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# Mixed chorangioma of the placental disk of a 29-year-old pregnant woman: A case report with literature review

*Eziagu UB*<sup>1</sup>\*, Wemimo RM<sup>2</sup>, Ndukwe CO<sup>3</sup>, Kudamnya IJ<sup>1</sup>, Utuk NM<sup>4</sup>, Oyewumi AO<sup>1</sup>, Eziagu ED<sup>5</sup>, Chibuike IO<sup>1</sup>

<sup>1</sup>Department of Histopathology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria.
<sup>2</sup>Department of Pathology, University of Ilorin Teaching Hospital, Ilorin, Kwara State.
<sup>3</sup>Department of Anatomic Pathology and Forensic Medicine, Nnamdi Azikiwe University, Awka/Nnewi, Anambra State, Nigeria.
<sup>4</sup>Department of Obstetrics and Gynaecology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria.
<sup>5</sup>Living Word Missions Hospital, Aba, Abia State, Nigeria.

# Abstract

A Chorangioma is a rare benign non-trophoblastic placental vascular neoplasm that develops from the placental primitive chorionic mesenchyme. It happens in 1% of pregnancies. Because Chorangioma may hurt the health of both the mother and the fetus, it is crucial to distinguish it from other placental disorders. In this article, we present a case study of an incidental Mixed Chorangioma variant found in a 29-year-old mother's placental disk during routine histopathological examinations as part of a large-scale prospective histopathological survey of the placenta in a tertiary healthcare facility in Uyo, Akwa Ibom State, Nigeria. In addition, we offer a comprehensive overview of the existing literature on Chorangiomas, focusing on their pathology, clinical importance, and treatment. This article aims to advance the understanding of Chorangiomas and increase clinicians' and pathologists' awareness of the need for early detection and suitable treatment.

Keywords: Chorangioma, Placental Hemangioma, placental neoplasm, placental disk, placental abnormalities, pregnancy, pregnancy outcomes

## Introduction

Chorangiomas are a rare but clinically significant subset of placental neoplasms.<sup>1-3</sup> It is a rare vascular neoplasm originating from the placental primitive chorionic mesenchyme and is characterized by the abnormal proliferation of capillaries within the placental disk tissue.<sup>1,3,4</sup> Chorangioma, also called placental hemangioma or Fibroangiomyxoma, is an uncommon benign non-trophoblastic neoplasm of the human placenta that manifests as a well-circumscribed placental neoplasm made up of capillaries, stromal cells, and surrounding trophoblast developing in the stem villus.<sup>3</sup> Histopathologically, Chorangioma is composed of well-circumscribed nodule(s) formed by the proliferation of capillaries in a

#### **Corresponding Author:**

Dr. Uchechukwu Brian Eziagu

Department of Histopathology, University of Uyo Teaching Hospital, P.M.B. 1136, Uyo, Akwa Ibom State, Nigeria. Postal code: 520001

uchechukwu.eziagu@npmcn.edu.ng | +2348095794223

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stem villus.<sup>2-8</sup> These rare placental neoplasms commonly present as asymptomatic lesions as well as incidental microscopic findings on histopathological evaluation of the placenta.<sup>3,4,9</sup> Complications with fetal hemodynamics arise when a Chorangioma manifests as a large mass (> 4 cm).<sup>1-4,7,9-11</sup> The clinical importance of Chorangiomas stems from their possible link to

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# unfavorable pregnancy outcomes.<sup>2–4,7,9,10,12–15</sup>

In this case report, we aim to present a rare case of Mixed Chorangioma of the placental disk in a pregnant woman, emphasizing its placental histopathological features. Furthermore, we will review relevant literature on Chorangioma of the placental disk, emphasizing its pathology (histopathological characteristics, classification, etiopathogenesis, and associated clinical correlations), classification, laboratory and radiological diagnosis, associated pregnancy outcomes, and management.

#### **Case Presentation:**

This is a case of a 29-year-old pregnant woman who received ante-natal care (ANC) at the Obstetrics and Gynecology (O&G) department of the University of Uyo Teaching Hospital (UUTH), Uyo, Akwa Ibom State, Nigeria. Her last menstrual period (L.M.P) was on the 1<sup>st</sup> of February 2015 and her expected date of delivery (E.D.D) was the 1<sup>st</sup> of November 2015. She was in her second pregnancy [G2P1+0(1A)]. She has an uneventful past obstetrics history as well as an unremarkable past medical and surgical history. She is HIV-negative. Her pack cell volume (PCV) in this pregnancy was 34%. All other routine investigations, such as urinalysis, random blood glucose, liver function test, and abdominopelvic ultrasound scan, carried out did not show any abnormality.

She had an uneventful pregnancy and eventually presented at the ante-natal ward at 38 weeks of gestation (Term) with complaints of lower abdominal pain, and an assessment of normal labor was made. Her 2.4 kilograms (normal range:  $\geq 2.5$  to 3.9 kg) live female baby was born through spontaneous vaginal delivery (SVD) at an estimated gestational age (EGA) of 38 weeks, with an APGAR score of 8 at the first minute, and 9 at five minutes. Her baby had a head circumference of 34 cm (normal range: 33 to 35.5 cm), a chest circumference of 29 cm (normal range: 30.5 to 33 cm), and a crown-heel length of 48 cm (normal range: 48 to 53 cm).<sup>16,17</sup>

Her placental delivery was spontaneous and complete, with clear amniotic fluid (liquor). Subsequently, a histopathological evaluation of her placenta (fetal membrane, umbilical cord, and disk) was done. The collection, fixation, grossing (macroscopy), Tissue processing, Embedding, Microtomy, Staining (with Haematoxylin and Eosin [H&E] staining), Microscopy (with CX22 Olympus light microscope) of her placenta were performed following standard histopathological techniques.<sup>18</sup> Grossly, her placental weight was 450 grams before fixation in 10% neutral buffered formalin (and 500 grams after 48 hours of fixation), giving a placentalbirthweight ratio of 18.75% (with an assessment of



Figure 1 (A-C): Gross photographs of the placenta showing (A) the opaque fetal surface of the placental disk {red star} with numerous patent connecting vessels as well as an umbilical cord false knot {*blue arrow*}, (B) excess torsion of the umbilical cord {*blue arrow*}, and (C) the maternal surface of the placental disk with diffuse to marginally adherent blood clots {red star}.



Figure 2 (A-D): Photomicrographs of the placental disk showing (A) a Chorangioma, composed of a well-circumscribed nodule formed by the proliferation of variably sized congested capillaries in a stem villus {blue arrow}surrounded by variably sized and shaped chorionic villi [H&E, x 40 mag.], (B) same focal lesion {*blue arrow*} at intermediate magnification [H&E, x 100 mag.], (C) a section of same focal lesion {*blue arrow*} at high magnification [H&E, x 400 mag.],and (D) another section of same focal lesion {*blue arrow*} at high magnification [H&E, x 400 mag.].



Figure 3 (A-D): Photomicrographs of the placental disk showing (A) another focus of Chorangioma, composed of a well-circumscribed nodule formed by the proliferation of variably sized congested capillaries in a stem villus {*black arrow*} surrounded by several variably sized and shaped terminal (with congested blood vessels) and chorionic villi [H&E, x 40 mag.], (B) same focal lesion {*black arrow*} at intermediate magnification [H&E, x 400 mag.], (C) a marginal section of the same focal lesion at high magnification [H&E, x 400 mag.], and (D) central section of the same focal lesion at high magnification [H&E, x 400 mag.].

large placenta with small for gestational age infant).<sup>19</sup> The fetal membrane was complete, opaque, and greyish-white, with its point of rupture being 14 cm from its marginal insertion to the placental disk (Figure 1). The umbilical cord measured 30 cm in length, and 1.1 cm in diameter, having three patent blood vessels (visualized in the transverse section), false knots, focal hematoma, excess torsion, and eccentric insertion to the disk (Figure 1). The placental disk was discoid shaped measuring 16.0 x 15.0 x 1.0 cm in its widest dimensions, having an opaque greyish-white fetal surface, patent connecting vessels, and complete soft to firm reddish-brown maternal surface with about 40 ml of clotted blood diffusely to marginally adherent to it, and its serial cut surfaces were similar being spongy, reddish-brown and interspersed by several septa-like whitish foci (Figure 1). Microscopically, the fetal membrane showed squamous metaplasia of amnion as well as Chronic Choriodeciduitis of the fetal membrane; the umbilical cord showed focal edema and hematoma; the placental disk showed Chorangioma (hemangioma-like vascular malformation in the placental disk) of the mixed variant, Chronic

Deciduitis (chronic inflammation of the decidua or endometrial tissue with pregnancy-induced changes), mild maternal floor infarct, perivillous fibrin deposition, Chronic Villitis (chronic inflammation of the chorionic villi), Chronic Intervillositis (chronic inflammation of the intervillous areas) and calcification of the disk (Figure 2 and 3). Ethical approval for this study was obtained from the UUTH Health Research Ethics Committee (UUTH/AD/S/96/VOL.XII/115) as a part of a larger study on placental pathology in HIVpositive pregnant women. Patient confidentiality was protected, and informed consent was obtained.

### Discussion

Placental vascular (nontrophoblastic) tissue gives rise to Chorangiomas, which are uncommon benign vascular neoplasms.1-4 These benign neoplasms derived from primitive chorionic mesenchyme are composed of proliferative capillary-sized vascular structures and can exhibit variable significant clinical implications for both the mother and the fetus.<sup>3-5,8</sup> Chorangiomas are most common in multiple gestation pregnancies or pregnancies complicated by preeclampsia.<sup>1-4,6,9,10,14,20</sup> This is in contrast to our case, which was a singleton gestation pregnancy and was not pre-eclamptic. Chorangioma, though a rare neoplasm, is the most common placental tumor, occurring in 0.5 to 1% of all placentas, and has an incidence of 1 in 100 placentas.<sup>2-4</sup>

The exact cause of Chorangiomas is still unknown, while numerous hypotheses have been put forth about their etiology and pathogenesis.<sup>1-4,9,21</sup> Although studies have shown that Chorangiomas arise from primitive chorionic mesenchyme, some researchers believe that these neoplasms arise from the disorganized proliferation of fetal blood vessels.<sup>2-4,10,11,21,22</sup> According to some researches, Chorangiomas could be hamartomatous lesions or vascular malformations brought on by abnormal placental angiogenesis in the early stages of embryonic development.<sup>2-4,10,11,21,23</sup> Other studies also consider it a reactive process secondary to hypoxia.<sup>2-4,20</sup> The etiology and pathogenesis of Chorangioma have been specifically associated in certain studies with high-altitude births, older mother age, hypertension including preeclampsia, multiple gestations, and co-occurrence with

infantile hemangioma.<sup>1-4,9-11,20,21</sup> Furthermore, in one study Infantile Hemangioma was found to occur in 55% of children whose placenta had Chorangioma.<sup>21</sup> In this case, none of these etiologic factors were present.

Histopathologically, Chorangiomas are typically well-circumscribed lesions located within the placental disk parenchyma.<sup>1-3,5-8,14,23</sup> On gross examination, they are usually imperceptible, however, they may also appear as single or multiple well-circumscribed spherical to oval reddish or brownish nodules, ranging in size from a few millimeters to 10 centimeters, with most lesions being  $< 4 \text{ cm.}^{2-4}$  In this case, there were no gross features suggestive of focal Chorangioma in the placental disk, however, the placental disk was diffusely reddish-brown. Microscopically, these tumors are composed of variably sized fetal capillaries lined by endothelial cells, often embedded in a fibrous stroma and trophoblast.<sup>2,3,5-8</sup> These fetal capillaries (vascular structures) may vary in size and shape, and their lumina can be filled with erythrocytes or fibrinoid material.<sup>2-5</sup> In larger Chorangiomas, some vessels may undergo thrombosis, infarction, fibrosis, hyalinization, hemosiderin deposition, or calcification.<sup>2-5,8,10</sup> Rarely, myxoid degeneration may be present.<sup>3,24</sup> These lesions are typically well-circumscribed but may be infiltrative, depending on their size and location within the placental disk.<sup>3</sup> Also, trophoblast proliferation may be present but will not display cytological atypia.<sup>3,8</sup> In atypical Chorangioma, the stroma can be cellular with increased mitoses and necrosis, however, no malignant transformation has been reported.<sup>3,8</sup> In this case, the microscopic features were classical in their presentation, being well-circumscribed and composed of a proliferation of capillary-sized vascular structures. It is important to note that the relationship between the incidental placental lesions (namely squamous metaplasia of the amnion, Chronic Choriodeciduitis, focal umbilical edema/hematoma/torsion, Chronic Deciduitis, maternal floor infarct, perivillous fibrin deposition, Chronic Deciduitis, Chronic Intervillositis, and Calcification) reported in this case with Chorangioma is unknown and it was not reported in the literature reviewed for this study. Hence, understanding the link between these lesions will require further research.

Furthermore, Chorangiomas are classified based on their location within the placenta as well as distinctive histopathological characteristics into three distinct types, namely marginal, central, and mixed variants.<sup>1</sup>

Mixed Chorangiomas display elements of both marginal and central types of Chorangioma, and they are regarded as a less clearly defined entity. Their clinical significance may vary depending on the proportion and location of the distinct components.<sup>2-4</sup> Interestingly, our case report's lesion falls into this category given that it has histopathological features of both Marginal and Central Chorangiomas.

Ancillary immunohistochemical studies have provided valuable insights into the cellular composition of Chorangiomas.<sup>3</sup> Endothelial markers, such as GLUT1, CD31, and CD34, are consistently positive in the vascular components of Chorangiomas, confirming their vascular nature.3 Other markers like VEGF (vascular endothelial growth factor) may also be expressed, reflecting the potential role of angiogenic factors in the pathogenesis of these tumors.<sup>2-4</sup> Also, Ki-67, a marker of cell proliferation, can be variably positive in Chorangiomas and may indicate their growth potential.<sup>2-4,8</sup> Furthermore, no copy number alteration has been identified in molecular biological and cytogenetic evaluations of Chorangiomas.<sup>3,25</sup>

The main clinical correlation in the pathology of Chorangioma is its association with pregnancy outcomes.<sup>2-4</sup> While the majority of Chorangiomas are small and clinically insignificant, larger lesions (> 4 cm) have been associated with adverse pregnancy outcomes.<sup>2,3,6,7,9,12,13,15,22,24</sup> Interestingly, the lesion, in this case, measured about 1 cm. Importantly, these adverse pregnancy outcomes may include polyhydramnios, preterm birth, placental abruption, fetal growth restriction, and fetal distress.<sup>2-4,9,12,13,15</sup> The exact mechanisms underlying these associations remain unclear, but possible explanations include mechanical disruption of the placental vasculature, alterations in blood flow, and hormonal imbalances induced by the neoplasm.<sup>2-4</sup>

Concerning maternal effects, most Chorangiomas are asymptomatic and do not directly impact the mother's health.<sup>3</sup> However, large or multiple Chorangiomas can lead to maternal complications such as placental abruption, polyhydramnios, maternal mirror syndrome, and preterm labor.<sup>2-4,6,9,13,24</sup> Maternal hemorrhage may occur if the neoplasm involves the maternal surface of the placenta.<sup>3,24</sup> Our case was asymptomatic as regards maternal effects.

For fetal effects, Chorangiomas can potentially affect fetal well-being particularly when large (> 4 cm).<sup>2-4,7,10-12,15,21,22</sup> These large Chorangiomas may be associated with perinatal morbidity and even mortality due to hemodynamic stresses on the fetus.<sup>3,7,9,12,13,15</sup> Complications such as intrauterine growth restriction (IUGR), fetal anemia, arteriovenous shunting, fetal cardiomegaly, fetal heart failure, fetal thrombocytopenia, and fetal hydrops have been reported.<sup>3,4,7,11–13,15,22</sup> The fetal effect of IUGR can be inferred in our case report given that the live female baby had a low birth weight (LBW) of 2.4 kg at term, reduced chest circumference (29 cm), and large placenta with small for gestational age infant assessment (18.75) from placenta-birth weight ratio calculation. However, the exact mechanism of these fetal effects in Chorangioma cases remains uncertain, but it is presumed that the neoplasm competes with the fetus for blood supply or produces vasoactive substances affecting fetal circulation.<sup>2-4,11</sup> This indeed calls for further research, given that these further fetal effects features could not be evaluated in our case.

In terms of diagnosis, Chorangiomas, particularly the large ones, are often detected incidentally during routine obstetric ultrasound examinations.<sup>3,26,27</sup> On ultrasound, they appear as hypoechoic or echogenic masses within the placenta.<sup>3,26–28</sup> Color Doppler imaging and Magnetic Resonance Imaging (MRI) can help delineate the vascular nature of the lesion.<sup>3,26,29</sup> Interestingly, the ultrasound scan performed in this case could not detect the Chorangioma present in the placental disk, this may be because of its small size rather than lack of expertise thereof.

Notably, postnatal histopathological examination of the placenta by a skilled anatomical pathologist is essential to confirm the diagnosis and characterize the tumor further. This was the case in this study, thereby emphasizing that histopathological valuation of the placenta is the gold standard in the diagnosis of Chorangioma. Hence, whenever

Obstetricians suspect it (in the presence of its associated clinical correlates enumerated above) they should request for histopathological evaluation of the placenta to confirm this diagnosis.

Concerning expert management, most Chorangiomas do not require specific treatment and resolve spontaneously postnatally with the delivery of the placenta.<sup>2,3</sup> Careful close antenatal monitoring is recommended for pregnancies with large or multiple Chorangiomas, as appropriate management can be initiated promptly if a fetal compromise such as hydrops is detected.<sup>2-4</sup> In severe symptomatic cases, fetal blood sampling, intrauterine transfusion, amniodrainage, or early delivery may be considered as treatment modalities.<sup>2-4</sup> Furthermore, interventions such as alcohol injection/ablation, micro-coil embolization, endoscopic devascularization, and interstitial laser coagulation therapy may be instituted in rare cases.2-4

As regards differential diagnosis, Chorangiomas should be distinguished from other placental vascular anomalies, such as placental Chorangiomatosis (no distinct mass, a nonexpansile proliferation of anastomosing capillaries at the periphery of stem villi or immature intermediate and terminal villi, unlike Chorangioma which involves the stem villi), placental Chorangiosis (no distinct mass, capillary hyperplasia in terminal villi due to chronic placental hypoperfusion or low-grade tissue hypoxia), placental Chorangiocarcinoma (comprised of features of Chorangioma and Choriocarcinoma, with extensive trophoblast proliferation, atypia, and necrosis), arteriovenous malformations, inflammatory myofibroblastic tumor, Leiomyoma, placental infarct, intervillous thrombus, and mesenchymal dysplasia.2,3,14,22,23,30 This differentiation is based on histopathological features, location, and immunohistochemical profile, as well as clinical correlations.

Overall, Chorangiomas represent a fascinating and rare group of benign placental neoplasms with potential clinical significance. A thorough understanding of their histopathological features, classification, etiopathogenesis, and clinical correlations is vital for early detection, accurate diagnosis, and appropriate management of these tumors. Further research is needed to unravel the exact mechanisms underlying their development and potential therapeutic interventions.

# Conclusion

This case report and literature review contribute to the current knowledge of Chorangioma, emphasizing the importance of histopathological evaluation of the placenta in making the diagnosis and a call for further research to better comprehend its pathogenesis and develop evidence-based management strategies.

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