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Research Article

Histologic Correlates of Single Artery Umbilical Cords with Clinical Implications

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Abstract

Single artery umbilical cords have conventionally been studied in relation to clinical abnormalities such as intrauterine growth restriction (IUGR) and chromosomal abnormalities. Literature on the histopathologic correlates of single artery umbilical cords is lacking. We evaluated umbilical cord, foetal membrane and placental histopathologic findings in 26 placentas with single artery umbilical cords to characterise any differences compared to normal three-vessel umbilical cord control cases. We found a greater prevalence of funisitis and acute chorioamnionitis, and greater prevalence of maternal vascular malperfusion. Umbilical cord and/or foetal membrane inflammation and placental histology of maternal vascular malperfusion often correlate with clinical infection and hypertension, respectively. Early in-utero detection of single artery umbilical cord may therefore help identify risk of potential infection and maternal/foetal hypertension and help prevent adverse clinical sequelae.

Keywords: Two-Vessel Umbilical Cord; Single Umbilical Artery; Funisitis; Chorioamnionitis; Maternal Vascular Malperfusion

Introduction

Literature in relation to single artery umbilical cords has concentrated on its association with clinical abnormalities, including intrauterine growth restriction and chromosomal abnormalities [1-6], or on best methods of single artery cord detection [7]. Pathology literature includes gross autopsy findings; [8] However, only a rare report includes histology findings, and only those of the umbilical cord [9]. We evaluated umbilical cord, foetal membrane and placental histologic findings in 26 placentas with single artery umbilical cords to characterise any potential histologic differences compared with normal three-vessel umbilical cord control cases. Following CoPath electronic archive search using keywords 'placenta' and 'two-vessel cord', anonymized final diagnosis summary reports from 46 singleton placenta (26 single artery cord cases and 20 normal control cases) from 2006 through 2022 were reviewed. Data on umbilical cord, membrane and placental histopathologic findings were recorded. Compared with normal control cases, placenta with single artery umbilical cords had a greater prevalence of acute funisitis and acute chorioamnionitis. There was also a greater prevalence of histologic findings of maternal vascular malperfusion, including increased syncytial knots (Tenney-Parker change), thickened arterial vessel walls in chorionic villi and distal villous hypoplasia.

Methods

CoPath electronic pathology data archive search using keywords 'placenta' and 'two-vessel umbilical cord' yielded final diagnosis summary reports from 46 clinical audit singleton placenta (26 single artery cord cases and 20 normal three-vessel cord control cases) from 2006 through 2022. Gross and histologic evaluation were performed by consultant pathologists, American Board Specialty-certified and/or on the specialist histopathology Medical Council of Ireland register. Hematoxylin and eosin-stained histology slides were available for all cases including umbilical cord, foetal membrane and full thickness placental sections. Data on maternal age, placental weight, and histopathologic findings of placenta, umbilical cord, and foetal membranes were recorded.

Results and Discussion

Study and control cases did not differ with regard to mean maternal age (32 vs. 33 years), while single umbilical artery cases showed less mean placental weight (362 vs. 480 grams). Compared with normal control cases, placenta with single artery umbilical cords had a greater prevalence of acute funisitis (5/26; 20% vs 2/20; 10%) and acute chorioamnionitis (12/26; 46% vs 8/20; 40%). There was also a greater prevalence of maternal vascular malperfusion (10/26; 39% vs 2/20; 10%, see (Figures 1-3), including increased syncytial knots (Tenney-Parker change), thickened arterial vessel walls in chorionic villi, distal villous hypoplasia and decidual vasculopathy.

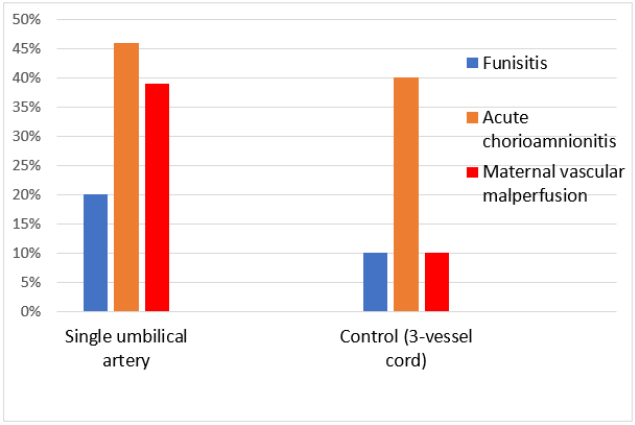

Figure 1: Acute inflammation and maternal vascular malperfusion in single artery umbilical cord cases (n = 26) compared with normal controls (n = 20).

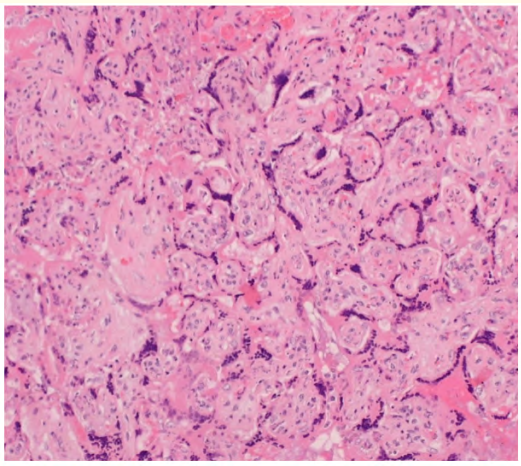

Figure 2: Increased syncytial knotting, H and E stain, medium power.

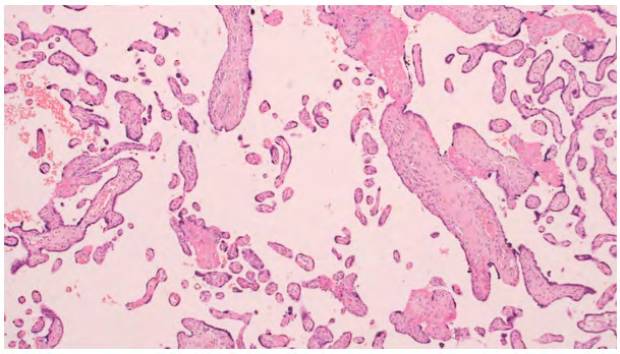

Figure 3: Distal villous hypoplasia, H and E stain, low power.

Literature in relation to single umbilical artery has concentrated on its association with clinical abnormalities, including intrauterine growth restriction (IUGR) and chromosomal abnormalities, [1-6] or on best methods of single artery cord detection [7]. Current medical literature is devoid of reports on the placental histopathologic correlates of single artery umbilical cords. We evaluated umbilical cord, foetal membrane and placental histopathologic findings in 26 placentas with single artery umbilical cords to characterise any potential histopathologic differences compared with normal three-vessel cord control cases and identify any clinical implications.

The prevalence of single artery umbilical cord is 0.5% to 1% in singleton pregnancies, [8] and this percentage increases to approximately 3.5% when in-vitro fertilisation (IVF) or other

pregnancy aiding practices have occurred [10]. A plethora of research on single artery umbilical cords and clinical correlates has established that single umbilical artery cords reduce, up to 50%, flow of oxygen, nutrients and waste products between foetus and mother, and that single umbilical artery is associated with prematurity, growth restriction, low birth weight, gestational diabetes and increased mortality rate [8,10,11].

Despite widely reported clinical associations with single artery umbilical cords and the potential clinical salience of histopathologic findings in placenta in general, no studies to date report on placental histopathology associated with single umbilical artery. We found single artery umbilical cords associated with a greater prevalence of umbilical cord and foetal membrane acute inflammation. While there is evidence to suggest that acute funisitis and acute chorioamnionitis are sometimes associated with intra-amniotic inflammation that occurs in the absence of demonstrable microorganisms, many of these lesions are infection-related [12,13]. Ascending infection, for example, with Streptococcus agalactiae or maternal blood-borne infection, for example, with Listeria monocytogenes, and many others, are frequent causes of acute funisitis and acute chorioamnionitis [12,14]. Early gestational detection of single umbilical artery may help identify and prevent increased risk for possible intra-amniotic infection.

Maternal vascular malperfusion has clinical correlates of hypertension and pre-eclampsia and histologic correlates of accelerated villous maturation, distal villous hypoplasia, increased syncytial knotting, increased peri- and intervillous thrombi, villous infarction, and decidual vasculopathy [13]. Our cases showed evidence of clinical hypertension and maternal vascular malperfusion including increased syncytial knotting (Tenney-Parker change), medial wall thickening of intermediate chorionic villi arterial vessels, distal villous hypoplasia and decidual vasculopathy. Pregnancies affected by maternal vascular malperfusion have a 4.5 times higher risk of developing a small for gestational age newborn or pre-eclampsia, [15] the latter potentially fatal for mother and neonate. To the extent that single umbilical artery is associated with maternal vascular malperfusion, early gestational detection of single umbilical artery may aid in prevention of the potentially severe clinical risks of maternal vascular malperfusion such as pre-eclampsia and maternal or foetal death [13,15].

Conclusions

We found single artery umbilical cords associated with a greater prevalence of umbilical cord and foetal membrane acute inflammation, as well as signs of maternal vascular malperfusion. If the number of cases with acute funisitis and acute chorioamnionitis in our study were combined, then single artery umbilical cord cases would have a prevalence 15% greater than normal control cases of potential infection. Acute inflammation of umbilical cord or foetal membranes, and maternal vascular malperfusion often correlate with clinical infection and hypertension, respectively. Therefore, early in-utero detection of single artery umbilical cord may help identify risk, not only of those conditions conventionally associated with single umbilical artery, but also of intra-amniotic infection and maternal/foetal hypertension and maternal vascular malperfusion and help prevent their potential adverse clinical sequelae. Future work with larger samples, microbial culture and clinical laboratory complete blood count and other clinical and serologic data would be beneficial, and perhaps further qualify and/or quantify maternal and/or foetal morbidity and mortality risk associated with single umbilical artery histopathologic findings.

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Conflict of Interest

Authors have no financial interest or any conflict of interest to declare.

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