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Chronic intervillositis of unknown etiology (CIUE): Relation between placental lesions and perinatal outcome

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ABSTRACT

Objectives: To evaluate perinatal outcome of pregnancies complicated by chronic intervillositis of unknown etiology (CIUE) and to study the relation between extent of such placental histological lesions and clinical expression.
Study design: Descriptive and retrospective study including all cases of CIUE diagnosed between 2000 and 2006 in the university hospital of Toulouse (France). Perinatal outcome was evaluated according to the extent of placental lesions assessed by semi-quantitative graduation.
Results: Twenty pregnancies complicated by CIUE were included (14 patients). Three pregnancies were prematurely interrupted spontaneously during the first trimester. Perinatal outcome of the remaining 17 pregnancies beyond 22 WG was: 4 intrauterine fetal deaths, 3 terminations of pregnancy for early and severe intrauterine growth restriction (IUGR), and 10 live births (58.8%). All fetal deaths, 82.3% of pregnancies beyond 22 WG and 70% of live births were growth restricted. Severe intervillositis with massive fibrinoid deposition was associated with a severe perinatal prognosis whereas focal forms had a best evolution. The rate of recurrence was 100% in the reported cases.
Conclusion: CIUE have a poor perinatal outcome and a high rate of recurrence. There is a relation between clinical expression and histological lesions.

1. Introduction

Chronic intervillositis of unknown etiology (CIUE) is a rare entity, initially described by Labarrere and Mullen in 1987 [1], defined by inflammatory placental lesions prevailing in the intervillous space (IVS). This pathology, also called *massive chronic intervillositis* or *chronic histiocytic intervillositis*, is characterized by an intervillous infiltrate of mononuclear cells (monocytes, lymphocytes, histiocytes) from maternal origin. This infiltrate, either massive or moderate, is frequently associated with villous and intervillous fibrinoid deposition. Chronic intervillositis can be associated to focal villitis, but the pathophysiologic distinction between these two entities is not clear.

CIUE is associated with a poor perinatal prognosis (intrauterine growth restriction (IUGR), intrauterine fetal death (IUFD), spontaneous miscarriage) by placental insufficiency. Since its first description, only a few cases have been reported.

The purpose of our study was to clarify the clinical relevance of this rare anatomoclinic entity and to evaluate the perinatal prognosis from 20 complicated pregnancies, while trying to establish a relationship between such placental lesions and pregnancies outcome.

2. Materials and methods

Paule de Viguier hospital (University of Toulouse) is a tertiary centre in the southwest of France, carrying out more than 4200 deliveries a year.

Patients were retrospectively identified from the department of histopathology database. All women managed in our institution between January 2000 and June 2006 whose placenta revealed lesions of CIUE at pathologic examination, were eligible for the study.

During the 6 years study period, about 22,000 deliveries occurred in our centre and 5276 placentas were submitted for pathologic examination (24% of deliveries). 2798 products of abortion were also analysed in the same department.

Placenta was submitted for pathologic examination in the main following situations: IUGR, preeclampsia, IUFD, unexplained perinatal asphyxia. A pathological examination is also performed

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for all spontaneous first trimester miscarriages. VIH, rubella, toxoplasmosis, hepatitis and CMV serological tests were systematically performed in order to exclude chronic infection. An immunological and thrombophilic assessment (factor V Leyden mutation, MTHFR mutation, factor II, S and C protein and antithrombin) is moreover performed in early (before 34 WG) and severe (<5th percentile) IUGR, IUFD or recurrent spontaneous miscarriages (3 or more).

Placentas were fixed in formaldehyde after gross examination and three samples randomly taken, were systematically analysed for each case. If abnormalities were suspected (cellular infiltrate or fibrinoid deposition), additional samples were taken (up to 8 by placenta) in order to detect confined lesions. Serial sections (5 μm) of tissues embedded in paraffin blocks were done and stained for basic visualization using hematoxilin–eosin–saffron (HES) staining. All the slides were reviewed by the same pathologist.

Following patterns, first described in 1987 by Labarrere and Mullen [1], were considered for diagnosis of CIUE: inflammatory mononuclear cells infiltrate (monocytes, histiocytes, lymphocytes) prevailing in the placental IVS with intervillous and perivillous fibrinoid deposition on materno–fetal interface, anchoring villi and adjacent decidua. These inflammatory lesions could also be observed in the chorionic plate and can be associated with thrombosis of the villous trunks, hemorrhagic endovascularitis, and chorioangiosis. Cases containing very focal chronic villitis were included. Immunohistochemical analysis, unnecessary for current diagnosis, could be useful to characterize the cells infiltrate and attest the mononuclear origin (CD45+ and CD68+). Moreover, this technique allowed quantifying the lesion spreading in the focal forms.

A semi-quantitative grading was used according to the extent of chronic inflammatory infiltrate and the amount of fibrinoid deposition in the IVS. For each specimen, the slides with the most significant lesions were considered and evaluated as following: focal (when intervillous mononuclear infiltrate and fibrinoid deposition were localised in less than 10% of the slide), moderate (10–50% of the intervillous space of the slide was involved) or massive (more than 50% of the slide).

In order to analyze the anatomoclinical relation, we considered schematically two histological levels of severity:

- *Moderate*: defined by focal or moderate intervillous lymphohistiocytic inflammatory infiltrate with mild or moderate fibrinoid deposition.
- *Severe*: defined by massive intervillous mononuclear inflammatory infiltrate with moderate or severe fibrinoid deposition. Massive and confluent perivillous fibrinoid deposition with mild mononuclear infiltrate was also considered in this level.

We excluded patients with immunologic disorder, infectious disease, obvious obstetrical pathology (such as preeclampsia) and if pathological diagnosis was unclear or uncertain.

For each patient the following data were recorded: obstetrical history, parity, treatment during pregnancy, characteristic of obstetrical follow-up (serum markers for down syndrome screening, sonography, uterine Doppler), outcome of the pregnancy, mode of delivery, neonatal characteristics (state of newborn, gestational age, birth weight), placental histological data (weight of the placenta, extent of cellular infiltration and/or fibrinoid deposition, associated lesions), and pediatric outcome at day 8.

3. Results

Twenty pregnancies and 14 patients (including five primigravidas) meeting the inclusion criteria, were analysed. Mean maternal age was 30 years (range: 24–39) and mean BMI was 21 (range: 19–27). Most patients were Caucasian. Two patients out of 14 had a history of recurrent spontaneous miscarriages. Among the 20 complicated pregnancies, 3 were spontaneously terminated before 22 WG (Table 1) and 17 were continued beyond 22 WG (Table 2).

Table 1
Perinatal outcome (pregnancies <22 WG).

Patient	Pregn.	Parity	Age (year)	Treatment during pregnancy	Pregnancy outcome	Gestational age (week)
B	2	G8P5	35	–	Miscarriage	14
G	10	G4P0	24	Aspirin	Miscarriage	10
	11	G5P0	25	Aspirin/corticoïd (prednisone 20 mg)	Miscarriage	8

Table 2
Perinatal outcome (pregnancies >22 WG).

Patient	Pregnancy	Parity	Age (year)	Treatment during pregnancy	Pregnancy outcome	Gestat age (weeks)	Fetal weight (g)	IUGR	Placenta			Pediatric outcome D8
									Weight (g)	Intensity	Other	
A	1	G1P0	35	–	Delivery	40.5	2550	+	420	+	Villitis	Alive
B	3	G9P5	37	–	IUFD	37	2160	+	327	+++	Villitis	Dead
	4	G10P6	38	Aspirin/corticoïd	Delivery	34	2410	0	335	+	Villitis	Alive
C	5	G2P1	29	–	Delivery	34	2310	0	360	+	Ischemy	Alive
D	6	G2P1	31	–	IUFD	23	180	++	100	+++		Dead
E	7	G2P1	31	–	TOP	22	190	++	148	+++		Dead
	8	G3P2	33	–	TOP	26	392	++	157	+++		Dead
F	9	G1P0	29	–	Delivery	37	2080	++	280	+	Ischemy	Alive
H	12	G3P0	25	–	Delivery	27.5	590	++	230	+++	Thromb.	Alive
	13	G4P1	29	Aspirin	IUFD	26.5	330	++	195	+++		Dead
I	14	G2P0	31	–	IUFD	28.5	160	++	260	+++		Dead
	15	G3P1	33	Aspirin/corticoïd (prednisone 5 mg)	TOP	22.5	215	++	150	+++		Dead
J	16	G3P2	28	Aspirin	Delivery	37	2760	0	565	+		Alive
K	17	G2P1	27	Aspirin	Delivery	37.5	2320	+	350	+	Ischemy	Alive
L	18	G1P0	39	–	Delivery	37	2400	+	395	+	Ischemy Villitis	Alive
M	19	G1P0	28	–	Delivery	37	2040	++	345	+	Ischemy Villitis	Alive
N	20	G1P0	39	–	Delivery	30	790	++	110	+	Ischemy Villitis	Alive

IUFD: intrauterine fetal death; TOP: termination of pregnancy; IUGR: intrauterine growth restriction: (0) none; (+) moderate; (+++) severe.

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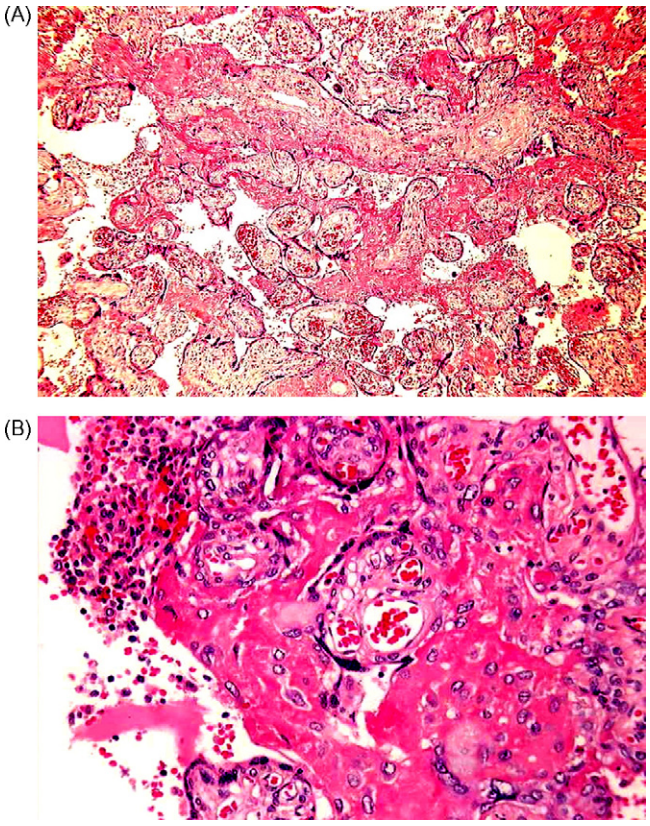

Fig. 1. (A and B) Chronic intervillositis of unknown etiology: massive mononuclear infiltrate in the intervillous spaces of the placenta in association with diffuse fibrinoid deposition surrounding villi [patient I] (*hematoxylin and eosin*). (A) Magnification 400×; (B) magnification 1200×.

Following results concern pregnancies >22 WG. CIUE was diagnosed in 0.32% of the placentas analysed (17 pregnancies/5276 placentas >22 WG). Clinical expressions were IUGR associated with oligohydramnios in 80% of cases. IUGR was the main obstetrical complication. It concerned 100% of fetal death, 82.3% of pregnancies evolving beyond 22 WG and 70% of live births. Termination of pregnancy (TOP) was performed in three cases between 22 and 26 WG because of a severe and early IUGR with interruption of fetal growth and severe oligohydramnios. All terminations of pregnancy were carried out at patient's request with agreement of the regional multidisciplinary prenatal diagnosis centre.

Gross placental examination did not show any specific abnormalities. The IVS infiltrate was massive in eight cases (Fig. 1A and B) and moderate in nine cases (Fig. 2). Associated villitis was observed in 30% of cases. There were no specific

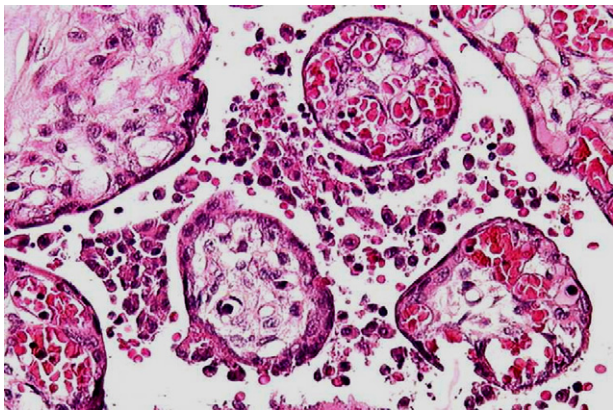

Fig. 2. Chronic intervillositis of unknown etiology. Moderate mononuclear inflammatory infiltrate in the intervillous spaces of the placenta with focal villitis (focused alteration of the villous trophoblasts) (*hematoxylin and eosin, original magnification* 400×).

abnormalities of second trimester serum markers for down syndrome screening and no arguments for an infectious disease. Uterine artery Doppler was available for 11 pregnancies >22 WG: the velocity waveforms were considered as normal in eight cases (pregnancies 1, 3, 4, 8, 14, 16, 17 and 18) and pathological in three cases: resistance index >0.6 with bilateral Notch (pregnancies 13, 19 and 20).

We observed two clinical expressions according to the severity of the histological lesions. When the cellular infiltrate and/or the fibrinoid deposition were massive (eight cases), perinatal prognosis was poor with constant, early and severe IUGR with oligohydramnios. Perinatal outcome was: one live birth, four IUFD and three TOP. When infiltrate was moderate (nine cases), perinatal prognosis was better: 100% live births including six IUGR.

Six pregnancies (30%) could reach 37 WG with a live birth. The global perinatal mortality rate was 41.2%. Some patients had a normal pregnancy before the occurrence of the first case of intervillositis (6 patients over 14), but after a complicated pregnancy, the placental disorder always recurred during the following pregnancies.

Three patients benefited, from a prophylactic treatment with corticosteroids (prednisone 20–40 mg/day) in association with aspirin (100–160 mg/day). The treatment was started as soon as possible at the beginning of pregnancy and continued up to delivery. This treatment allowed obtaining one live birth over the three overall treated patients. In all cases, in spite of the treatment, chronical intervillositis placental lesions were present at pathologic examination.

Table 3 summarizes the suggestive obstetrical history of patient B. She had four normal pregnancies before the occurrence of

Table 3
Obstetrical history of patient B.

	Maternal age	Pregnancy outcome	Treatment	Gestational age (week pregnancy)	Weight (g)	Placental pathology
1	22	Delivery	–	41	2950	Not done
2	24	Delivery	–	41	2900	Not done
3	26	Delivery	–	41	2950	Not done
4	29	Delivery	–	38	2950	Not done
5	29	IUFD	–	23	–	NS
6	34	Miscarriage	–	17	–	NS
7	35	Miscarriage	–	15	–	NS
8	35	Miscarriage	–	14	–	*Intervillitis*
9	37	IUFD	–	37	2160	*Intervillitis*
10	38	Delivery	Aspirin + corticoïd	34	2410	*Intervillitis*

IUFD: intrauterine fetal death; NS: non-specific.

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placental lesions and always recurred in the following pregnancies, without change in paternity. The diagnosis was formally made for the last three pregnancies but was probable for the three preceding ones. She benefited, with success, from a prophylactic treatment (aspirin + prednisone) for her last pregnancy.

4. Comment

Inflammatory placental lesions of chronic villitis or intervillositis are found in variable proportions according to the studied populations and the number of biopsies done on the placentas. Incidence ranges from 10 to 33% for placentas examined in high-risk pregnancies, 12% after birth of normal weighted babies and from 8 to 14% in population studies [2–4].

Chronic intervillositis, whose frequency is unknown, is probably much less frequent. Our study did not allow us to estimate the incidence of CIUE because placentas from uncomplicated pregnancy are infrequently submitted for pathologic examination. Twenty-four percent of our placentas were examined. This rate is consistent with published data. A recent US study suggested that in a university practice, almost 40% of placentas were eligible for pathologic examination according to the national guidelines (not available in France), but less than half of those were really submitted [5]. Nevertheless, 20 diagnosis of CIUE were done in our hospital, during a 6 years period (22,000 births). Interestingly, Boyd found similar values; 6/10,000 placentas analysed in the second and third trimester [6]. In a larger epidemiologic study concerning 668 first trimester miscarriages, the rate of intervillositis was 4.4% when karyotype was normal versus 0.3% if not [7].

Intervillositis is frequently associated with villitis (30% in our study, 25% for Rota et al. [8]) but the pathophysiologic distinction between these two entities is not clearly defined. Contrary to chronic villitis, intervillositis lesions are primarily found in placental IVS (thus on the maternal side). One can admit that the immune reaction develops first in the IVS, and then affects villi [4]. In our experience, associated villitis is focused and limited to villous trophoblast without invasion of the villous tree, even in the most severe patterns of CIUE. Conversely, when villitis lesions are prominent with infiltration of the villous tree, prognosis and etiological context are different (infectious factor?). Thus, we consider, in agreement with clinical patterns, that CIUE and CVUE are two different entities; data are insufficient to consider that CVUE should be a more pejorative state of the same disease. The maternal origin of inflammatory cells and the participation of CD3+ T-lymphocytes were shown in chronic villitis, using in situ hybridization and immunohistochemical techniques [6,9]. Similar observations were made in some cases of our study.

Recent pathophysiologic findings have argued in favour of an immune response resulting from a maternal reaction against placental tissue, comparable to a host-versus-graft reaction [6]. Whereas inflammatory reaction preferentially implies T-lymphocytes, some studies are in progress to assess the potential role of maternofetal placental allo-immunization.

Chronic intervillositis patterns were sometimes related to an antiphospholipid syndrome [10] or a massive malaria infection where pigmented depositions of hematozoa or parasitized erythrocytes are observed [11,12]. In all our cases, the etiology of intervillositis remained unknown. The hypothesis of infection by unidentified pathogen factors (virus?), suggested by the similarity of the lesions with those of viral placentitis (CMV, rubella, etc.), is rendered unlikely by the normal development of the surviving neonates [2] and the recurrence of these lesions at the time of a later pregnancy. However, the long-term neurodevelopment of survivors has never been studied.

References concerning perinatal prognosis related to CIUE is poor, in contrast to chronic villitis of unknown etiology (CVUE). As in our study (only 10 live birth among 20 complicated pregnancies), most publications reveal a poor perinatal outcome. The clinical features include either early recurrent spontaneous miscarriages or consequences of placental insufficiency for pregnancies evolving beyond 22 WG. The first study, published in 1987 by Labarrere and Mullen [1], described six cases of CIUE resulting in five IUGR and one perinatal death. In another study with six cases, reported by Jacques and Qureshi in 1993 [13], perinatal mortality was 83%. In this study, the high frequency of associated pathologies (two preeclampsia, two systemic lupus erythematosus) and associated microscopic placental lesions (infarct, two cases; aspect of atheroma in decidual vessels, two cases; acute chorioamniotitis, two cases) make difficult any interpretation of the clinical results. Recently, Rota et al. reported a series of 25 patients (25% associated villitis) with similar results: rate of fetal loss 55%, perinatal mortality 29%, and small for gestational age fetuses 77%. Only 32% of the babies were alive 1 week after birth [8]. These authors emphasized the possibility of a prenatal diagnosis by obtaining at the same time the fetal karyotype and a histological probe at placentocentesis. Such an attitude has not yet been validated. Moreover, a small placental sample, randomly taken, is unlikely to be accurate for the diagnosis of focal CIUE. The most important published study [6] reported 31 cases of exclusive CIUE without villous extension in 21 patients between 1993 and 2000. The prognosis of these pregnancies was: perinatal death 77%, IUGR 57% with only 18% pregnancies reaching 37 WG. However, in this study, most cases (23/31) were early spontaneous miscarriages and only eight cases concerned pregnancies after 22 WG (five IUGR over eight pregnancies). Recently, Boog et al. [4] reported one case of intervillositis with associated villitis. The patient had a history of three perinatal deaths between 23 and 31 WG, with at least two of them associated with CVUE and CIUE inflammatory lesions. Chronic intervillositis is a probable cause of several «unexplained» IUFD [14].

Doss et al. [7] described one case with 10 spontaneous miscarriages due to recurrent massive CIUE. Similarly, patient G of our study had five early recurrent spontaneous miscarriages with CIUE for the last ones. In the other miscarriages, microscopic analysis showed atypical placental abnormalities not obviously related with CIUE. Pathologic examination of the product of abortion researching intervillositis, seems thus to be useful in recurrent miscarriage assessment. While hydropic and dysmorphic villi evoke chromosomal abnormalities with a positive predictive value (PPV) of 90% before 6 WG, the CIUE aspect has a PPV of 85% for a normal karyotype in miscarriages after 11.5 WG [4,10,15].

High rate of recurrence is currently reported. This rate is about 67% for Boyd and Redline [6], and reaches 100% in our study, with a similar intensity in this five patients for whom such information was available. For Boog et al. [4], clinical recurrences are more and more early.

The results of our study suggest a relation between intensity of placental inflammatory histological lesions and severity of clinical outcomes. They confirm the poor perinatal prognosis and probably a high rate of recurrence. We highlighted two clinical expressions:

- *Massive CIUE with diffuse fibrinoid deposition*, characterized by a poor pregnancy outcome: midtrimester recurrent IUFD, early and severe IUGR with oligohydramnios. This severe clinical feature is associated with massive fibrinoid deposition surrounding villi. Immunohistochemical analysis can be useful in order to display the cellular infiltrate.
- *Moderate CIUE with focal fibrinoid deposition*, characterized by a favourable evolution with an active obstetrical management: progressive IUGR (2/3 of cases), late IUFD.

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Diagnosis of focal forms is difficult and probably underestimated with current placental examination. Numerous placental samples and immunohistochemical analysis thus may be useful.

According to the hypothesis of a maternal immunological origin, an early corticosteroid treatment should be useful during pregnancy. In our study, three patients had a combined treatment with aspirin and prednisone. Aspirin is often prescribed because of frequent obliterative vascular lesions observed in association with lympho-plasmocyte infiltrate. For patient B, the outcome of the last treated pregnancy was favourable (elective caesarean delivery at 34 WG with corticosteroid-induced gestational diabetes). Patient I, with aspirin and prednisone (5 mg/J), had a recurrence of massive CIUE leading to a TOP because of major IUGR at 22.5 WG. The corticosteroid posology seems to have been inadequate. Despite the treatment, persistent histological lesions of CIUE were observed in all cases. In the two cases reported by Boog et al. [4], the first patient was treated with 2 mg betamethasone per day. Such treatment allowed a live birth, but did not induce the disappearance of placental lesions. In the second case, the treatment was prednisone 20 mg/day and no placental inflammatory lesions were seen at pathological examination.

Although no treatment has been yet fully validated, we suggest prescribing corticosteroid (prednisone, at least 20 mg/day) as early as possible during pregnancy, especially in patients with history of severe CIUE with moderate fibrinoid deposition. A closed fetal monitoring must be established during the second trimester with a discussion for fetal extraction as soon as 34 WG in case of IUGR.

Further studies are needed in order to assess the efficiency of such an attitude and to confirm the immunological origin of this entity. Pathologists should be aware of these placental lesions in the event of an evocative clinical context.

References

[1] Labarrere C, Mullen E. Fibrinoid and trophoblastic necrosis with massive chronic intervillositis: an extreme variant of villitis of unknown etiology. Am J Reprod Immunol Microbiol 1987;15:85–91.
[2] Nessmann C, Larroche JC. Villite et intervillite chroniques sans étiologie connue. In: Atlas de pathologie placentaire. Paris: Masson; 2001. pp. 67–68.
[3] Becroft DM, Thompson JM, Mitchell EA. Placental villitis of unknown origin: epidemiologic associations. Am J Obstet Gynecol 2005;192:264–71.
[4] Boog G, Le Vaillant C, Alnoukari F, Jossic F, Barrier J, Muller JY. Combining corticosteroid and aspirin for the prevention of recurrent villitis or intervillositis of unknown etiology. J Gynecol Obstet Biol Reprod 2006;35:396–404.
[5] Curtin WM, Krauss S, Metlay LA, Katzman PJ. Pathologic examination of the placenta and observed practice. Obstet Gynecol 2007;109:35–41.
[6] Boyd TK, Redline RW. Chronic histiocytic intervillositis: a placental lesion associated with recurrent reproductive loss. Hum Pathol 2000;31:1389–96.
[7] Doss BJ, Greene MF, Hill J, Heffner LJ, Bieber FR, Genest DR. Massive chronic intervillositis associated with recurrent abortions. Hum Pathol 1995;26:1245–51.
[8] Rota C, Carles D, Schaeffer V, Guyon F, Saura R, Horovitz J. Perinatal prognosis of pregnancies complicated by placental chronic intervillitis. J Gynecol Obstet Biol Reprod 2006;35:711–9.
[9] Redline RW, Patterson P. Villitis of unknown etiology is associated with major infiltration of fetal tissue by maternal inflammatory cells. Am J Pathol 1993;143:473–9.
[10] Salafia C, Maier D, Vogel C, Pezzullo J, Burns J, Silberman L. Placental and decidual histology in spontaneous abortion: detailed description and correlations with chromosome number. Obstet Gynecol 1993;82:295–303.
[11] Nebuloni M, Palloti F, Polizzotti G, Pellegrinelli A, Tosi D, Giordano F. Malaria placental infection with massive chronic intervillositis in a gravida 4 woman. Hum Pathol 2001;32:1022–3.
[12] Ordi J, Ismail MR, Ventura PJ, et al. Massive chronic intervillositis of the placenta associated with malaria infection. Am J Surg Pathol 1998;22:1006–11.
[13] Jacques SM, Qureshi F. Chronic intervillositis of the placenta. Arch Pathol Lab Med 1993;117:1032–5.
[14] Hors Y, Jacob B, Brousse H, Beniada A, Herlicoviez M, Dreyfus M. Villites et intervillites chroniques placentaires: une cause de mort fœtale in utero inexpliquée. J Gynecol Obstet Biol Reprod 2000;29:712.
[15] Redline RW, Zaragoza M, Hassold T. Prevalence of developmental and inflammatory lesions in nonmolar first-trimester spontaneous abortions. Hum Pathol 1999;30:93–100.

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