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Report

Fetal Thrombotic Vasculopathy in Association with Umbilical Artery Thrombosis and Single Umbilical Artery

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Fetal thrombotic vasculopathy (FTV) is a lesion due to thrombotic occlusion of large vessels of the placenta, and secondarily makes chorionic villi degenerative changes peripheral to the thrombotic occlusion. Although both umbilical vessel thrombosis and FTV are the lesions of vessels derived from the fetus, very few references report on their relationship.

We encountered a case of secondary single umbilical artery (SUA) caused by complete thrombotic occlusion, which was accompanied with FTV. Based on our placental pathology registry in the last 5 years we found 4 cases of umbilical artery thrombosis, of which 2 cases showed FTV. This fact suggests that umbilical artery thrombosis may be a cause of FTV and the detection rate of FTV accompanied by umbilical artery thrombosis may be greater if more attention was paid to FTV.

We found 3 out of 9 cases for SUA accompanied by FTV, and of which 1 had no arterial remnant. Therefore we can conclude that not all FTV lesions accompanied by SUA result from arterial occlusion. However, we obtained a case of umbilical artery thrombosis which brought the artery to atrophy. We speculated umbilical artery thrombosis as one of the causes of SUA.

Key words: fetal thrombotic vasculopathy, single umbilical artery, umbilical artery thrombosis, placenta, umbilical cord

Introduction

Fetal thrombotic vasculopathy (FTV) has pale wedge-shaped areas where villi are fibrotic and avascular with mural thrombi or obliteration in chorionic vessels or in villous stem vessels[1]. Cases of FTV with small foci are asymptomatic at birth, but thrombi may be present in somatic vessels of the neonates. The latter may cause infarction in the organs and limbs[2)~4)].

Single umbilical artery (SUA) is known to be associated with fetal congenital malformation. However its etiology, and whether it results from primary aplasia or secondary atrophy are controversial points[5)].

Although both umbilical vessel thrombosis and FTV are lesions of the vessels derived from the fetus, there are only limited references to be found concerning their possible relationship.

In the present study, we describe the relationship between FTV and umbilical arterial lesion, SUA and umbilical artery thrombosis. Furthermore, we give consideration to the cause of secondary umbilical arterial atresia.

Materials and Methods

Materials subject for this study were obtained from placental pathology archives of Tokyo Women's Medical University Medical Center East and Kanto Rosai Hospital registered between January 2004 and February 2009. All placentas were examined by authors (MF, MA) and gross findings were recorded and photographed.

In each of the cases, tissue samples were obtained

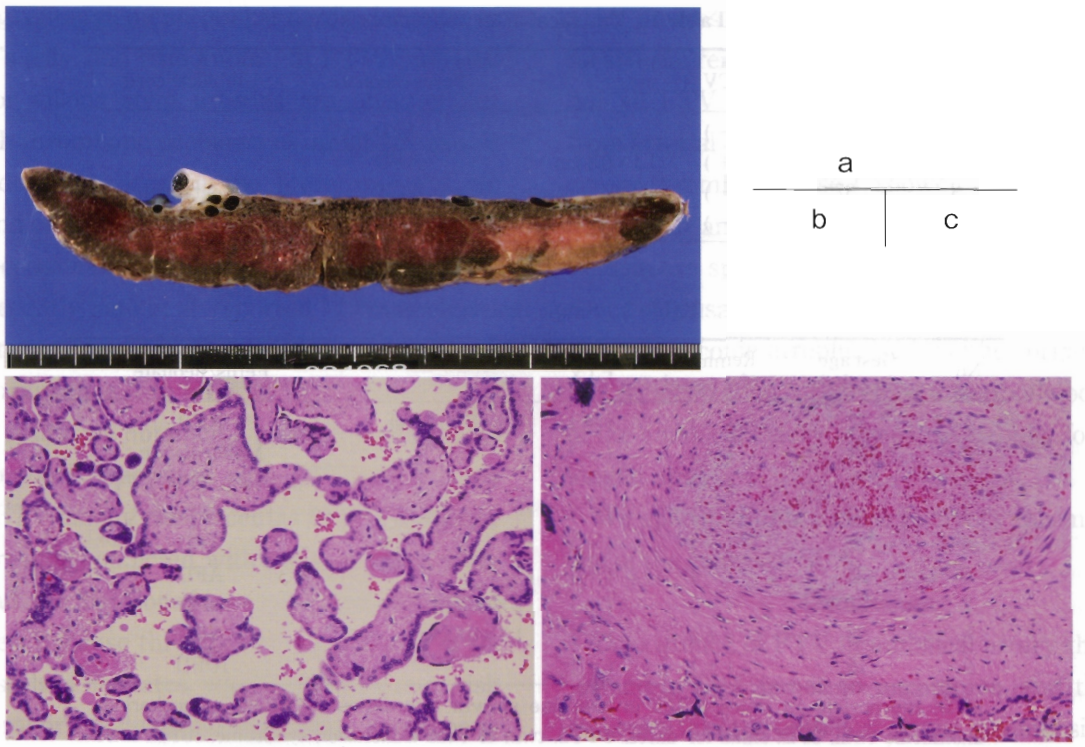

Fig. 1 Fetal thrombotic vasculopathy
a: A pale area at the periphery of the placenta.
b: A microscopic photograph of 1-a. An area of a group of avascular villi. ×200
c: An occluded vessel of the stem villus. ×200

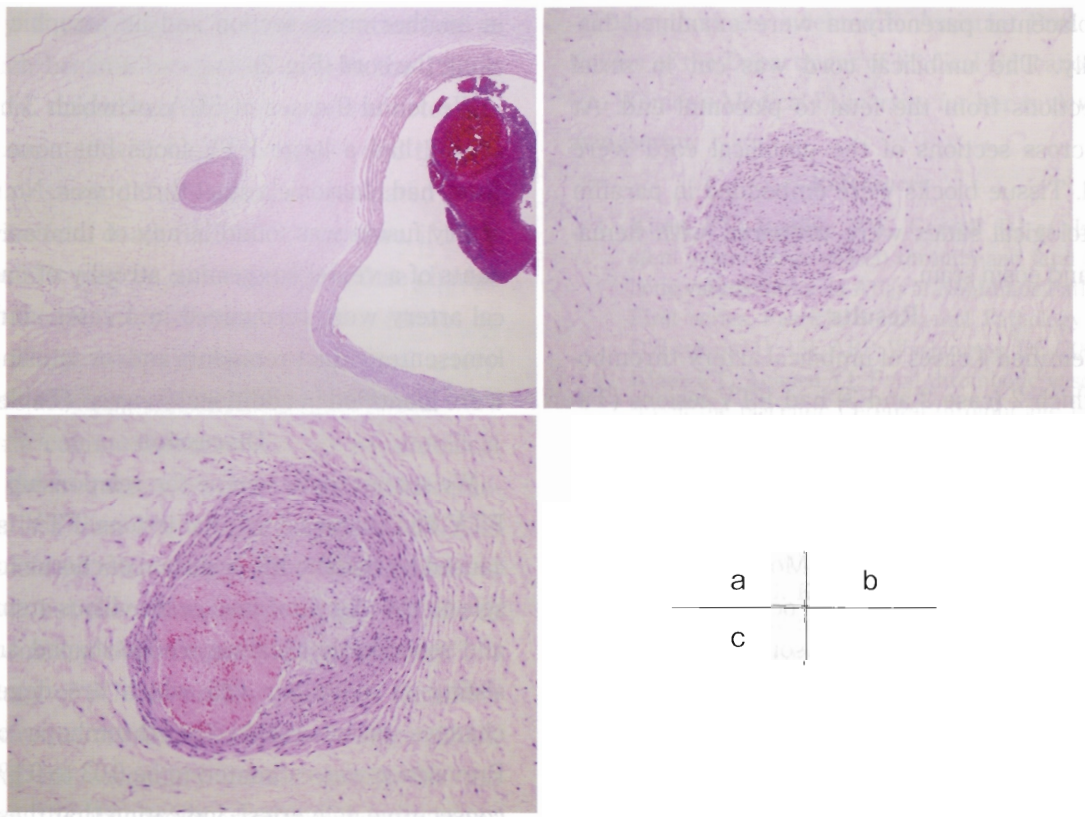

Fig. 2 Umbilical artery thrombosis with arterial atrophy
a: Thrombosed and atrophied umbilical artery. ×20
b: Atrophied umbilical artery. Cross section 8 cm from the umbilicus. ×200
c: Thrombosed and atrophied umbilical artery. ×200

Table 1 Umbilical artery thrombosis

No.	Gest.age (weeks)	FTV		Fetus/neonate	Umbilical cord
1	36	(−)		AFD	
2	38	(+)	1.4×0.8 cm	AFD	
3	37	(+)	small, multiple	IUGR	Hypercoiling
4	37	(−)		IUGR	Hypercoiling, 69 cm

Table 2 Single umbilical artery

No.	Gest.age (weeks)	Remnant of a vessel	FTV		Fetus/neonate
1	37	(−)	(+)	4.5×3×1.5 cm	AFD
2	21	(−)	(−)		Malformation
3	31	(−)	(−)		MD twin, SFD, TTTS
4	33	(+)	(−)		SFD
5	27	(−)	(−)		AFD
6	38	(−)	(−)		AFD
7	37	(+)	(+)	2×0.5 cm	SFD
8	38	(+)	(+)	1.3×0.8 cm	AFD
9	16	(+)	(−)		IUFD

AFD: appropriate for dates, IUGR: intrauterine growth retardation, MD twin: monochorionic diamnionic twin, SFD: small for dates, TTTS: twin to twin transfusion syndrome, IUFD: intrauterine fetal death.

after formalin fixation. One roll of free membrane and more than 5 sections including 3 normal parts of the placental parenchyma were examined histologically. The umbilical cord was cut in serial cross sections from the fetal to placental end. At least 3 cross sections of the umbilical cord were sampled. Tissue blocks were embedded in paraffin and histological slides were prepared with hematoxylin and eosin stain.

Results

We identified 4 cases of umbilical artery thrombosis, of which 2 (case 2 and 3) had FTV lesions (Table 1). These areas were sharply demarcated from the surrounding villous tissue at cross sections. The areas were made up of avascular villi with fibrous and hyalinized villous stroma. Most vessels of the villous stem show complete occlusion with fibromuscular hypertrophy, and some showed fibroblastic proliferation with extravasated erythrocytes (Fig. 1). We excluded foci consisting of less than 20 avascular villi which could be lesions of miscellaneous degenerative changes.

Umbilical arteries showed necrosis of the whole arterial wall, occlusion with thrombi, and atrophy partly along the cord. In case 3, calcification was found in the arterial wall. Case 1 had showed complete occlusion with a thrombus, showing necrosis in another cross section and an atrophic remnant along the cord (Fig. 2).

We found 9 cases of SUA, of which 3 had FTV. Case 1 had a large FTV focus but none of the 9 cases had chorionic vessel thrombosis. No umbilical artery fusion was found in any of the cases[6]. Remnants of a vessel suggesting atrophy of one umbilical artery were recognized in 4 cases, and omphalomesenteric duct remnants and/or vitelline vessels were identified in additional 5 cases[7] (Table 2).

Discussion

We set out to determine the relationship between FTV and umbilical arterial lesions. FTV is a lesion caused by thrombotic occlusion of chorionic (i.e. vessels on the placental surface) or villous stem vessels, and secondarily creating wedge-shaped areas consisting of avascular villi which are degenerative changes peripheral to the thrombotic occlusion. Prevalence was estimated to be 0.03 to 0.1% among consecutive deliveries[3], indicating that these lesions are rare.

FTV is often associated with umbilical cord disorders such as marginal or velamentous insertion, hy-

percoiling, entanglement, nuchal cords, decrease in Wharton's jelly, and true knots[8]. In FTV, chorionic vessels or villous stem arteries are affected but FTV with thrombotic occlusion of umbilical vessels have seldom appeared in the literature, and we have found only one report[9]. FTV were reported to be only occasionally accompanied by thrombi in the cord[10]. Recently Sato et al. reported 11 cases of umbilical artery thrombosis, but there was no description on coexistence with FTV[11].

In this study, we obtained 2 cases of umbilical artery thrombosis associated with FTV and 2 cases without FTV among the placentas from 2 hospitals, and our results conflicted with those of other studies which have mentioned a very limited number of such cases. Because thrombi are also present in somatic vessels of neonates, which places them at risk for cerebral or renal infarcts and other thromboembolic diseases in FTV[2)-4)], it can be said that FTV is associated with umbilical artery thrombosis. Furthermore we assume that FTV accompanied by umbilical artery thrombosis can be detected more frequently if pathologists pay closer attention to FTV which became recognized only in the 1990's. In addition, thrombosis of the umbilical artery is closely associated with fetal mortality[1)], and the placentas may show diffuse changes associated with intrauterine fetal death (IUFD)[12]. Therefore, if FTV lesion exists, it may be concealed by diffuse change due to fetal circulatory disruption, and it cannot be detected. In this study, no cases of umbilical artery thrombosis accompanied by IUFD were found.

SUA is a common abnormality of the umbilical cord, but the frequency reported in consecutive deliveries is less than 1%[13,14]. The fact that SUA is often associated with congenital malformations is well known but there is no malformation specific to this abnormality. Any organ can be affected[15)-17)]. The etiology of SUA is unclear. Arterial remnants are not infrequently found in the cords with a SUA, supporting the secondary atresia theory. On the other hand, the absence of arterial remnants keeps the possibility of congenital aplasia[18].

We could not find any reports in the literature on FTV coexistent with SUA, but in our 9 cases of SUA, 3 cases had FTV. Among 3 cases, 1 case had no arterial remnant, therefore we can conclude that not all FTV lesions accompanied by SUA result from arterial occlusion. However 1 case of umbilical artery thrombosis, case 1, showed umbilical arterial atrophy at another part of the cord. The umbilical vessels are specifically characteristized by the absence of "vasa vasorum", thus vessels occluded with thrombi become atrophic with neither organization nor recanalization[19], therefore thrombotic occlusion of the umbilical artery may cause atrophy for a prolonged time.

We speculate that umbilical artery thrombosis is one of the causes of SUA.

Conclusion

Coexistence of FTV in umbilical artery thrombosis and in SUA is not so uncommon, and this fact suggests that the umbilical artery thrombosis is one of the causes of FTV and also secondary atresia type SUA.

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臍帯動脈血栓症および単一臍帯動脈と，Fetal thrombotic vasculopathy との関係について

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Fetal thrombotic vasculopathy（FTV）は胎児由来の胎盤の血管（chorionic vessel および絨毛幹血管）の血栓性閉塞による，下流の絨毛の変性（硬化）である．同じ胎児由来の血管でありながら，臍帯血管の閉塞と FTV で見られる絨毛の病変の関係についてはこれまでほとんど論じられていない．

我々は臍帯動脈血栓症を原因とする単一臍帯動脈（SUA）の胎盤に FTV を合併した症例を経験した．そこで5年間の2施設の胎盤病理記録を検索したところ，4例の臍帯動脈血栓症の2例に FTV が合併していた．我々が収集した症例数は少ないが，臍帯動脈血栓症に FTV が合併したという報告が極めてまれであるということとは一致しない．FTV の病変を念頭に置いて見逃さなければ，その頻度はもっと高く，臍帯動脈血栓症が FTV の成因の一つであると推測する．

SUA は成因によって無形成と後天的退縮の2つに分けられる．9例の SUA のうち3例に FTV が合併していた．このうちの1例には後天的退縮を示唆する動脈の痕跡がなかったので，FTV を合併している SUA の全部が動脈の閉塞に因るとは断定できない．しかし我々は明らかに臍帯動脈血栓症が臍帯動脈の萎縮をもたらした1例を経験した．これらのことから臍帯動脈血栓症が SUA の成因の1つであると推察した．