

## Wharton's jelly absence: a possible cause of stillbirth

Eduarda Bittencourt Damasceno<sup>a</sup>, Patrícia Picciarelli de Lima<sup>b</sup>

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### ABSTRACT

The umbilical cord is a structure that provides vascular flow between the fetus and the placenta. It contains two arteries and one vein, which are surrounded and supported by gelatinous tissue known as Wharton's jelly. There are many umbilical cord abnormalities that are related to the prognosis of fetus survival and birth weight. The authors report a case of umbilical cord constriction due to the localized absence of Wharton's jelly, which was undiagnosed antenatally and had a fatal outcome. A review of the association between the absence of Wharton's jelly and an unfavorable pregnancy outcome was undertaken.

**Keywords:** Umbilical Cord; Wharton Jelly; Stillbirth.

### CASE REPORT

A male stillborn fetus was delivered at 33 weeks and 4 days of gestational age through a vaginal birth, which was the second pregnancy of a 32-year-old woman. The mother had a history of a previous ectopic pregnancy and left salpingectomy, plus type II diabetes mellitus

and arterial hypertension—the latter two without medical control. The woman stopped feeling the fetal movements 6 hours before hospital admission. An ultrasound examination diagnosed intrauterine fetal demise, and the labor was induced with misoprostol.

### AUTOPSY FINDINGS

The external examination showed a male stillbirth, weighing 2.260 g (z score: 0.59, 72 percentile, small for gestational age),<sup>1</sup> with marked maceration. A marked reduction of diameter over a 1-cm length segment of the umbilical cord at 3 cm distant from the fetal insertion site. No external or internal malformations were found (Figure 1A and 1B).

On gross examination, the placenta measured 15.0 × 14.0cm in diameters, corresponding to an area of 164 square centimeters (−1,4 z score and 1 percentile, small for gestational age),<sup>2</sup> 2.5cm of mean thickness (3.0 z score and 99 percentile, large for gestational age)<sup>2</sup> and weighed 425.0 g (1.1 z score and 87 percentile, adequate for gestational age).<sup>2</sup> The insertion of the umbilical

<sup>a</sup> Department of Pathology – Faculdade de Medicina – Universidade de São Paulo, São Paulo/SP – Brazil.

<sup>b</sup> Anatomic Pathology Service – Hospital Universitário – Universidade de São Paulo, São Paulo/SP – Brazil.

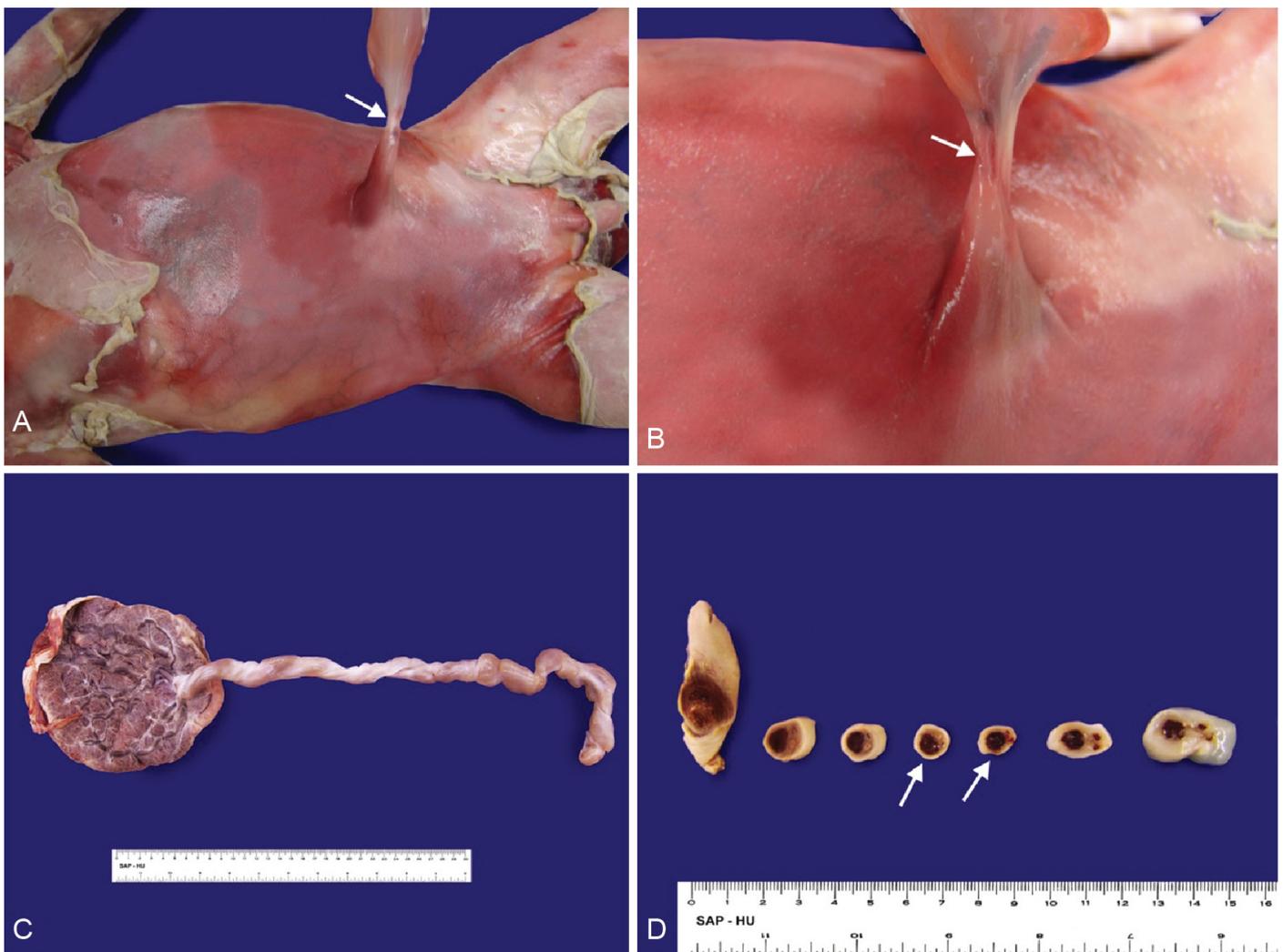
cord was marginal (Figure 1C). At microscopy, there were a mild subchorionic hematoma with thrombosis and few foci of dystrophic calcification of the trophoblastic villi. Thrombosis, hemorrhagic endovasculopathy or villi fibrosclerosis, which could be also associated with obstruction of fetoplacental circulation, were not present.

The umbilical cord measured 73.0 cm of length (4.5 z score and 99 percentile, large for gestational age),<sup>2</sup> and 2.2 cm in diameter (measured 3 cm from the fetal skin) (3.3 z score and 99 percentile, large for gestational age),<sup>2</sup> and was composed of three vessels. In the segment close to the placenta, the umbilical cord was morphologically normal, without areas of constriction. The umbilical coil index was 0,12, just above the lower limit of normality. In contrast, close to its insertion into the fetal abdomen, it presented an abrupt reduction in the diameter (corresponding to a 50% in the diameter reduction) (Figures 1A, 1B, 1D and 2A).

At microscopy, absence of Wharton's jelly was evidenced in the constricted segment. (Figures 2B and 2C).

## DISCUSSION

The umbilical cord—the fetal lifeline—is a structure that connects the fetus to the placenta, and is crucial for fetal development. It is composed of two arteries and one vein and is cushioned by a special type of mucous connective tissue known as Wharton's jelly. At birth, the average diameter and circumference of the umbilical cord in a normal-term infant is 1.5 cm and 3.6 cm, respectively.<sup>3,4</sup> Wharton's jelly seems to have the function of the adventitia layer, which is lacking in the umbilical cord, and binds and encases the umbilical vessels. Wharton's jelly is an amorphous substance, which is rich in glycosaminoglycans, proteoglycans, and



**Figure 1** – Gross examination of the stillbirth. **A** and **B** – Constriction of the umbilical cord close to its insertion into the fetal surface; **C** – External examination of the placenta and the umbilical cord. Note the marginal insertion of the umbilical cord at the placenta; **D** – Sequential cuts of the umbilical cord.



**Figure 2** – Gross and microscopy examination of the umbilical cord, showing the morphology of the constricted segment. **A** – Gross aspect of the constricted segment of the umbilical cord showing the absence of Wharton's jelly; **B** – The absence of Wharton's jelly at the umbilical cord; **C** – A segment of the umbilical cord with scant Wharton's jelly.

predominantly hyaluronic acid. It is surrounded by myofibroblasts, which are mesenchymal cells with the characteristics of both fibroblasts and smooth-muscle cells. Myofibroblasts have both fibrogenesis and contractile functions and produce increasing amounts of type I, II, and V collagen fibrils during the pregnancy, giving Wharton's jelly elastic and contractile properties as well as microfibrils.<sup>5</sup> Hyaluronic acid is the most common glycosaminoglycan—a hydrophilic component of Wharton's jelly that absorbs water and electrolytes. Umbilical cord elasticity confers resistance to external pressure, and acts as a physical buffer in the regulation of fetoplacental blood circulation and umbilical vessels.<sup>5,6</sup> It has been speculated that the cells of Wharton's jelly may participate in the regulation of umbilical blood flow. In some cases, the reduction in fetal growth could be directly associated with Wharton's jelly decrement, leading to hypoplasia of the umbilical vessels. If Wharton's jelly is poorly developed, or if the vessels remain unprotected, they become more prone to compression.<sup>7,8</sup>

The sonographic umbilical cord diameter and area increase as a function of gestational age until the 32nd week of pregnancy. After that, a reduction in the diameter of the umbilical cord can be observed due to the water content of Wharton's jelly at the end of the pregnancy.<sup>8</sup> Over a 1 year period, Proctor et al.<sup>9</sup> studied 497 umbilical cords of gestational ages ranging from 18 weeks to 41 weeks. They found that the umbilical cord diameter increases as the gestational age progresses until 28 weeks when it reaches a plateau at approximately 1.0 cm. These findings are in agreement with the antenatal ultrasound assessment of the umbilical cord that describes an increase in diameter

with gestational age until the third trimester.<sup>9</sup> Using Proctor's nomogram, they identified and classified the umbilical cord diameter as thin (< 10<sup>th</sup> percentile), average (10<sup>th</sup>–90<sup>th</sup> percentile) and thick (> 90<sup>th</sup> percentile), and concluded that the umbilical cord components were responsible for the diameter variation. According to this standard, the cord of the present case was a thick one. Their findings show that a significant increase in the vessel area (specifically an increase in the umbilical artery wall area) is responsible for a thick umbilical cord diameter, while a significant decrease in Wharton's jelly area is responsible for a thin umbilical cord diameter.<sup>9</sup>

Pathologic studies and case reports demonstrated that a thin umbilical cord is associated with oligohydramnios, fetal distress, and adverse pregnancy outcome.<sup>9</sup> Silver et al.<sup>10</sup> reported that in post-term pregnancies, the umbilical cord diameter is smaller in patients with oligohydramnios compared with normal amniotic fluid. In addition, these authors found a higher incidence of antepartum variable decelerations in patients with a small umbilical cord diameter compared with those with a normal umbilical cord. Raio et al.<sup>11</sup> found an association between the presence of a thin umbilical cord and the delivery of an infant who is small for its gestational age. Proctor et al.<sup>9</sup> showed that there was a relationship between the umbilical cord diameter and gross placental pathologic features. A thin umbilical cord was associated with low placental weight percentile, a single umbilical artery, and a marginal umbilical cord insertion.

Marked reductions in the diameter of the umbilical cord may be referred to as constrictions, stricture, torsion, and coarctation. When present,

they are frequently found close to the fetal insertion site, as was observed in our case. They are more prevalent in long cords and marked coiled cords. In these cases, the obstruction of blood flow occurs by the same mechanism as with excessive coiling. None morphological evidence of fetoplacental vascular obstruction was observed in the present case. Some authors suggested that it is either a primary deficiency of Wharton's jelly, or is due to a secondary phenomenon caused by a gradual decrease in Wharton's jelly at the fetal end of the cord.<sup>7</sup> It has been suggested that the umbilical cord constriction could be due to a degeneration of Wharton's jelly around the vessels, since normal development of the vessel would not be possible in the absence of embryonal mesenchyme, although no mucoid or degenerative changes were demonstrated.<sup>7</sup> Other possible physiopathologic mechanisms for this anomaly could be an incomplete fusion of the amniotic covering and the mesenchyme of the umbilical cord during early development, or a hypoplasia of this amniotic covering with a secondary loss of Wharton's jelly.<sup>7</sup> In 1961, Bergman, Lundin and Malmstrom<sup>12</sup> described the first case in which a segment of the umbilical arteries were devoid of their Wharton's jelly covering. The most common complication of this anomaly results in fetal demise, but cord constrictions have also been implicated in fetal growth restriction and fetal intolerance to labor;<sup>5</sup> in the present case, fetal weight was adequate for gestation age.

A different umbilical cord anomaly related to the lack of Wharton's jelly is known as *insertio funiculi furcate*. In those cases, the insertion site is normal, but as the cord vessels loose the Wharton's jelly their vessels become separated before reaching the placental surface. In a velamentous insertion, the umbilical cord is inserted into the membranes and the umbilical vessels remain unprotected for some distance before reaching the placenta. An increased incidence of fetal distress and perinatal mortality has been described in association with both velamentous insertion and *insertio funiculi furcata*.<sup>7</sup>

Baergen<sup>13</sup> describes four cases of stillbirth and umbilical cord constriction. In all the four cases, the absence of Wharton's jelly around the umbilical cord arteries described so far were associated with acute fetal distress and perinatal death, and this may have been due to compression of the unprotected vessels. According to Baergen,<sup>13</sup> this is consistent with animal studies in which fetal lambs that were subjected to intermittent partial chord

occlusion develop cerebral necrosis and serious fetal neurologic damage. Chronic partial obstruction can also lead to fetal growth restriction. Abnormally coiled cords, abnormally short or long cords, velamentous cord insertions, constrictions, true knots, cord entanglement, and cord prolapse have all been associated with an increased risk of fetal demise, neurologic injury, or abnormal development outcome.<sup>13</sup> In the present case, we observe a thick and under to normal coiled cord.

Filiz et al.<sup>5</sup> investigated the relationship between the amount of Wharton's jelly and its protective role in umbilical cord vessels, and hence, on fetal growth. Their study enrolled 299 women and concluded that the "quality" and characteristics of Wharton's jelly were both important in its protective role. Abnormal situations, such as a decrease in the hyaluronic acid content of Wharton's jelly and Wharton's jelly fibrosis, may affect the mechanical characteristics of the cord, which leads to impaired fetal circulation, anoxia, and fetal death.<sup>5</sup>

## CONCLUSION

The changes in the quantity or quality of Wharton's jelly affects the diameter of the umbilical cord and the hemodynamics of its vessels, leading to impaired fetal blood flow and consequently low weight gain and fetal demise. The constriction in the umbilical cord due to the absence of Wharton's jelly, which was seen in our case, much probably was the cause of fetal death since the autopsy did not show any malformations or other disorders. We highlight the need to study the umbilical cords in all cases of stillbirth.

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**Conflict of interest:** None

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**Correspondence:** Departamento de Patologia  
Hospital das Clínicas  
Faculdade de Medicina  
Universidade de São Paulo  
Av. Dr. Enéas Carvalho de Aguiar, 155 – 10 andar – São Paulo/SP – Brazil  
CEP: 05503-000 – Phone: +55 (11) 2661.6092  
E-mail: dudabd93@yahoo.com.br

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