## Histopathological Findings in Spontaneous Hematoma of the Umbilical Cord

Severe Hypoxic-Ischemic Encephalopathy in a Term Survived Newborn

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**Background:** Spontaneous hematoma of the umbilical cord is a rare, unpreventable, and dramatic event mainly due to a disruption of the vascular wall, often resulting in adverse perinatal outcome.

**Case:** We describe a case of a term fetus with acute hemorrhage in the cord occurred intrapartum during spontaneous vaginal delivery. No iatrogenic factors were involved because no drugs, obstetric instruments, or procedures were applied. Umbilical hematoma probably developed in a time frame of 90 seconds, when the electronic fetal monitoring tracing detected a loss of fetal heart rate. At birth, the baby was in serious conditions with a low Apgar score (always 3 at 1, 5, and 10 minutes) and severe mixed acidosis. He was intubated, was ventilated, and underwent therapeutic hypothermia. Although all standard emergency procedures had been immediately applied, hypoxic-ischemic encephalopathy ensued within 24 hours postnatal. Placental examination revealed in the cord disruption of the elastic fibers in the vessels walls. Moreover, myofibroblasts in the Wharton's jelly appeared reduced in number and blunted, instead of their usual stellate shape. Chorioamnionitis but no funisitis was also present.

Clinical follow-up of the child, aged 4 years, showed spastic tetraplegia, seizures, central deafness, and blindness.

**Conclusions:** Intrinsic anomalies of the cord favored vascular rupture, hematoma of the cord, and acute fetal hypoxia. Placental examination played a key role in excluding medical malpractice because hematoma of the cord was a damaging, not otherwise preventable, event.

Key Words: umbilical cord hematoma, vascular elastic fiber disruption, myofibroblasts, hypoxic-ischemic encephalopathy, cerebral palsy

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**S** pontaneous hematoma of the umbilical cord is a rare, unpreventable, and dramatic event due to a disruption of the vascular walls, often resulting in adverse perinatal outcome.<sup>1–5</sup> Hemorrhage within the Wharton's jelly may result in compression of the vessels leading to a reduced blood flow to the fetus and consequent fetal hypoxia. Hematoma can occur during the pregnancy but is more frequent during labor, requiring immediate fetal extraction. Even though urgent procedures are promptly performed, fetal mortality is considerably high. A very few cases of spontaneous hematoma of the cord are described in literature, mostly associated with stillbirth. Nevertheless, some infants reported

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did not experience any consequences, at least at birth, and were discharged well. However, in none of these patients, long-term follow-up was available.<sup>4,6</sup>

The causes of rupture of umbilical cord vessels are mainly unknown,<sup>4</sup> although some favoring factors have been identified, such as intrinsic degeneration of the vessel wall, anomalous cord insertion (marginal or velamentous), length of the cord (too short or too long), traumatic events, and placental infections including funisitis. Funisitis is a negative additional factor to poor outcome and fetal demise, as it may further contribute to weaken the vascular wall. Only in 1 case,<sup>6</sup> the infant survived, admitted to neonatal intensive care unit, and then discharged in good conditions after 14 days. Of note, in spontaneous hematoma of the cord, funisitis and chorioamnionitis seem to be an infrequent association, as it was reported only in 1 case<sup>7</sup> where the baby died in utero.

We present a case of a 4-year-old child who experienced hypoxic-ischemic encephalopathy (HIE) at birth and then developed cerebral palsy. Placental examination showed hematoma in the cord and *Escherichia coli* chorioamnionitis but no evidence of funisitis. Umbilical cord displayed unusual findings such as vascular disruption of the elastic fibers and reduction in stromal myofibroblasts, which were abnormally shaped, blunted instead of stellate. These intrinsic anomalies probably favored vascular rupture, hematoma of the cord, and acute fetal hypoxia. This lethal event was otherwise not preventable, and placental examination played a key role in excluding medical malpractice.

## CASE REPORT

The mother was a 19-year-old primigravida at term with unremarkable medical history and uneventful pregnancy. The couple was consanguineous. Labor went on for 2 hours and 25 minutes monitored by continuous electronic fetal monitoring (EFM). No drugs or other medical aids were used to induce and favor delivery, which was spontaneous and vaginal. At birth, there was a loss of fetal heart rate lasting 90 seconds. Apgar score was 3 at 1, 5, and 10 minutes, respectively. The newborn infant was immediately intubated and ventilated. Umbilical artery sampling displayed severe mixed acidosis (pH 6.68; PCO<sub>2</sub>, 116 mm Hg; standard bicarbonate, -24 mEq/L) and fetal anemia (hemoglobin level, 11 g/L). Systemic therapeutic hypothermia was immediately started (mean rectal temperature of 33.5°C for 72 hours, followed by slow rewarming). Severe HIE ensued after the first 24 hours in postnatal period.

Gross placenta examination revealed an amniotic band at umbilical cord insertion into the chorionic plate, markedly congested chorionic vessels with dispersed distribution, and convoluted decourse. In the cord, a fresh hematoma was detected. Histological examination showed a rupture in the wall of the umbilical vein with discontinuity in the layers of the subintimal and internal elastic lamina. One umbilical artery presented peripheral dissection, subintimal myxoid degeneration, and widespread disruption of the elastic fibers (Fig. 1).

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**FIGURE 1.** Umbilical cord hematoma (hematoxylin-eosin staining,  $\times$  2). Extensive spontaneous hemorrhage of the cord surrounding the artery (A) and vein (V). The latter also shows dissection of the vascular wall.

Immunohistochemistry for desmin documented a marked reduction in myofibroblasts in the Wharton's jelly, which also presented a blunted shape (Fig. 2). The membranes had diffuse chorioamnionitis (maternal inflammatory response, stage 2, grade 1) in which bacteriologic investigation using polymerase chain reaction DNA analysis (Roche, Basel, Switzerland) performed on chorionic villi demonstrated the presence of *E. coli* infection.

Postnatal T2-weighted magnetic resonance single-shot-spin echo imaging using a 1.5 T (Siemens, Germany) performed at 10 and 21 postnatal days demonstrated abnormal signal intensity in the lentiform nuclei and thalami, as well as absence of normal signal of the rolandic cortex bilaterally. A diffuse hyperintensity of the white matter throughout the centrum semiovale was also seen bilaterally. Neurodevelopmental follow-up at the age of 4 years showed spastic tetraplegia, seizures, central deafness, and blindness.

## DISCUSSION

Spontaneous hematoma of the umbilical cord, due to disruption of the vessels, is a rare but dramatic obstetric event (1/5500 births).<sup>8</sup> Acute hemorrhage, often caused by rupture of the umbilical vein, determines sudden deterioration of fetal conditions, detected by rapid changes in EFM tracing, that leads to death or HIE in survivors. Favoring and adverse factors are infective funisitis,<sup>9</sup> short cord,<sup>10</sup> entangling and knotting,<sup>11</sup> twisting and traction,<sup>4</sup> and postmaturity.<sup>12</sup> In addition, prolonged meconium exposure of the cord may cause myonecrosis of the vessel walls and blood extravasation.<sup>11</sup> Moreover, meconium has a vasoconstrictive effect, worsening fetal hypoperfusion, and hypoxia. Umbilical cord hematoma, associated with poor outcome, may also be a rare complication of cord cyst and hemangioma.<sup>13–17</sup>

In our case, pregnancy was unremarkable; the delivery was spontaneous; and no drugs, iatrogenic procedures, or invasive procedures were applied. Fetal distress acutely occurred at birth, when fetal heart rate was not detected for 90 seconds at EFM tracing. Rupture of the umbilical cord vessels likely happened during this time. The amount and duration of fetal blood loss mutually could have probably determined the severity of acute fetal hypoxia with mixed acidosis and anemia. Moreover, *E. coli* chorioamnionitis was a further contributory factor in worsening clinical conditions. Nevertheless, the infant survived, maybe because the hemorrhage occurred just before birth and blood loss was not considerable

enough to cause death. Hypoxic-ischemic encephalopathy was then the result of acute disruption of umbilical cord vessels, not counteracted by systemic hypothermia, considered helpful in lowering neuronal metabolic demand, and beneficial in reducing brain damage.<sup>2,9,18</sup> Moreover, histological examination of the cord showed multiple constitutional anomalies. First of all, an artery and a vein displayed elastorrhexis, characterized by widespread disruption and fragmentation of elastic fibers. Splitting of the elastic lamina was described only in the umbilical vein in 2 other cases of spontaneous hematoma of the cord.<sup>7,12</sup> Elastic fibers are essential components of extracellular matrix endowing the fundamental properties of resistance and resilience. These features are particularly important for arteries, which require high deformability and passive recoil with no need of energy. Elastic fibers include a central core of elastin and an outer structure made of microfibrils, rich in fibrillin. Gene mutations in each component, such as elastin and fibrillin 1 and 2, are encountered in connective tissue disorders, characterized by variability in expression, severity, and inheritance. Considering our case, we found abnormal elastic fibers in the umbilical cord with elastorrhexis. This may have determined altered elastic resistance, limiting the vascular capacity for reacting to compression or stretching forces, which are particularly powerful during labor. This anomaly may disclose an underlying connective tissue disorder event though the child does not currently present specific symptoms. However, fibrillin 1 mutations, mainly associated with Marfan syndrome (OMIM #154700), also include a wide spectrum of Marfan-like phenotypes, some of them restricted to cardiovascular disorders, in the absence of skeletal or ocular manifestations.<sup>19,20</sup> Marfan-like pattern has also been described in aneurismatic vascular dilatation and in some hematologic diseases such sickle cell anemia.<sup>21</sup> Of note, parent consanguinity may have contributed to the expression of a connective tissue disease although inheritance, in that kind of disorders, is mainly autosomal dominant.<sup>20</sup> The second abnormal finding observed in the umbilical cord was that myofibroblasts, the main stromal cells of Wharton's jelly, were markedly reduced in number exhibiting an unusual blunted shape, instead of being fusiform or stellate.<sup>22</sup> In normal condition, the contractile property of myofibroblasts helps to maintain Wharton's jelly elasticity, which attenuates the effects of external forces on umbilical cord vessels.23



**FIGURE 2.** Histology of the Wharton's jelly in the umbilical cord. A, Our case: myofibroblasts in the Wharton's jelly are markedly reduced and show a blunted shape. B, Uneventful pregnancy at 40 weeks' gestational age: myofibroblasts in the Wharton's jelly have a high stromal density and a spindle appearance (smooth muscle actin staining, brown cells, ×40).

In our case, Wharton's jelly myofibroblasts were defective in number and probably in functionality and contraction because of their unusual aspect. Therefore, overall elasticity of the cord was severely compromised, considering the additional adverse factors of vascular elastorrhexis and abnormal myofibroblasts, favoring together tears and lacerations. Placenta and umbilical cord examination should be mandatory in all cases of fetal hypoxia and adverse perinatal outcome because this may strongly help to discriminate biological natural causes of perinatal mortality and morbidity from extrinsic medical factors.

Analysis of the placenta is fundamental in differentiating between medical malpractice (eg, a delay in performing obstetrical procedures) and intrinsic placental anomalies, as in the case reported, such as defective components of Wharton's jelly and vascular elastic fibers. Constitutional anomalies of the cord were the critical biological factors that led to fetal acute hypoxia and HIE. Those findings were fundamental in preventing legal action by the family because no act of malpractice could be attributed to the operators.

## REFERENCES

- Naidu M, Nama V, Karoshi M, et al. Umbilical cord rupture: a case report and review of the literature. Int J Fertil Womens Med. 2007;52:107–110.
- Lyonnet R, Blanc PM. Rupture of the funicular vessels having caused the death of the fetus. *Bull Fed Soc Gynecol Obstet Lang Fr.* 1960;12:170–171.
- Leroux O, Michon G. Apropos of another case of hematoma of the cord caused by rupture of the umbilical vein with death of the fetus. *Bull Fed Soc Gynecol Obstet Lang Fr.* 1960;12:322–324.
- Gualandri G, Rivasi F, Santunione AL, et al. Spontaneous umbilical cord hematoma: an unusual cause of fetal mortality: a report of 3 cases and review of the literature. *Am J Forensic Med Pathol.* 2008;29:185–190.
- Baergen R. Cord abnormalities, structural lesions, and cord "accidents". Semin Diagn Pathol. 2007;24:23–32.
- Kumar A, Kaplan C, Mokrian S, et al. Intact newborn survival after spontaneous umbilical cord vascular rupture before labor. *Obstet Gynecol*. 2012;120:489–490.
- Summerville JW, Powar JS, Ueland K. Umbilical cord hematoma resulting in intrauterine fetal demise. A case report. *J Reprod Med.* 1987;32: 213–216.
- Sizun J, Soupre D, Broussine L, et al. Spontaneous umbilical cord hematoma, a rare cause of acute fetal distress. *Arch Pediatr.* 1995;2: 1182–1183.

- Tonni G, Leoncini S, Signorini C, et al. Pathology of perinatal brain damage: background and oxidative stress markers. *Arch Gynecol Obstet*. 2014;290:13–20.
- Seoud M, Aboul-Hosn L, Nassar A, et al. Spontaneous umbilical cord hematoma: a rare cause of acute fetal distress. *Am J Perinatol.* 2001;18: 99–102.
- Benirschke K. Obstetrically important lesions of the umbilical cord. J Reprod Med. 1994;39:262–272.
- Clare NM, Hayashi R, Khodr G. Intrauterine death from umbilical cord hematoma. Arch Pathol Lab Med. 1979;103:46–47.
- Brown R, Nicolaides K. Umbilical cord hematoma associated with an umbilical cord cyst and fetal death at 28 weeks of gestation. J Ultrasound Med. 2000;19:223–225.
- Sepulveda W, Wong AE, Gonzales R, et al. Fetal death due to umbilical cord hematoma: a rare complication of umbilical cord cyst. *J Matern Fetal Neonatal Med.* 2005;18:387–390.
- Søndergaard G. Hemangioma of the umbilical cord. Acta Obstet Gynecol Scand. 1994;73:434–436.
- Vougiouklakis T, Mitselou A, Zikopoulos K, et al. Ruptured hemangioma of the umbilical cord and intrauterine fetal death, with review data. *Pathol Res Pract.* 2006;202:537–540.
- Dombroswski MP, Budev H, Wolfe HM, et al. Fetal hemorrhage from umbilical cord hemangioma. *Obstet Gynecol.* 1987;70:439–442.
- Kasdorf E, Perlman JM. Hyperthermia, inflammation, and perinatal brain injury. *Pediatr Neurol.* 2013;49:8–14.
- Kielty CM, Sherrat MJ, Shuttelworth CA. Elastic fibres. J Cell Sci. 2002; 115:2817–2828.
- Milewicz DM, Urban Z, Boyd C. Genetic disorders of elastic fibre system. Matrix Biol. 2000;19:471–480.
- Tsomi K, Karagiorga-Lagana M, Karabatsos F, et al. Arterial elastorrhexis in beta-thalassaemia intermedia, sickle cell thalassaemia and hereditary spherocytosis. *Eur J Haematol.* 2001;67:135–141.
- Ryu YJ, Sook SH, Cho TJ, et al. Comparison of the ultrastructural and immunophenotypic characteristics of human umbilical cord-derived mesenchymal stromal cells and in situ cells in Wharton's jelly. *Ultrastruct Pathol.* 2013;37:196–203.
- Kobayashi K, Kubota T, Aso T. Study on myofibroblast differentiation in the stromal cells of Wharton's jelly. Expression and localization of alpha-smooth muscle actin. *Early Hum Dev.* 1998;51: 223–233.