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Case report

Two cases of pseudo-partial mole of placenta

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Background : Though pseudo-partial mole was not a gestational trophoblastic disease, it was frequently treated as partial mole. In a meaning to avoid a useless treatment, the spread and the establishment of diagnosis of this disease were recommended. Cases : Two cases with pseudo-partial mole of placenta in mid-and late trimesters were reported. Each placenta was very heavy in spite of appropriate-for-gestational-aged female babies. Placental stem villous hydrops was pathognomonic and each placenta revealed diploid pattern of 46, XX by fluorescence in situ hybridization (FISH). Our cases were diagnosed as pseudo-partial mole because of a genetically diploid pattern, a pregnancy sustained until mid-trimester, and a defect of chorionic epithelial proliferation. Conclusion : FISH was very effective method to confirm pseudo-partial mole as to omit an unnecessary treatment against gestational trophoblastic disease.

Key words : pseudo-partial mole, placental stem villous hydrops, mesenchymal dysplasia of placenta, chorioangioma, diploid, fluorescence in situ hybridization (FISH)

Case report

Case 1 (Fig. 1-4, 9, 10, Table 1).

A 30-year-old mother with neurofibromatosis (Recklinghausen's disease) admitted because of premature rupture of membranes and a female baby was delivered transvaginally at 23 weeks of gestation in 1990. Neonate weighed 590g (appropriate for gestational age) and had a minor anomaly of right-sided iris defect. She gained a normal weight increment but was complicated with bronchopulmonary dysplasia of IV stage, apnea attack, retinopathy of prematurity of III stage, cardiac hypertrophy, and dilatation of cerebral ventricles. The placenta weighed 500g (normal range＝140±30g) and the ratio against fetal weight reached 0.85(normal range＝0.27). Placenta was half replaced by vesicular chorionic villi, reached up to 2 x 1 cm in diameter. Vesicular villi dispersedly intermingled with normal villi in whole placenta, which neglected multiple pregnancies. Chorionic stem villi were microscopically swollen with central cistern formation but no chorionic epithelial proliferation and atypism were found. Based on the diagnosis of partial mole, she was treated with intrauterine curettage and urine β-human chorionic gonadotropin (HCG) had come down into normal range for 8 months after delivery. Basal body temperature (BBT) became biphasic and no silhouette was found in chest radiograph. Fluorescent in situ hybridization (FISH) for formalin-fixed paraffin-embedded specimens with anti-centromeres for both X- (red spot) and Y-chromosome (green spot) revealed that there were 113 cells with 2 red spots (diploid pattern of 46, XX, 97%) and 4 cells of 3 red spots (triploid pattern of 69, XXX, including X trisomy pattern, 3 %, Table 1) (3, 4). In spite of a chromosomal mosaicism, the previous diagnosis of partial mole was corrected as pseudo-partial mole on the basis of diploid pattern.

Case 2 (Fig. 5-10, Table 1)

A 29-year-old mother delivered female baby, 2065g (small-for-date), Apgar 9, at 37 weeks of gestation in 2002. Placenta weighed 930g and revealed solid hydropic

Table 1. FISH results for X-and Y-centromeres

Case	examined nuclei	results		
	total numbers	X	XX	XXX
1	185	68	113	4
	%	37%	63%	
			97%	3 %
2	286	140	142	4
	%	49%	51%	
			97%	3 %

villi, reached up to 5 mm in diameter and occupied more than half volume of placenta. Vesicular villi dispersedly intermingled with normal villi in whole placenta, which neglected multiple pregnancies. Stem villous hydropic change accompanied hypovascular change. Thrombosis and vasculitis were found. There was a small chorioangioma up to 1.5cm in diameter. There was a weak tendency in cistern formation but no trophoblastic epithelial proliferation and atypism could be found. Fluorescent in situ hybridization (FISH) for formalin-fixed paraffin-embedded specimens with anti-centromeres for both X- (red spot) and Y-chromosome (green spot) revealed that there were 142cells with 2 red spots (diploid pattern of 46, XX, 97%) and 4 cells of 3 red spots (triploid pattern of 69, XXX, including X trisomy pattern, 3%) (3,4). In spite of a chromosomal mosaicism, the diploid pattern indicated pseudo-partial mole. It was diagnosed as pseudo-partial mole of placenta with chorangioma by Masahiro Nakayama, a pathologist in Osaka Medical Center and Research Institute for Maternal and Child Health, on the mail consultation of the Japanese Society of Pathology.

Discussion

Differential diagnosis consisted of gestational trophoblastic diseases: partial mole and total mole (Table 2) (1-3). A gestational duration of pseudo-partial mole was longer than those of moles, i.e. occurred more often in second trimester than in first trimester. Pseudo-partial mole and total mole were genetically diploid but partial mole was triploid. Moles showed trophoblastic epithelial proliferation with atypism. Both pseudo-partial mole and partial mole had evidence of fetus, i.e. nucleated erythrocytes, but total mole lacked it. As to hydropic villous changes in early abortion before an establishment of hematopoiesis evidence of nucleated erythrocytes was not available for reconfirmation of fetus, which required genetic analysis for objective diagnostic criteria.

Paradinas reviewed the pathognomonic mechanism of pseudo-partial moles as follows(2): half cases of pseudo-partial moles tended to complicate Beckwith-Wiedemann syndrome, which complicated overgrowth of both fetus, including omphalocele with or without macrosomia, and placenta because of up-regulation of genes by deregulation of the normal expression of imprinted genes. Normally in chromosome 11p the gene of insulin-like growth factor II (IGF 2) as a cell-cycle accelerator was activated only in paternal allele and the gene of p57Kip 2 as a cell-cycle repressor was activated only in maternal allele, i.e. imprinted. Conversely in the case of Beckwith-Wiedemann syndrome IGF 2 was up-regulated and p57Kip 2 was down-regulated because the imprinted suppression in maternal allele were replaced by paternal one or there were two paternal copies of these regions. Pseudo-partial moles without Beckwith-Wiedemann syndrome had a possibility of minute abnormality at a gene level because we could not reveal triploid by usual FISH chromosomal examination. Genetic rearrangement analysis should be done with single-stranded conformation polymorphism (SSCP) or restriction fragment length polymorphism (RFLP) after polymerase chain reaction (PCR).

References

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偽部分奇胎の2症例

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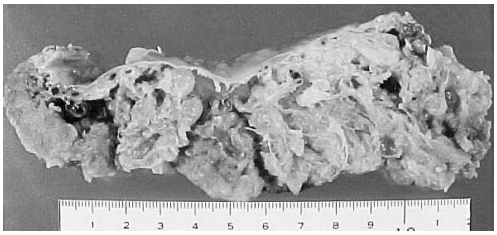
背景：絨毛性疾患でない偽部分奇胎が部分奇胎として治療されている。無用な治療を避ける意味で、偽部分奇胎の疾患概念の普及と診断確立が望まれている。症例：妊娠中期と後期まで妊娠が継続した偽部分奇胎の2症例を経験したので報告した。各症例の出生時女児体重は正常範囲で Beckwith-Wiedemann 症候群は認められなかった。胎盤は重く、びまん性・散在性に胎盤全体に水腫様幹絨毛が認められた。胎盤絨毛の染色体は fluorescence in situ hybridization (FISH) 検査上、二倍体の46, XX と判断された。顕微鏡所見上、絨毛上皮細胞の増生と異型性は認められなかった。以上より、本症例は偽部分奇胎（別称：胎盤幹血管水腫、胎盤間葉異形成など）と診断された。結論：妊娠早期における奇胎からの偽部分奇胎の組織学的診断は困難な場合が多く、FISH による染色体検査は 補助診断として極めて有効であった。

キーワード：偽部分奇胎、胎盤幹血管水腫、胎盤間葉異形成、絨毛血管腫、二倍体、蛍光 ISH (FISH)

Table 2. Clinico-pathological differential diagnosis for gestational trophoblastic diseases.

classification	histology					trophoblastic disease								
	non－trophoblastic			trophoblastic		molar	molar			nonmolar				
	villous	implantation site	chorionic－type	cytotrophoblast	syncytiotrophoblast	mole			invasive	choriocarcinoma	implantation site IT in anchoring foci		chorionic－type IT in laeve	
						pseudo－partilal mole	partial	complete			exaggerated placental site	placental site trophoblastic tumor	placental site nodule	epithelioid trophoblastic tumor
developmental genetics						diploid	triploid 69XXY（diandry）＝dispermy（23X＋23Y)＋egg(23X)	diploid 46XX，46XY（diandry）＝dispermy（23X，23Y)＋empty egg						
presentation						3rd＜2nd＜1st trimester	1st trimester	1st trimester		after mole		missed abortion		spotting
embryo						＋	＋	－						
villous outline						scalloped	scalloped	round						
trophoblast proliferation						－	focal, minimal	variable，marked						
trophoblastic atypism						－	－	often						
p57（kip2）							＋, diffuse	－／weak						
villi						＋	＋	＋	＋	－	－	－	－	－
terminal villous hydrops						weak	＋	＋	＋					
terminal villous cistern						－	＋	＋	＋					
trophoblastic inclusion						－	＋							
stem villous hydrops						＋	possible	possible	possible					
stem villous aneurysmal dilatation						＋	－	－	－					
stem villous peripheral chorioangiomatoid						＋	－	－	－					
extramedullary hematopoiesis						＋	－	－	－					

classification	histology					trophoblastic disease								
	non－trophoblastic			trophoblastic		molar	molar			nonmolar				
	villous	implantation site	chorionic － type	cytotrophoblast	syncytiotrophoblast	mole			invasive	choriocarcinoma	implantation site IT in anchoring foci		chorionic － type IT in laeve	
						pseudo － partilal mole	partial	complete			exaggerated placental site	placental site trophoblastic tumor	placental site nodule	epithelioid trophoblastic tumor
cell										dimorphic : primitive previllous － type trophoblastic		monomorphic IT , large, pleomorphic , abundant , eosinophilic		monomorphic IT , small, round, uniform, eosinophilic or clear
infiltration										expansile , dimorphic		infiltrating single cell or confluent cells		expansile epithelioid nest or cord or solid mass
necrosis										++		－		++
calcification										－		－		＋
vascular invasion										from lumen to periphery		from periphery to lumen		－
fibrinoid										－		＋		＋
mitosis／10 HPF										2 －22		0 － 6		1 －10
HLA－G	++++	++++	+++ eosinophilic cytoplasm	－	－					+ in IT	++++	++++	++++ in eosinophilic cytoplasm	++++ in eosinophilic cytoplasm
β－HCG	－	－, ＋ in multinucleated IT	－	－	++++					+ in ST	－	+ in multinucleated IT	－	－
inhibin－α	－										＋	＋	＋	＋
CK－18	－										＋	＋	＋	＋
HPL	－／＋＋ toward distal end	++++	－／＋	－	++++					+ in IT	＋	＋	－／focal	－／focal
Mel－CAM, CD146	－／＋＋＋＋ toward distal end	++++	－／＋	－	－					+ in IT	＋	＋	－／focal	－／focal
PlAP	－	－	+++	－	－					－	－／＋	－／＋	+/++	+/++
Ki－67 index	90%＜	0	3 －10%	25－50%	0					90%＜単核	＜１%	10%＜	＜10%	10－20%
chemotherapy effect										good		variable		variable
treatment										chemotheray		hysterectomy		hysterectomy



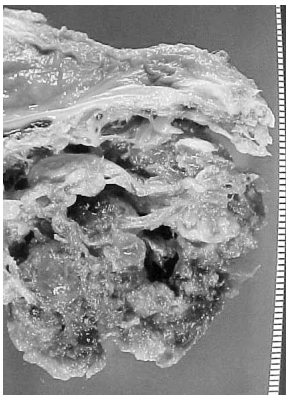
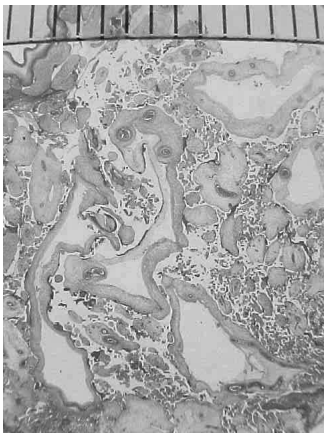


Fig 1．Case 1．Enlarged placenta consisted of normal villi intermingled with vesicular ones, the latter of which occupied around half volume of placenta. Vesicular diameter reached up to 1 cm in close-up picture.



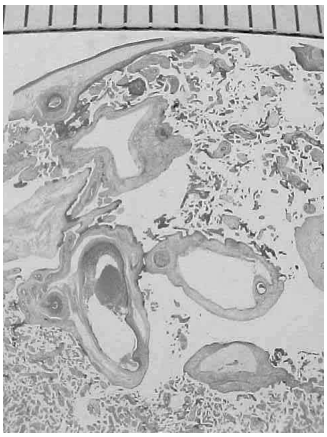
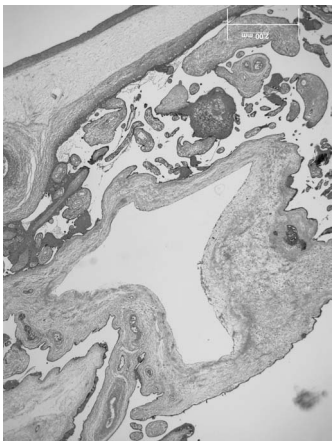


Fig 2．Case 1．Stem villous hydropic change and cistern formation on scanning microscopy, graduated in millimeters.



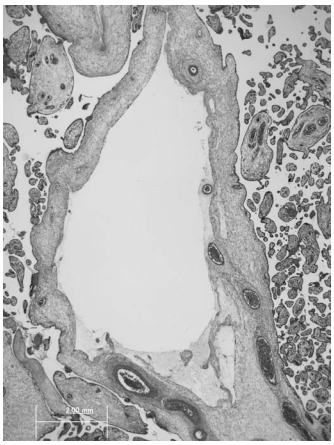


Fig 3．Case 1．Stem villous hydropic change without any trophoblastic epithelial proliferation and atypism, scaled 2 mm in length.

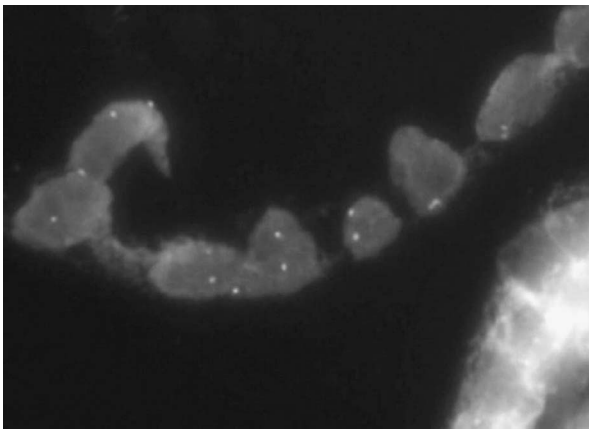


Fig 4 . Case 1 . Most chorionic cells had two red spots in FISH.

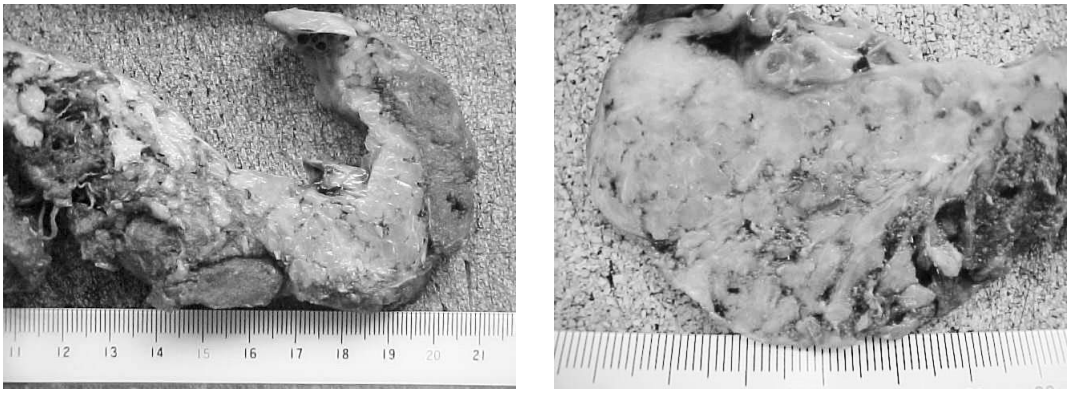
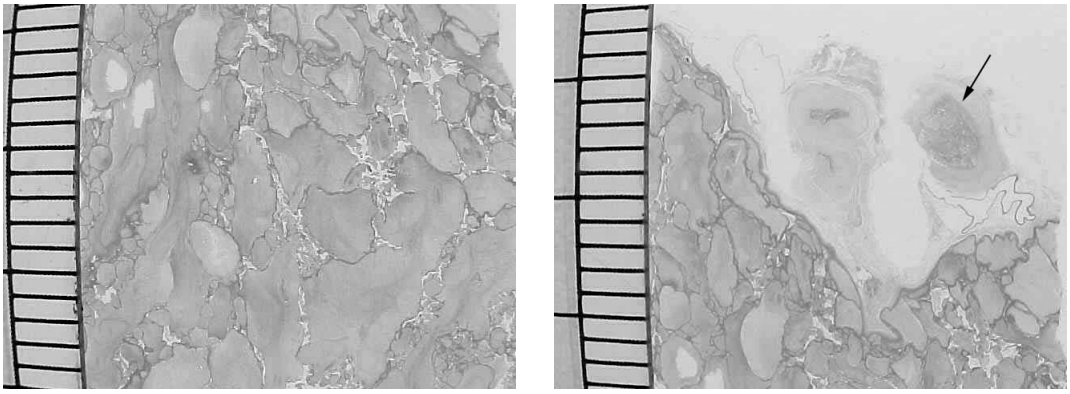


Fig 5 . Case 2 . Enlarged placenta consisted of normal villi intermingled with vesicular ones, the latter of which occupied more than half volume of placenta.



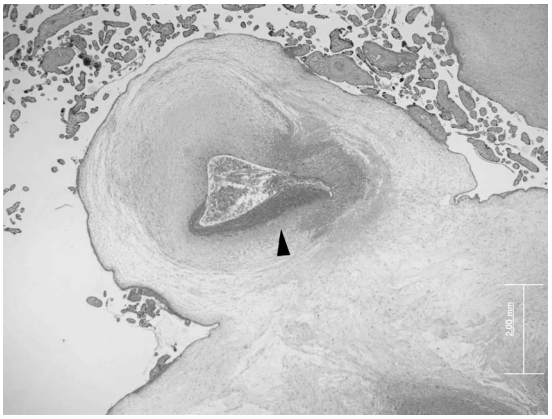
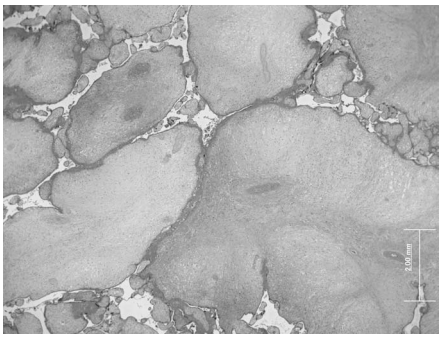
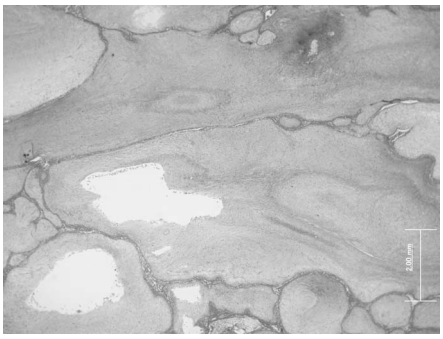


Fig 6．Case 2．Stem villous hydropic change with hypovascular change. Thrombosis (arrow) and vasculitis (arrow head) were found, graduated in millimeters or bar of 2 mm in length.





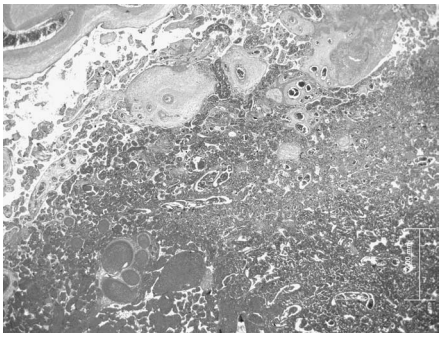


Fig 7．Case 2．Stem villous hydropic change was confirmed with hypovascular change and cistern formation without any trophoblastic epithelial proliferation and atypism, scaled 2 mm in length. Chorangioma was found in the left picture.

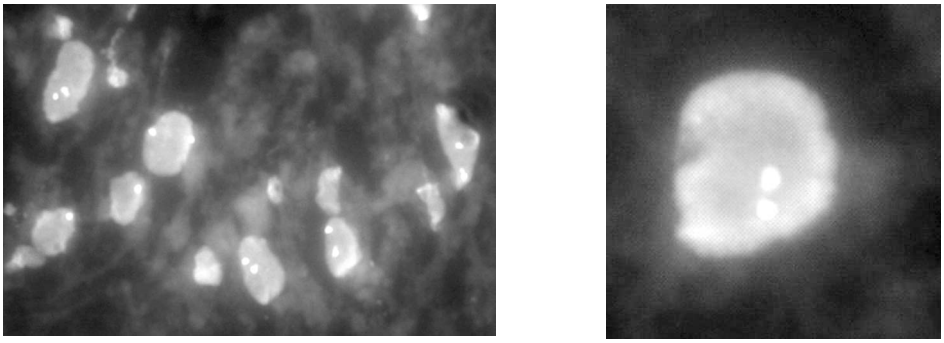


Fig 8. Case 2. Most chorionic cells had two red spots in FISH.

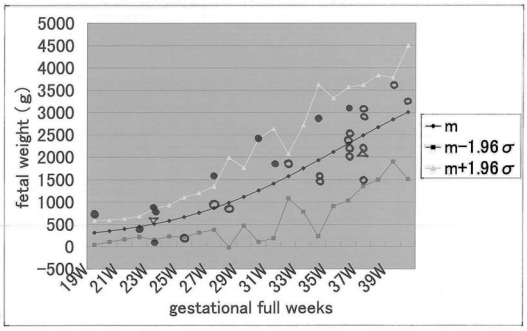


Fig 9. Fetal weight of pseudo-partial mole from reference, which was limited within normal range. Closed circle (●) was complicated with Beckwith-Wiedemann syndrome and open circle (○) was free from this syndrome(1). There was no significant difference between them. Our Case 1 (▽) and Case 2 (△) were also drawn.

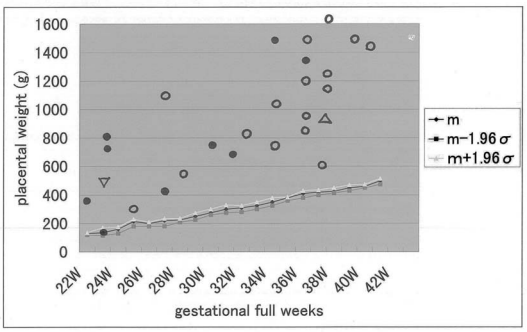


Fig10. Placental weight of reported cases was very heavy(1). Symbol marks were same as above and no statistical difference was found.