnancies in 8 women resulted in 2 miscarriages, 2 terminations of pregnancy for FGR, 1 early neonatal death and 9 living babies (9/14; 64.3%). Histopathologically confirmed CIUE recurred in 5 out of 10 subsequent pregnancies. Two pregnancies with recurrent CIUE were terminated, one pregnancy ended in a late miscarriage and another resulted in term birth complicated by FGR. Recurrent CIUE can also be accompanied by an uncomplicated pregnancy (1/5; 20%).

Conclusion: This study provides additional insight into the clinical phenotype of CIUE and emphasises the need for further research to understand the pathophysiology behind different pregnancy outcomes in CIUE.

1. Introduction

Chronic intervillositis of unknown etiology (CIUE) is a rare, poorly understood histopathological lesion which was first described by Labarrere and Mullen in 1987 as massive chronic intervillositis [1]. An intervillous infiltrate may occur in every trimester [2] and it is estimated that the lesion is found in approximately 1:10000 placentas [3]. A variety of terms have been used to describe CIUE, including chronic intervillositis, chronic histiocytic intervillositis of unknown etiology, chronic histiocytic intervillositis, massive histiocytic chronic intervillositis, massive perivillous histiocytosis, intervillitis and massive chronic intervillositis [4]. Although different criteria have been used to define CIUE [5], it has repeatedly been shown that an intervillous infiltrate of histiocytes is associated with adverse pregnancy outcome [5–7]. Miscarriages, fetal growth restriction (FGR) and intrauterine fetal death (IUFD) are frequently associated with CIUE [5]. Furthermore, a high recurrence rate of the intervillous infiltrate and associated adverse pregnancy outcomes, emphasises the clinical importance of CIUE [5, 7–9].

Previous studies of CIUE relied on diverse selection criteria and do not extensively report on pregnancy outcomes [5]. In this study CIUE was defined as an infiltrate occupying 5% or more of the intervillous space of approximately 80% of mononuclear cells positive for CD68 in the absence of clinical or histopathological signs of an infection [5]. Our objective was to report the obstetric and perinatal outcomes in a cohort of pregnancies affected by CIUE.

Abbreviations: CIUE, Chronic Intervillositis of Unknown Etiology; FGR, Fetal Growth Restriction; IUFD, Intra Uterine Fetal Death; TOP, Termination Of Pregnancy.

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2. Methods

2.1. Patient selection

In this retrospective descriptive study, patient samples were selected from the pathology department of the University Medical Center Utrecht (UMCU) between 2000 and 2015 using the hospitals' pathology registry. In this time period, there were approximately 33200 (1700-2300/year) clinical deliveries at the UMCU and approximately 13300 (600-1150/year) placentas were studied at the pathology department. Placentas were sent to the pathology department when the pregnancy was complicated by pre-term birth, fetal growth restriction, pre-eclampsia, pregnancy induced hypertension, gestational diabetes, pre-term premature rupture of membranes, asphyxia of the new born or intra uterine fetal demise (IUFD). Placentas were also studied from twin pregnancies, fetuses with (suspected) congenital defects and when the pregnancy was terminated. Between 2006 and 2007, placentas from uneventful pregnancies were also examined as part of a separate study by Houben et al. [10]. All placental samples in the UMCU were assessed according to a standardized protocol. From each placenta, samples were taken from the umbilical cord, fetal membranes and 3 full-thickness samples of normal-appearing placenta parenchyma. Samples reported as showing 'chronic intervillositis' were selected. Cases were reviewed by an experienced pathologist and the diagnosis for CIUE was based on our previously described criteria [5].

We defined CIUE as the presence of an infiltrate occupying 5% or more of the intervillous space with approximately 80% of mononuclear cells positive for CD68 [5]. Furthermore, clinical or histopathological signs of infection should be absent [5]. Patient characteristics and pregnancy outcomes were obtained from the medical records. This study was approved by the UMCU biobank committee (TC-BIO number: 16-434). The pregnancy in which the diagnosis CIUE was made for the first time, was defined as the index pregnancy.

2.2. Clinical definitions

Miscarriage was defined as a spontaneous fetal loss within the first 24 weeks of pregnancy [11,12]. Early and late miscarriages were defined as a miscarriage $\leq$10 weeks and 10–24 weeks of gestation, respectively [11,13]. Recurrent miscarriage was defined as two or more pregnancy losses, either consecutive or not, before 24 weeks of gestation [11]. Termination of pregnancy (TOP) was an induced pregnancy loss within 24 weeks of gestation for medical reasons, for example fetal congenital anomalies, severe fetal growth restriction (FGR) or severe early-onset pre-eclampsia [14]. Abortion was defined as an induced pregnancy loss within 24 weeks of gestation for psychosocial reasons [15]. IUFD was defined as spontaneous fetal loss after 24 weeks of gestation. Early neonatal death refers to death during birth and within the first 7 days after birth. Term pregnancy was defined as birth from 37 weeks of pregnancy onwards, and preterm birth was defined as birth between 24 and 37 weeks of gestation. Fetal growth restriction (FGR) was defined as a birthweight below the 3rd percentile [16,17]. The overall fetal outcome was depicted by the number of pregnancies resulting in a living baby 7 days post-partum.

2.3. Statistical analysis

Where applicable, in the case of sufficient events, statistical analysis was performed to test significance between previous pregnancies, index pregnancies and subsequent pregnancies. For categorical outcomes within patients, repeated measures ordinal logistic regression was performed to test significance. For repeated continuous outcomes, a linear mixed model was used to test significance. $P \leq 0.05$ was considered statistically significant. Analyses were performed using the SPSS statistics software (version 23.0, Armonk, NY: IBM Corp).

3. Results

3.1. Selection of cases

Forty-five placentas with an intervillous infiltrate were identified from the UMCU pathology archives between 2000 and 2015. Three cases were excluded due to intercurrent infection, including parvo virus and rubella. Four twin pregnancies were excluded. Thirty-eight cases fulfilled the diagnostic criteria for CIUE [5].

3.2. Previous pregnancies

Maternal characteristics and pregnancy outcome are depicted in Table 1. Most women with CIUE in the index pregnancy were multigravida (28/38; 26.3%). The 28 women who had a previous pregnancy, had 78 pregnancies between them. Out of these 78 pregnancies there were 10 pre-term deliveries, 1 IUFD and 27 miscarriages. Twenty-seven spontaneous miscarriages were observed in 16 women (16/38; 42.1%) and 6 out of 27 miscarriages were late miscarriages (6/27; 22.2%). Furthermore, 7 out of 38 women have experienced recurrent miscarriages (7/38; 18.4%; 2 to 4 miscarriages per women). Twelve babies were FGR (12/43; 27.9%). Two early neonatal deaths in the same women were observed. Forty-one out of 78 pregnancies resulted in a living baby (41/78; 52.6%) and 14 women had at least one uneventful pregnancy before the index pregnancy (14/38; 36.8%). The placenta was available for re-assessment in 6 out of 78 (7.7%) previous pregnancies and CIUE was found in 2 placentas (2/6; 33.3%).

3.3. Index pregnancy

Out of 38 index pregnancies, 13 pregnancies resulted in term birth (13/38; 34.2%, Table 1, Fig. 1 A and 1 B), 21 fetuses were born pre-term (21/38; 55.3%, Fig. 1 C) and 4 pregnancies resulted in a fetal loss before 24 weeks of gestation (4/38; 10.5%, Fig. 1 D). Thirteen out of 38 pregnancies were complicated by hypertensive complications (34.2%, PIH or pre-eclampsia). Sixteen neonates were FGR (16/31; 51.6%). Five FGR neonates were born term and 11 FGR neonates were born pre-term. There were 2 early neonatal deaths: One baby died during induction of labour for severe pre-eclampsia at 25 + 6 weeks, weighing 580 g. The other baby died 5 days post-partum, following an emergency caesarean section for fetal distress at 32 + 2 weeks, weighing 1240 g. The 38 index pregnancies resulted in 29 living babies 7 days post-partum (76.3%).

3.4. Subsequent pregnancies

Follow-up information was available for 15 out of 38 women (39.5%). Seven of these 15 women did not have a further pregnancy after the index pregnancy. Eight women with previous CIUE had 14 subsequent pregnancies, which resulted in 2 miscarriages, 2 TOPs and 10 live births, but 9 living babies at 7 days post-partum (9/14; 64.3%). This early neonatal death was due to a congenital cardiomyopathy. This woman had experienced 2 earlier neonatal deaths due to a congenital cardiomyopathy as well. Seven out of 8 (87.5%) women who wished to get pregnant after the index pregnancy eventually had a pregnancy resulting in a living baby. None of the 9 successful pregnancies received prophylaxis against recurrent CIUE.

The placenta was analysed in 10 out of 14 subsequent pregnancies (71.4%) and recurrent CIUE was present in 5 placentas (5/10; 50%). Pregnancies accompanied by recurrent CIUE were observed in 3 women. The first woman had CIUE in 4 consecutive pregnancies with fetal losses. IUFD was diagnosed in combination with growth restriction in the index pregnancy at 22 + 1 weeks. Her second pregnancy was terminated for FGR at 21 + 5 weeks. During the third pregnancy, she was treated with aspirin and prednisone from 6 weeks of pregnancy. This pregnancy was terminated at 17 + 5 weeks for FGR. In her fourth pregnancy, the patient was treated with aspirin and low molecular weight heparin from 6

Table 1

	Previous	Index	Subsequent	
Maternal characteristics				
Maternal age, mean (SD) [Range]		34 (4.5) [24â€“43]		
Gravidity, median [Range]		3 [1â€“8]		
Primi-gravida, n (%)		10 (26.3)		
Parity, median [Range]		1 [0â€“5]		
Nulli-parous, n (%)		16 (42.1)		
Pregnancy characteristics				**Significance**
Number of pregnancies	78	38	14	
Term, n (%)	34 (43.6)	13 (34.2)	8 (57.1)	0.473
Gestational age [weeksÂ +Â days], mean (SD [days]) [range [weeksÂ +Â days]]	40Â +Â 2 (10) [37Â +Â 5 - 42Â +Â 0]	38Â +Â 5 (9) [37Â +Â 0 - 41Â +Â 2]	39Â +Â 6 (11) [37Â +Â 2 - 42Â +Â 1]	0.505
IUFD, n (%)	0	2 (15.4)	0	NA
Pre-term, n (%)	10 (12.8)	21 (55.3)	2 (14.3)	0.473
Gestational age [weeksÂ +Â days], mean (SD [days]) [range [weeksÂ +Â days]]	34Â +Â 1 (23) [27Â +Â 1 - 36Â +Â 6]	31Â +Â 5 (24) [25Â +Â 3 - 36Â +Â 6]	34Â +Â 2 (6) [33Â +Â 4 - 34Â +Â 6]	0.505
IUFD, n (%)	1 (10.0)	1 (4.8)	0	NA
Gestational age <24wkn, n (%)	34 (43.6)	4 (10.5)	4 (28.6)	0.473
Gestational age [weeksÂ +Â days], mean (SD [days]) [range [weeksÂ +Â days]]	13Â +Â 0 (39) [6Â +Â 0 - 22Â +Â 0]	22Â +Â 5 (8) [21Â +Â 2 - 23Â +Â 6]	15Â +Â 6 (37) [9Â +Â 0 - 21Â +Â 5]	0.505
Miscarriage, n (%)	27 (79.4)	1 (25.0)	2 (50.0)	0.219
Late miscarriage, n (%)	6 (22.2)	1 (100.0)	1 (50.0)	NA
Abortion, n (%)	3 (8.8)	0	0	NA
TOP, n (%)	3 (8.8)	3 (75.0)	2 (50.0)	0.011
TOP for congenital problem, n (%)	2 (66.7)	1 (33.3)	0	NA
TOP for FGR, n (%)	1 (33.3)	2 (66.7)	2 (100)	NA
Hypertensive complications of pregnancy, n (%)	5 (6.4)	13 (34.2)	1 (7.1)	<0.001
Pregnancy induced hypertension, n (%)	1 (20)	5 (38.5)	1 (100)	NA
Pre-eclampsia, n (%)	4 (80)	8 (61.5)	0	NA
Fetal characteristics				
Number of live born fetuses	43 (55.1)	31 (81.6)	10 (71.4)	0.05
Male, n (%)	23 (56.1)	15 (48.4)	3 (30.0)	0.786
FGR, n (%)	12 (27.9)	16 (51.6)	3 (30.0)	0.058
Early neonatal death, n (%)	2 (4.7)	2 (6.5)	1 (10.0)	0.198
Overall fetal outcome				
Living baby 7 days after birth, n (%)	41 (52.6)	29 (76.3)	9 (64.3)	0.084

Table to show pregnancy outcomes for women with CIUE in the index pregnancy according to pregnancy order; previous pregnancy, index pregnancy or subsequent pregnancy.
TOP, hypertensive complications of pregnancy and number of live born fetuses was associated with pregnancy order. NA; not applicable.

weeks of pregnancy. At 14 + 6 weeks, this pregnancy ended in a spontaneous miscarriage. The second woman had an index pregnancy which resulted in a FGR baby (2250 g) born at 38 weeks. She has also had 3 miscarriages and one abortion. Her last pregnancy resulted in a healthy girl born at 37 + 4 weeks weighting 3255 g. This last pregnancy was associated with CIUE and not treated. A third woman had 4 pregnancies in total of which 2 were accompanied by CIUE. Her first pregnancy was terminated for a psychosocial indication. Her second pregnancy was affected by CIUE and resulted in IUFD at 27 + 3 weeks with a baby weighting 450 g. The third pregnancy was associated with CIUE and resulted in a FGR girl (2130 g) at 37 + 2 weeks, without treatment. Last, this women had a pregnancy without histopathological confirmation of CIUE, which resulted in a preterm FGR baby (34 + 6 weeks, 1468 g). This pregnancy was not treated as well. None of the pregnancies in these three women were accompanied by hypertensive pregnancy complications.

TOP, hypertensive complications of pregnancy and number of live born fetuses was associated with whether a pregnancy was a previous pregnancy, index pregnancy or subsequent pregnancy (Table 1).

4. Discussion

The aim of this study was to investigate the clinical outcomes from pregnancies affected by CIUE. We identified 38 cases which fulfilled the diagnostic criteria for CIUE [5], also 78 previous pregnancies and 14 subsequent pregnancies were identified. Pregnancies affected by CIUE frequently resulted in FGR, pre-term birth and previous miscarriages are often observed in these women. Early neonatal survival was 76.3%. Recurrent CIUE was accompanied by FGR, miscarriage or the pregnancy was terminated due to severe FGR. However, a pregnancy with recurrent CIUE can also be without complications (1/5; 20%).

Other publications also mentioned FGR in pregnancies affected with CIUE [5], and in one study severity of the infiltrate was reported to associate with severity of FGR [6]. FGR is tightly linked to chronic placental dysfunction and the intervillous infiltrate might contribute to a diminished exchange capacity in these placentas. Furthermore, CIUE is frequently associated with villitis of unknown etiology, massive perivillous fibrin depositions and trophoblast necrosis [5], which may also contribute to a diminished placenta function. Compared to other studies on CIUE, early neonatal survival seems higher in our study (76.3%) [6,8]. Women with a pregnancy affected by CIUE had frequently had a previous miscarriage (16/38; 42.1%). Compared to women without CIUE in history, the frequency of miscarriage and recurrent miscarriages in our cohort of women with CIUE was 3 and 6 times higher, respectively [18–20].

The pathophysiology of CIUE appears to be immunologically driven and several treatment strategies which suppress the immune system have been proposed for CIUE. Treatment with corticosteroids, hydroxychloroquine, intravenous immunoglobulin, aspirin and heparin have had variable efficacy to prevent recurrent CIUE [6,7,9,21,22]. In our

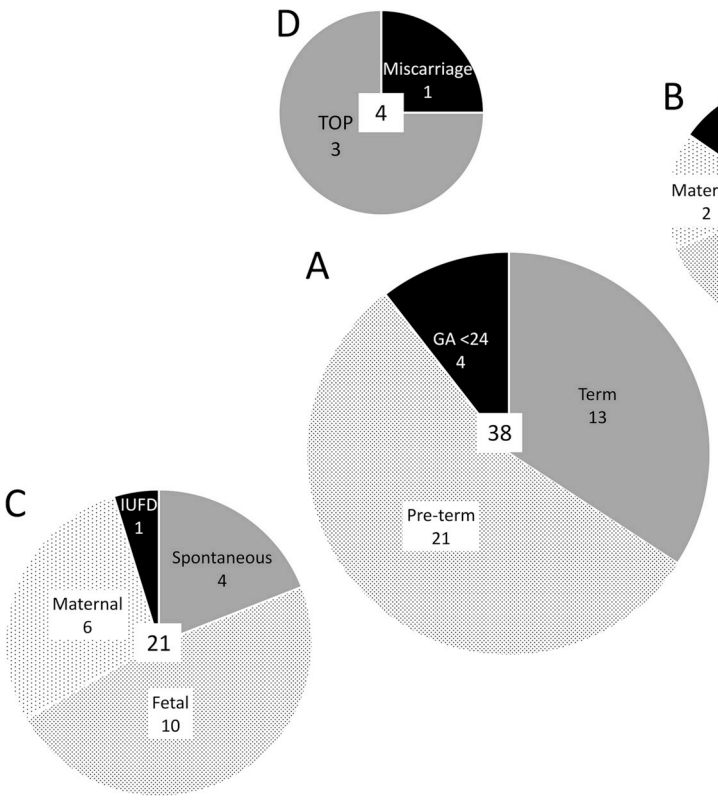

Fig. 1. Pregnancy characteristics index pregnanciesA Twenty-one fetuses were born pre-term and 4 pregnancies ended before 24 weeks of gestation. **B** Four out of 6 iatrogenic births at term were for a fetal indication (66.7%; fetal distress, FGR or macrosomia associated with gestational diabetes). Maternal indications were pre-eclampsia and a caesarean section in the medical history.**C** In 10 out of 16 pre-term births induction of labour was for a fetal indication (10/16; 62.5%; fetal distress or FGR). Maternal indications were hypertensive complications of pregnancy, abruption of the placenta or a prolonged delivery. **D** Four pregnancies resulted in a fetal loss. One pregnancy ended in a late miscarriage, 2 pregnancies were terminated for severe FGR (associated with PIH) and 1 pregnancy was terminated for congenital defects.

study, one patient was treated specifically for CIUE without an effect. Ten out of 14 (71.4%) subsequent pregnancies resulted in a living baby without treatment, although 3 out of 10 had FGR and 1 baby died within 7 days of birth. In 10 subsequent pregnancies the placenta was analysed, 5 had recurrent CIUE. Two pregnancies with recurrent CIUE were terminated for FGR, 1 pregnancy ended in a late miscarriage (14 + 3 weeks) and another resulted in term birth complicated by FGR. Recurrent CIUE can also be accompanied by an uncomplicated pregnancy without treatment (1/5; 20%). Henceforth, treatment for CIUE should be within the realms of well-conducted research and mindful of guidelines to prevent recurrent IUFD, FGR, pre-eclampsia or miscarriages.

Chronic intervillositis has been described before in cases with malaria, acute cytomegalovirus infection and dengue [23–25]. We identified one case with a parvovirus infection and another with rubella virus infection early in pregnancy. These infections have not previously been described in association with a chronic intervillous infiltrate. These cases show again the importance of excluding an infectious cause when considering the diagnosis CIUE [5]. Further research is needed to evaluate the diagnostic criteria for CIUE and should focus on inter-observer variability and associations between the intervillous infiltrate and clinical outcomes.

A strength of this study is the use of well-defined criteria to diagnose CIUE and associated clinical outcomes. Similar to most studies on CIUE, this study is limited by its retrospective design, which encourages selection bias. A retrospective design makes it more difficult to exclude for example, infectious causes for an intervillous infiltrate. Furthermore, indications for placenta examination and experience of the pathologist at a hospital also results in selection bias. The indications for placenta examination at our hospital can probably explain the significant association between TOP and hypertensive complications of pregnancy, and if a pregnancy was the previous, index or subsequent pregnancy. Interestingly, between 2006 and 2007, we studied 591 placentas from uncomplicated pregnancies [10] and did not identify CIUE in any of these cases. It is unlikely therefore that we are overestimating the clinical impact of CIUE. Due to the presumed low incidence of CIUE, only a multi-center prospective study on placental histology in complicated and uncomplicated pregnancies could overcome selection bias and provide a clear answer to the prevalence of CIUE and the incidence of accompanied pregnancy complications. In conclusion, CIUE is often accompanied by unfavourable pregnancy outcomes, but can also be accompanied by an uncomplicated pregnancy. Our study provides additional insight into the clinical phenotype of CIUE. Therewith, this study emphasises the need for further research to understand the pathophysiology behind different pregnancy outcomes in CIUE.

Author contribution and conflicts of interest

M. Bos: 'I declare that I participated in conceptualization of the study, data collection, data analysis and writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

E.T.M.S. Harris-Mostert: 'I declare that I participated in data collection, data analysis and writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

L.E. van der Meeren: 'I declare that I participated in writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

J.J. Baelde: 'I declare that I participated in conceptualization of the study and writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

D.J. Williams: 'I declare that I participated in writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

P.G.J. Nikkels: 'I declare that I participated in conceptualization of the study and writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

K.W.M. Bloemenkamp: 'I declare that I participated in conceptualization of the study, data analysis and writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

M.L.P. van der Hoorn: 'I declare that I participated in conceptualization of the study, data analysis and writing the manuscript and that I have seen and approved the final version. I don't have conflicts of interest'.

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References

[1] C. Labarrere, E. Mullen, Fibrinoid and trophoblastic necrosis with massive chronic intervillositis: an extreme variant of villitis of unknown etiology, Am. J. Reprod. Immunol. Microbiol. 15 (3) (1987) 85–91.
[2] E.E. Mooney, Chronic Histiocytic Intervillositis: A Practical Guide, 2019, pp. 207–211.
[3] J. Man, J.C. Hutchinson, A.E. Heazell, M. Ashworth, S. Levine, N.J. Sebire, Stillbirth and intrauterine fetal death: factors affecting determination of cause of death at autopsy, Ultrasound Obstet. Gynecol.: Off. J. Int. Soc. Ultrasound Obstet. Gynecol. 48 (5) (2016) 566–573.
[4] C.A. Labarrere, E. Bammerlin, J.W. Hardin, H.L. Dicarlo, Intercellular adhesion molecule-1 expression in massive chronic intervillositis: implications for the invasion of maternal cells into fetal tissues, Placenta 35 (5) (2014) 311–317.
[5] M. Bos, P.G.J. Nikkels, D. Cohen, J.W. Schoones, K.W.M. Bloemenkamp, J. A. Bruijn, H.J. Baelde, M.L.P. van der Hoorn, R.J. Turner, Towards standardized criteria for diagnosing chronic intervillositis of unknown etiology: a systematic review, Placenta 61 (2018) 80–88.
[6] O. Parant, J. Capdet, S. Kessler, J. Aziza, A. Berrebi, Chronic intervillositis of unknown etiology (CIUE): relation between placental lesions and perinatal outcome, Eur. J. Obstet. Gynecol. Reprod. Biol. 143 (1) (2009) 9–13.
[7] T.K. Boyd, R.W. Redline, Chronic histiocytic intervillositis: a placental lesion associated with recurrent reproductive loss, Hum. Pathol. 31 (11) (2000) 1389–1396.
[8] C. Capuani, F. Meggetto, I. Duga, M. Danjoux, M. March, O. Parant, P. Brousset, J. Aziza, Specific infiltration pattern of FOXP3+ regulatory T cells in chronic histiocytic intervillositis of unknown etiology, Placenta 34 (2) (2013) 149–154.
[9] A. Mekinian, N. Costedoat-Chalumeau, A. Masseau, A. Botta, A. Chudzinski, A. Theulin, V. Emmanuelli, E. Hachulla, C.S. De, A. Revaux, P. Nicaise, F. Cornelis, D. Subtil, F. Montestruc, M. Bucourt, S. Chollet-Martin, L. Carbillon, O. Fain, Chronic histiocytic intervillositis: outcome, associated diseases and treatment in a multicenter prospective study, Autoimmunity 48 (1) (2015) 40–45.
[10] M.L. Houben, P.G. Nikkels, G.M. van Bleek, G.H. Visser, M.M. Rovers, H. Kessel, W. J. de Waal, L. Schuijff, A. Evers, J.L. Kimpen, L. Bont, The association between intrauterine inflammation and spontaneous vaginal delivery at term: a cross-sectional study, PLoS One 4 (8) (2009), e6572.
[11] The Eshre Guideline Group on Recurrent Pregnancy Loss, R. Bender Atik, O. B. Christiansen, J. Elson, A.M. Kolte, S. Lewis, S. Middeldorp, W. Nelen, B. Peramo, S. Quenby, N. Vermeulen, M. Goddijn, ESHRE guideline: recurrent pregnancy loss, Human Reprod. Open 2018 (2) (2018) hoy004-hoy004.
[12] Green-Top Guideline, The Investigation and Treatment of Couples with Recurrent First-Trimester and Second-Trimester Miscarriage, 2011.
[13] A.M. Kolte, L.A. Bernardi, O.B. Christiansen, S. Quenby, R.G. Farquharson, M. Goddijn, M.D. Stephenson, Terminology for pregnancy loss prior to viability: a consensus statement from the ESHRE early pregnancy special interest group, Human Reprod. (Oxford, England) 30 (3) (2015) 495–498.
[14] G. Kleiverda, J. Derksen, Zwangerschapsafbreking Tot 24 Weken [Termination of Pregnancy until 24 Weeks of Gestational Age], Guidelines of the Netherlands Association for Obstetrics and Gynaecology (NVOG), 2015.
[15] R.M. Silver, D.W. Branch, R. Goldenberg, J.D. Iams, M.A. Klebanoff, Nomenclature for pregnancy outcomes: time for a change, Obstet. Gynecol. 118 (6) (2011) 1402–1408.
[16] F.C. Battaglia, L.O. Lubchenco, A practical classification of newborn infants by weight and gestational age, J. Pediatr. 71 (2) (1967) 159–163.
[17] G.H. Visser, P.H. Eilers, P.M. Elferink-Stinkens, H.M. Merkus, J.M. Wit, New Dutch reference curves for birthweight by gestational age, Early Hum. Dev. 85 (12) (2009) 737–744.
[18] R. Rai, L. Regan, Recurrent miscarriage, Lancet (London, England) 368 (9535) (2006) 601–611.
[19] E. Jauniaux, R.G. Farquharson, O.B. Christiansen, N. Exalto, Evidence-based guidelines for the investigation and medical treatment of recurrent miscarriage, Human Reprod. (Oxford, England) 21 (9) (2006) 2216–2222.
[20] A. Youssef, N. Vermeulen, E.L.O. Lashley, M. Goddijn, M.L.P. van der Hoorn, Comparison and appraisal of (Inter) national recurrent pregnancy loss guidelines, Reprod. Biomed. Online (2019).
[21] C. Rota, D. Carles, V. Schaeffer, F. Guyon, R. Saura, J. Horovitz, Perinatal prognosis of pregnancies complicated by placental chronic intervillitis, J. Gynecol. Obstet. Biol. Reprod. 35 (7) (2006) 711–719.
[22] S. Abdulghani, F. Moretti, A. Gruslin, D. Grynspan, Recurrent massive perivillous fibrin deposition and chronic intervillositis treated with heparin and intravenous immunoglobulin: a case report, J. Obstet. Gynaecol. Can. : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 39 (8) (2017) 676–681.
[23] J. Ordi, M.R. Ismail, P.J. Ventura, E. Kahigwa, R. Hirt, A. Cardesa, P.L. Alonso, C. Menendez, Massive chronic intervillositis of the placenta associated with malaria infection, Am. J. Surg. Pathol. 22 (8) (1998) 1006–1011.
[24] M. Taweevisit, K. Sukpan, S. Siriaunkgul, P.S. Thorner, Chronic histiocytic intervillositis with cytomegalovirus placentitis in a case of hydrops fetalis, Fetal Pediatr. Pathol. 31 (6) (2012) 394–400.
[25] C.F. Ribeiro, V.G.S. Lopes, P. Brasil, A.R.C. Pires, R. Rohloff, R.M.R. Nogueira, Dengue infection in pregnancy and its impact on the placenta, Int. J. Infect. Dis. : IJID: Off. Publ. Int. Soc. Infect. Dis. 55 (2017) 109–112.