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Japanese case series and review of the literature

Makiko Ohyama

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CASE REPORT

Umbilical cord ulcer: Japanese case series and review of the literature

Makiko Ohyama

Abstract:

Background: The association of umbilical cord ulcer (UCU) and congenital upper intestinal atresia (CUIA) has been reported since 1991. CUIA is a treatable disease itself with fair prognosis. It is not well acknowledged that some infants who have CUIA and UCU develop hemorrhagic shock followed by intrauterine demise/neonatal death. Most of the reported cases were from Asia, especially from Japan.

Objective: We reviewed reported cases with CUIA accompanied by UCU. We intend to find out clinic-pathological characteristics of this serious condition.

Method: We searched the above-mentioned association using Pub Med, Japanese journals, and congress abstracts. We reviewed clinical summaries the specimens of placentas and the umbilical cords of patients with CUIA who or or who's mothers were admitted to our hospital.

Result: Sixty-four cases with CUIA accompanied by UCU have been identified. Only 7 cases of this association have been published in countries other than Japan. In contrast, in Japan, the reported number of cases has increased since the first report from our hospital in 1996. As of December 2011 57 cases have been reported in Japan, including 15 cases from our hospital. Outcome was described in 63 of the 64 cases: 28 infants (44%) resulted in intrauterine or neonatal death, while 35 lived, of whom 8 had severe sequel. Pathological examination of 108 placentas of infants with CUIA in our hospital revealed 15 of complete/lacerated and 1 of abortive UCU were found.

Conclusion: Mortality rate of the association is as high as 44%. Close observation using fetal ultrasonography might predict massive hemorrhagic event.

Keywords: *intestinal atresia, umbilical cord ulcer*

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Introduction

Congenital upper intestinal atresia (CUIA) including duodenal and jejunal atresia are basically common congenital disease with fair prognosis. However, recent knowledge revealed the prognosis is poor when CUIA is accompanied with umbilical cord ulcer (UCU)[1-3]. About 40% of fetus or infants with this association were reported to be died of hemorrhagic shock. Hemorrhagic points are ulcerated umbilical vessels. This life-threatening event occurs at around delivery. Most of the published cases were from Asia, especially from Japan.

The objective of this study is to review reported cases with CUIA accompanied by UCU to find out clinic-pathological characteristics of this serious condition.

Method

We searched the above-mentioned association using Pub Med, Japan Medical Abstracts Society, and congress abstracts related to perinatal medicine as late as Dec. 2011.

We reviewed clinical summaries and placentas of patients with CUIA admitted to our hospital between 1992 and 2010. Detailed method of placental examination was previously described [2].

Statistical analyses were performed using JMP 7, SAS (SAS Institute Inc., Cary, NC, USA). Contingency table analysis using the Fisher's exact probability test assessed the statistical difference in categorical variables.

Literature review

We identified 64 cases of UCU in association with CUIA. The clinical characteristics of these 64 infants identified as of December 2011 are shown in the Table 1.

Median gestational age at delivery was 34 (28 to 37) weeks and median birth weight was 1998 (884 to 2870) grams. Polyhydramnios was detected in 43 of 49 reported cases. Modes of delivery were 38 of caesarian including 35 of emergency caesarean, 21 of vaginal and 5 of unknown. The type of the intestinal atresia associated with the UCU is duodenal or jejunal atresia (duodenal; 32, jejunal; 29, duodenal and jejunal 1, unknown 2). Associated anomalies other than CUIA were observed in 14 cases; 6 of chromosomal anomalies including 4 of trisomy 21, and 8 of other congenital anomalies. Reported hemoglobin levels ranged from 1.4g/dl to 19.4g/dl with 7.8g/dl of median. Hemorrhagic shock was present in 33 of 51 live births.

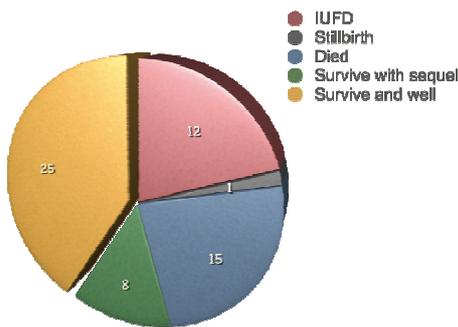


Fig.1 Outcome of literally reported cases with 53 CUIA with UCU up to Dec.2011.

Adding patients of anemia without shock, either hemorrhagic shock or anemia was observed in 78.4% of live births. Outcome was described in 63 of 64. There were 12 intrauterine fetal deaths, 1 stillbirth, and 15 infantile deaths. Eleven of infantile death occurred before 1 month. In total, 28 patients (44%) died as intra-uterine demise or after birth. Thirty-five were alive, but eight patients had moderate to severe sequel. Combined mortality/morbidity was 54%. (Fig.1)

Review of our own CUIA patients with or without UCU

Case presentation

A 33-weeker diagnosed as jejunal atresia antenatally was born by emergent caesarean section due to non-reassuring fetal status. Following delivery, the infant died of hemorrhagic shock from a ruptured umbilical vessel. Her hemoglobin level was 1.4g/dL. The umbilical arteries were engorged and coiled like a telephone cable (Fig.2).



Fig.2. Coiled telephone-line like engorgement of the umbilical arteries

We reviewed the incidence of UCU in cases of CUIA treated at our hospital. Between 1993 and 2010, 108 infants with CUIA were admitted to our hospital. Pathological examination of 86 placentas revealed 15 cases of complete/lacerated UCU and 1 case of abortive UCU.

Next we sought the relationship between UCU and congenital anomalies in addition to CUIA. Of 108 infants with CUIA 58 had additional congenital anomalies and 50 had not. Seven of former and 9 of latter group developed UCU. (Table 2) No relationship was observed between additional congenital anomalies and UCU in patients with CUIA.

Table 2. Additional congenital anomalies with or without UCU

	UCU		Subtotal
	Yes	No	
Congenital anomalies			
Yes	7	51	58
No	9	41	50

Of 108 infants with CUIA 34 had chromosomal anomalies. Two of 34 developed UCU. Four of 74 infants without chromosomal anomalies developed UCU. (Table 3) No relationship was observed between chromosomal anomalies and UCU in CUIA.

Table 3. Chromosomal anomalies with or without UCU

	UCU		Subtotal
	Yes	No	
Chromosomal anomalies			
Yes	2	32	34
No	14	60	74

Color of vomitus in 15 patients with UCU at our hospital was examined. Ten had bile-stained vomitus and 2 had brown-tan colored vomitus.

Placental pathology of UCU in our series revealed one or several spots of the linear ulcer along with the umbilical vessels macroscopically. The ulcer is usually seen on the arterial wall, sometimes on the wall of vein. Characteristic microscope findings are thinning or the tear of the umbilical vessel accompanied by degeneration of the neighboring Wharton's Jelly. (Fig.3)



Figure3. Randomly distributed multiple small ulcers were observed in a linear fashion along the spirals of the umbilical arteries after fixation.

Microscopically, an artery protruded over Wharton's jelly. (Fig.4,5)

Sometimes degenerative vessels lost their original structure and were replaced by degenerative myocytes, macrophages and some inflammatory cells (Fig.6)

There was one abortive case, in a baby with duodenal atresia who did not develop anemia or shock. (Fig. 7)

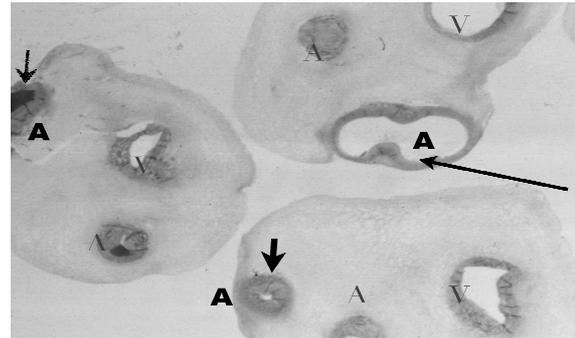


Figure 4. Serial cut sections of an affected umbilical cord. Wharton's jelly is defected and the arteries are exposed. The short arrows indicate degenerated umbilical artery. The long arrow shows a dilated thin-walled artery. Bold capital

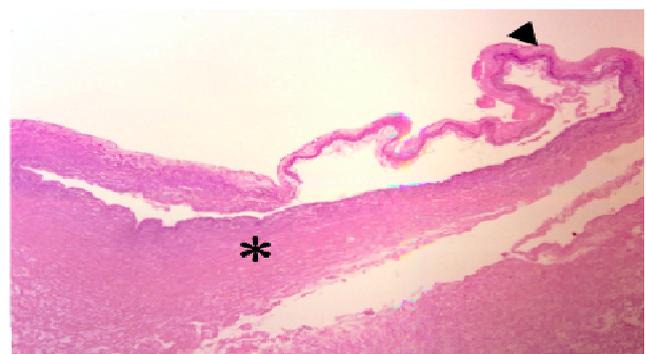
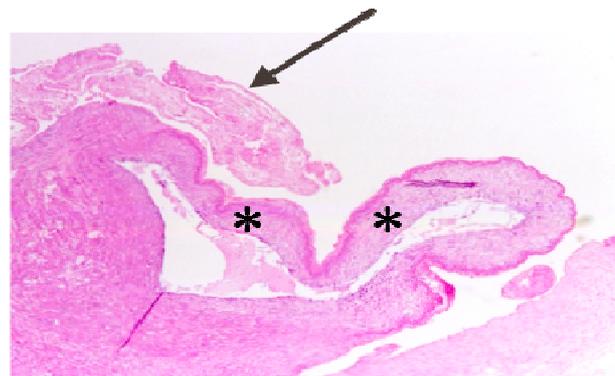


Fig.5 A low-power view of a severely dilated affected artery. The asterisks indicate necrotic arterial media. The arrow shows degenerated Wharton's jelly. The arrowhead indicates attenuated dilated vessel wall.

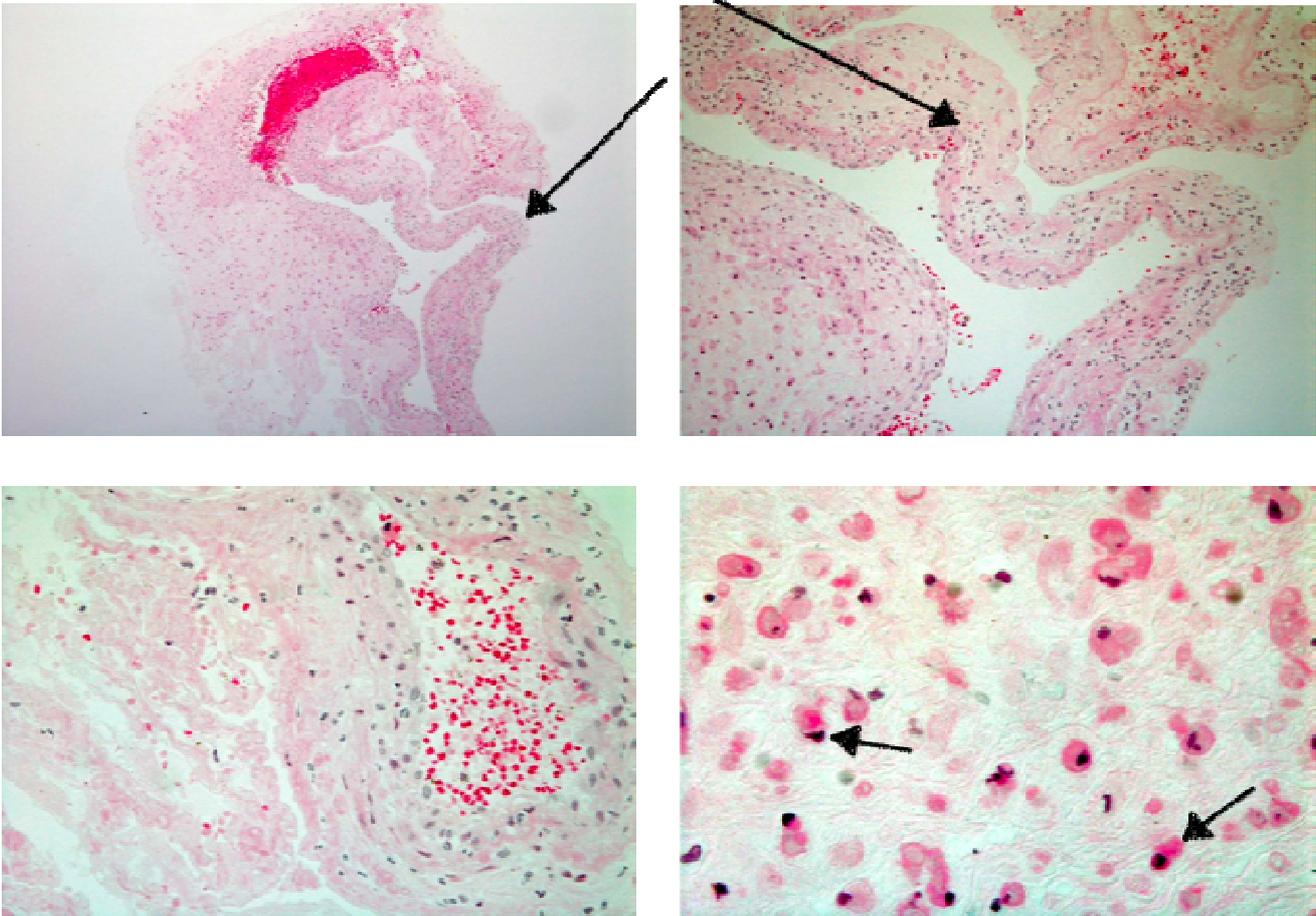


Fig.6 Low-power views of the umbilical vein show thinning of the winding dilated wall (long arrows). Lower right photo indicates the possible presence of degenerative myocytes (short arrows).

Discussion

An association between UCU and CUIA was first reported in 1991 by Bendon et al who described three cases [4]. One of his patients was stillbirth. Khong reported the 4th case in 1994[5]. His patient was severely asphyxiated due to hemorrhagic shock and died of sequel. We encountered the 5th case in 1994 [1]. In December 2011, we identified 64cases of UCU in association with CUIA. Only 7 cases were reported outside of Japan. [4-8]. In contrast, 57 cases were reported in Japan, including 15 cases from our hospital [1-3,9-15].

We considered that the mechanism of the UCU is injury of Wharton's jelly and the umbilical vessels by the bile constituent vomited by a fetus, considering that the atresia is distal from the papilla of Vater [2,3].

Altshuler et al [16] reported the concept of meconium-induced necrosis of fetal surface and umbilical cord vascular necrosis and ulceration]. They reported 2 cases of UCU. Their patients did not develop bleeding. Wang et al reported prolonged umbilical cord encirclement resulting in lineal ulcer-like lesion on the Wharton's jelly [17]. Again, no bleeding event occurred in the report. Literature cases of UCU resulting in vascular rupture were always associated with CUIA.

Ichinose et al. developed original grading of degenerative changes of UCU and found clinical symptom of UCU occurred as grade increased up to 3 or 4 [18]. On the other hand, findings similar to their grade 3 are not so rare findings on umbilical cords in routine placental examination. We reported 3 abortive cases with UCU in the previous article [2]. We omit 2 cases through reviewing specimens of CUIA. The remaining abortive case showed severe degeneration of Wharton's jelly without degeneration of vessel wall. Ichinose et al pointed that the number of macrophages was significantly increased in the Wharton's jelly in the intestinal atresia

cases. This finding favors the degeneration theory of UCU proposed by us [2].

In UCU series, sites of intestinal atresia are either duodenal or jejunal (33 or 28, respectively). In general, more than 80% of duodenal obstruction occurs at or below the ampulla of Vater [19]. In our cases, most of vomit appeared bile. Subsequently, bile must be responsible for degeneration of Wharton's jelly. Another author suspects trypsin or gastric juice as criminal [18]. These speculations await further study.

When a fetus vomits in utero, vomitus may be diluted in amniotic fluid, especially when polyhydramnionic status. The vomitus may hit the nearest segment of his umbilical cord. Concentration of vomitus might be higher there than other area. Prolonged exposure of bile or other digestive enzymes may lead to severe damage on Wharton's jelly and on umbilical vessels. The composition of bile is similar to meconium. Fetal surface of the placenta with UCU also showed necrosis as well as umbilical cord. Chronic exposure to bile might lead to degeneration of both Wharton's jelly and fetal surface.

We consider genetic cause is unlikely in UCU because of following findings. In our 108 cases, patients with CUIA were commonly associated with additional congenital anomalies or chromosomal anomalies (53.7% and 31.8%, respectively). However, we found no relationship between UCU in CUIA and additional congenital or chromosomal anomalies. Chromosomal anomalies in 64 cases of UCU were reported as trisomy 21 in 4, and partial 13 monosomy in 3. These anomalies are well known to be associated with CUIA.

According to our own study, incidence of the UCU in infants with the CUIA was 14.8%, if there were no case of the UCU in the unexamined placentas. The incidence of association of the UCU and CUIA is different according to the site of atresia. Incidence of the UCU was higher in the jejunal atresia (25%) than in the duodenal atresia (10.5%), although not statistically significant ($P>0.05$). We speculate the reason of lower incidence of the UCU in the duodenal atresia is some infants with the duodenal atresia did not vomit bile because their sites of atresia were oral to the papilla of Vater [2].

A fatality rate of the UCU is extremely high. Once the UCU developed, the mortality rate was 44%, which is similar to other reports [2, 8] Previous reports described features common to NRFS, such as disappearance of fetal heart-rate variability, continuous bradycardia, and loss of fetal biophysical profile, at the beginning of the bleeding

event. However, prognosis did not necessarily improve following emergent caesarean section. Of the 35 infants delivered by urgent caesarean section after the onset of NRFS, 14 infants died and 5 developed severe sequel

Recent fetal ultrasonographic approach showed some promising findings; a spot of bleeding from the tortuously winding ulcerative umbilical vein, and fibrinous material in amniotic fluid [8]. Histological findings of the ulcerative lesion showed denatured and stretched vessel walls [2]. Therefore, detecting a winding vessels or a small amount of bleeding may predict upcoming massive bleeding.

The change of the intrauterine pressure is considered to lead tear of the denatured blood vessel [1,2]. It is important to observe umbilical cord in detail by ultrasound as well as continuous fetal heart rate monitoring during labor or when rupture of membranes occur.

Conclusion

It is clinically important to acknowledge the association between UCU and CUIA because the mortality rate for this association can be as high as 44%.

Close observation using fetal ultrasonography may enable prediction of massive hemorrhagic events.

Finally, both clinicians and pathologists are encouraged to closely examine the umbilical cord of CUIA.

References

1. Yamanaka M, Ohyama M, Koresawa M, et al: Umbilical cord ulceration and intestinal atresia *Eur J Obstet Gynecol Reprod Biol* 1996; 70:209–212.
2. Ohyama M, Itani Y, Yamanaka M, et al, Umbilical cord ulcer: a serious in utero complication of intestinal atresia. *Placenta* 2000; 21:432–435.
3. Ohyama M, Itani Y, Ishikawa Y, et al, Is Umbilical cord ulcer associated with congenital upper intestinal atresia so rare? Japanese case series and review of the literature. *Fetal Diag Therapy* 2010; 28: 236.
4. Bendon RW, Tyson RW, Baldwin VJ, Cashner KA, Mimouni F, Miodovnik M: Umbilical cord ulceration and intestinal atresia: A new association? *Am J Obstet Gynecol* 1991; 164: 582-586.
5. Khong TY, Ford WDA, Haan EA: Umbilical cord ulceration in association with intestinal atresia in a child with deletion 13q and Hirschsprung's disease. *Arch Dis Child* 1994; 71: F212-3.

6. Khurana A, Huettner PC, Cole FS: Umbilical cord ulceration as a cause of hypoxic-ischemic encephalopathy: report of a case and review of the literature. *J Perinatol* 1995; **15**: 423-425.
7. Chan SS, Lau AP, To KF, Leung TY, Lau TK, Leung TN: Umbilical cord ulceration causing foetal hemorrhage and stillbirth. *Hong Kong Med J* 2008; **14**: 148-51.
8. Nijagal A, Rand L, Goldstein R, et al., Intrauterine umbilical cord hemorrhage with associated jejunal atresia captured by real-time ultrasound. *Am J Obstet Gynecol* 2009; **200**: e5-6. PMID: 18992865
9. Kimura T, Usui N, Kamata S, et al, Umbilical cord ulcer associated with fetal jejunal atresia: report of 2 cases. *Fetal Diag Ther* 2003; **18**: 144-147. PMID: 12711866
10. Anami A, Morokuma S, Tsukimori K, et al, Sudden fetal death associated with both duodenal atresia and umbilical cord ulcer: a case report and review. *Am J Perinatol* 2006; **23**:183-188. PMID: 16586238
11. Shimizu S, Kawagishi R, Arimoto-Ishida E, et al, Fetal hemorrhage associated with congenital intestinal atresia. *J Obstet Gynaecol Res* 2007; **33**: 726-30. PMID: 14641701
12. Hidaka N, Chiba Y: Intrauterine hemorrhage from an umbilical cord ulcer associated with fetal duodenal atresia: a case report. *Arch Gynecol Obstet* 2007; **275**: 219-22. PMID: 16900345
13. Miyachi K, Kikuchi A, Kitsunezaki M, et al, Sudden fetal hemorrhage from umbilical cord ulcer associated with congenital intestinal atresia. *J Obstet Gynaecol Res* 2007; **33**: 726-730. PMID: 17845338
14. Miyake H, Yamamoto A, Yamada T, Okazaki K, Morita K, Kondo M, Ishida T, Nishina T, Yokota A, Nakai A, Takeshita T: Umbilical cord ulceration after prenatal diagnosis of duodenal atresia with interstitial deletion of chromosome 13q: a case report. *Fetal Diag Ther* 2008; **24**: 115-118. PMID: 18648211
15. Ohyama M: Perinatal diseases recognized by placental examination. *Perinatal Medicine (Tokyo)* 2010; **40**: (article in Japanese)
16. Altshuler G, Arizawa M, Molnar-Nadasdy G. Meconium-induced umbilical cord vascular necrosis and ulceration: a potential link between the placenta and poor pregnancy outcome. *Obstet Gynecol.* 1992;**79**:760-6. PMID: 1565362
17. Wang G, Bove KE, Stanek J. Pathological evidence of prolonged umbilical cord encirclement as a cause of fetal death. *Am. J Perinatol.* 1998; **15**: 585-588. PMID: 9926881
18. Ichinose M, Takemura T, Andoh K, et al., Pathological analysis of umbilical cord ulceration associated with fetal duodenal and jejunal atresia. *Placenta* 2010; **31**: 1015-1018.
19. DeLorimier AA, Fonkalsrud EW, Hays DM. Congenital atresia and stenosis of the jejunum and ileum. *Surgery* 1969;**65**:819-27.

