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Antenatal Diagnosis of Retroperitoneal Cystic Mass: Fetiform Teratoma or Fetus in Fetu? A Case Report

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
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Manuscript Preparation E
Literature Search F
Funds Collection G

BEF 1 **Spencer Pace**
BEF 2 **Marla A. Sacks**
EF 2 **Laura F. Goodman**
EF 2 **Edward P. Tagge**
ABEF 2 **Andrei Radulescu**

1 School of Medicine, Touro University California, Vallejo, CA, U.S.A.

2 Department of Surgery, Division of Pediatric Surgery, Loma Linda University Children's Hospital, Loma Linda, CA, U.S.A.

Corresponding Author: Andrei Radulescu, e-mail: ARadulescu@llu.edu

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Patient: Male, newborn
Final Diagnosis: Fetiform teratoma
Symptoms: Abdomen distension
Medication: —
Clinical Procedure: Surgical removal
Specialty: Pediatrics and Neonatology

Objective: Unknown etiology

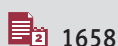
Background: Teratoma, a tumor containing a variety of tissues, is a broad diagnosis containing mature teratoma, immature teratoma, and teratomas with malignant transformation. The tumor forms during embryological development secondary to unsuccessful migration of primordial germ cells. A specific type of mature teratoma, containing human-like features, is called a fetiform teratoma. The fetiform teratoma is often compared and confused with fetus in fetu, a reabsorbed twin. While these tumors have commonly been described in the gonads, the retroperitoneal location finding on antenatal imaging is rare. The distinction between the aforementioned subtypes is not well established, proving a challenging diagnosis prior to resection.

Case Report: We present a case of a newborn male with a prenatal diagnosis of retroperitoneal cystic mass. Although prenatal imaging was obtained, the diagnosis remained unclear. After birth, planned surgical excision on day of life 7 showed the suprarenal mass contained contiguous intestinal elements. Histopathology examination revealed a mature cystic teratoma with multiple tissue types, including colonic, brain, respiratory, lymphatics, and nerves, reminiscent of fetiform teratoma. This case report presents an interesting example of differentiating elements straddling the diagnoses mentioned above.

Conclusions: This is the first reported case of fetiform teratoma diagnosed in a newborn and is especially unique for having the element of intestinal duplication within the retroperitoneal mass. The differentiating features of fetus in fetu and fetiform teratoma depend on subjective distinctions. The case provides an opportunity to discuss the differentials and management strategies.

Keywords: Embryonic and Fetal Development • Fetal Organ Maturity • Teratoma

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Background

Teratomas, derived from the Greek word “teras” meaning monsters and “onkoma” meaning swelling or tumor [1,2], contain multiple types of differentiated tissues, complete with hair, teeth, skin, and, in some cases, thyroid tissue. In the context of fetal tumors, the diagnosis may not be clear prior to resection. When considering a highly differentiated fetal tumor with multiple types of tissue, there are a few chief entities to consider: mature teratoma, fetiform teratoma (FT), and fetus in fetu (FIF), which is a resorbed twin [3].

Teratomas contain cell populations derived from 2 or more germ layers, such as endoderm, mesoderm, or ectoderm [4]. They occur during embryonic development and may be diagnosed at any age. Teratomas typically occur along the midline of the body, anywhere from the coccyx to the pineal gland. Primordial germ cells are initially found within the yolk sac wall outside of the developing embryo. At 4 to 6 weeks of gestation, these cells move along the hindgut and dorsal mesentery to reach the genital ridges on either side of midline, while continuing to undergo mitosis. Upon reaching the genital ridge, they contribute to the development of primitive sex cords, which themselves form from “finger-like projections of proliferating mesothelium”. The primitive sex cords and primordial germ cells then combine to form the primitive gonad, which gives rise to the fully developed ovary or testis. Teratomas are thought to arise from unsuccessful migration of these primordial germ cells, which fail to degenerate and continue to proliferate at abnormal locations along the midline. The pluripotent abilities of these cells are thus able to give rise to a wide spectrum of tissues, leading to their unique appearance [5].

There are four histologic variants: mature teratoma (MT), immature teratoma, teratoma with malignant transformation, and monodermal teratoma. MT is a benign neoplasm that is usually cystic and composed of well-differentiated structures derived from ectoderm, mesoderm, and endoderm [4,6]. A fifth histologic variant, the fetiform teratoma (FT), was seen in this case. Fetiform teratoma (also known as “homunculus” – Latin for little person) is a term that has been given to a rare subtype of mature cystic teratoma (MCT) that is so highly differentiated and organized that it misleadingly resembles a malformed fetus [3,7]. It is a very rare entity, with few cases described in the literature (only 25 reported cases as of 2006 [8]).

Mature teratomas are the most common form of teratoma [9] and are confirmed after surgical excision for definitive diagnosis. Due to the rarity of both FT and FIF, a well-defined diagnostic criteria has yet to be established. Currently, a diagnosis of FT is made upon gross pathologic examination, with typical features including the presence of a bony skeleton and the absence of visceral organ development and skeletal muscle tissue [8]. In contrast, FIF is usually diagnosed with gross

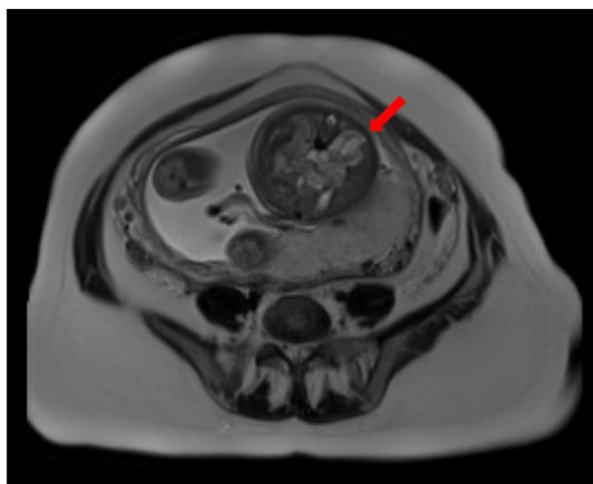


Figure 1. Prenatal MRI image showing a solid and cystic retroperitoneal mass with associated calcifications.

pathologic examination showing a well-developed and segmental axial skeleton [8], although some authors believe this definition is too restrictive, stating that FIF encompasses any “highly organized” fetiform mass [5].

In this case report, we present a case of fetiform teratoma in a newborn male who was diagnosed prenatally with an abdominal mass. The clinical, radiologic, and histopathology pathological features will also be reviewed, which can aid in confirming a diagnosis.

Case Report

Here, we present the case of a newborn male who was found to have a retroperitoneal abdominal mass on prenatal imaging studies. The patient's mother was a 42-year-old G7P6 female with a past medical history of obesity (BMI 37), herpes simplex virus 1 (HSV1) positivity, and antimitochondrial antibody (AMA) positivity, who initially presented to the Emergency Department with vaginal bleeding and was found to have a 10-week-old viable intrauterine pregnancy on pelvic ultrasound. Routine prenatal care ensued, which included repeat ultrasound (US) at 10 weeks of gestation to confirm gestational age and survey fetal anatomy. The US at 24 weeks of gestation showed a 2.1×3.0×2.4 cm right upper-quadrant mass and additional large calcifications. Subsequently, a fetal magnetic resonance imaging (MRI) study done at 30 weeks of gestation re-demonstrated the retroperitoneal mass 4.9×4.2×3.0 cm solid and cystic components with calcifications, distinctively separate from the liver and right kidney, as well as anterior displacement of the inferior vena cava (IVC) (Figure 1).

At 33 weeks of gestation, a repeat US showed the mass was enlarging, now measuring 6.1×3.8×5.7 cm in the RUQ, with



Figure 2. Post-natal computerized tomography (CT) images demonstrating a right retroperitoneal mass with soft tissue, fat, and calcifications and regional mass effect.

multiple large calcifications. The child was delivered by means of elective cesarean section at 38 weeks gestation. In the immediate postdelivery days, tumor markers obtained showed alpha fetoprotein (AFP) 32,135 ng/mL (normal <8.7), and beta human chorionic gonadotropin (B-hCG) 9.2 mIU/mL (normal <1). Homovanillic acid (HVA) and vanillylmandelic acid (VMA) were noted to be within normal ranges. Post-natal imaging performed included US, abdominopelvic MRI, and computed tomography (CT) scan (**Figure 2**). The CT scan re-demonstrated the heterogeneously enhancing right retroperitoneal mass, measuring approximately 5.6 (anteroposterior)×5.9 (transverse)×9.0 (craniocaudal) cm, with soft-tissue elements and calcifications, causing a significant regional mass effect.

The infant underwent a planned surgical exploration with mass resection on day of life (DOL) 7. A large cystic tumor was found without gross invasion of surrounding structures. It was noted that there were multiple fully-formed bowel loops and apparent appendices coming through the posterior aspect of the mass (**Figure 3**). Following resection, pathologic examination

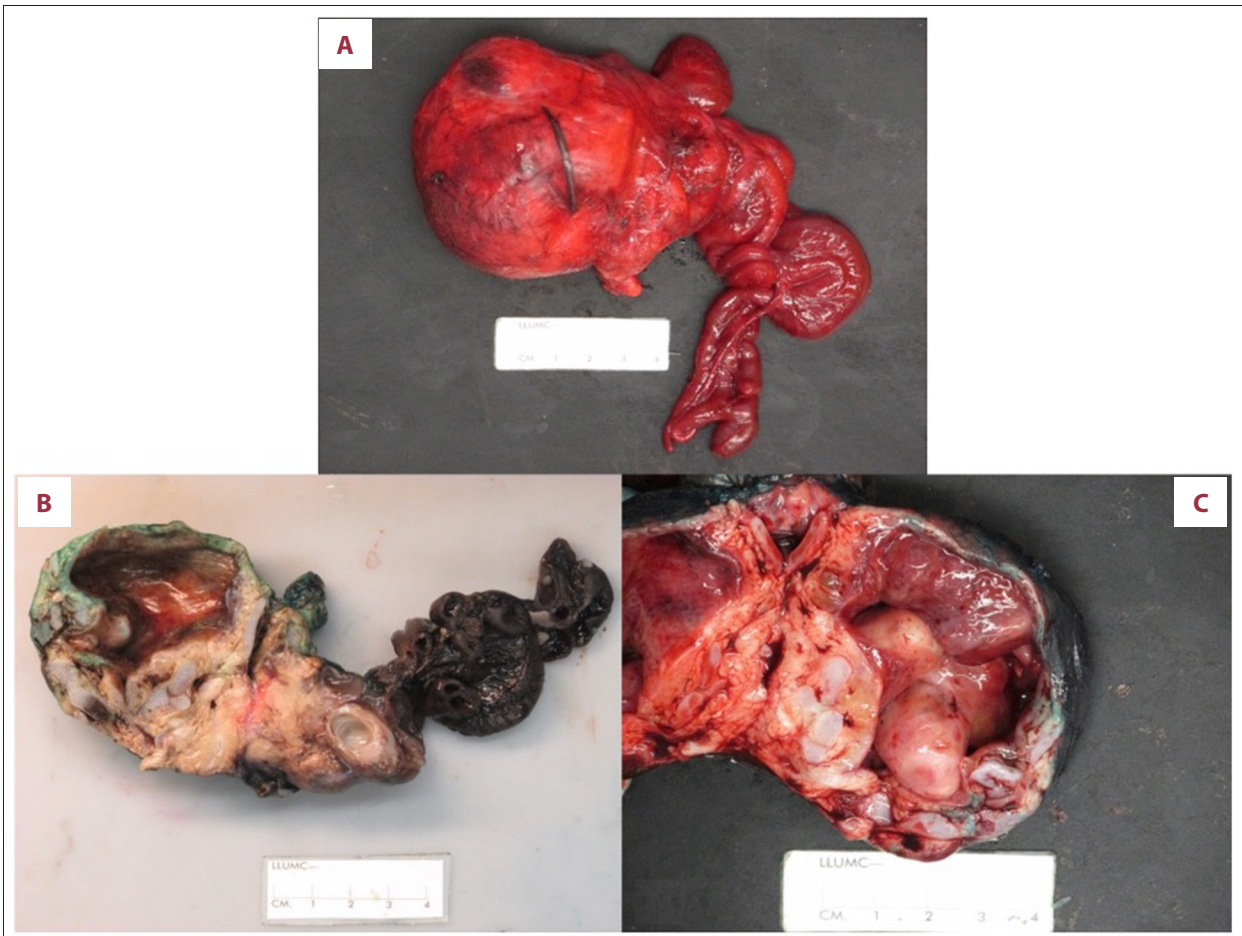


Figure 3. Intraoperative findings of right retroperitoneal mass with adjacent well-formed yet discontinuous and vermiform bowel segments. External surface of resected mass (**A**), and cross-sections of the mass revealing a unilocular cyst with multiple sessile masses and irregular cartilaginous and cystic lesions filled with mucoid material (**B, C**).

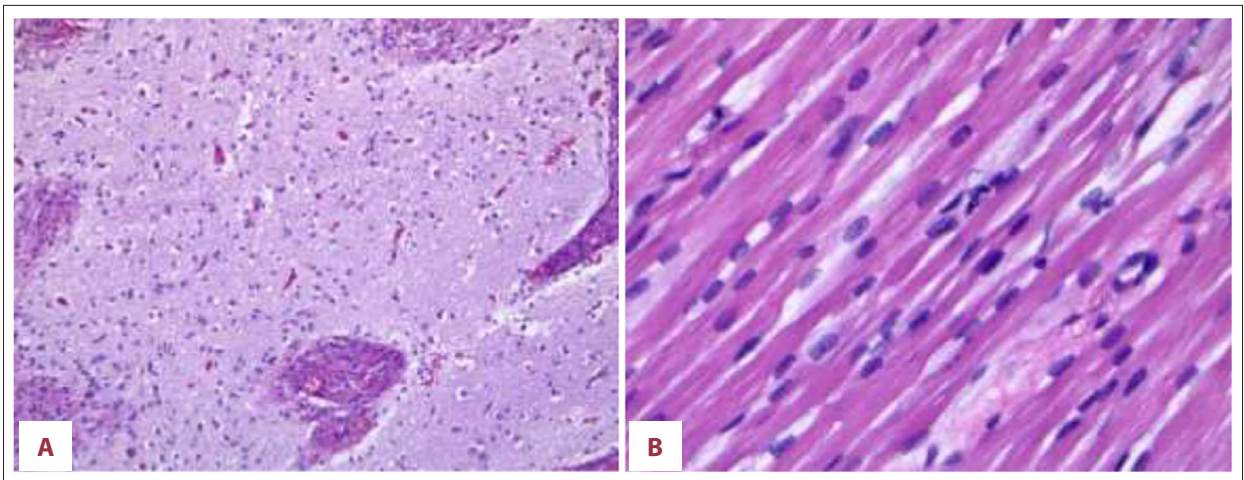


Figure 4. Pathologic examination of right retroperitoneal mass, with hematoxylin eosin staining demonstrating malformed brain parenchyma (A) and striated cardiac musculature (B).

revealed a mature cystic teratoma with areas showing well-differentiated loops of colon and small bowel, complete with mucosal, submucosal, and serosal elements. Within the cyst, there were disorganized areas of brain tissue, striated cardiac-type musculature, salivary glandular tissue, skin, bone, respiratory-type epithelium, lymphatics, and peripheral nerve bundles (Figure 4). The well-formed nature of the attached loops of bowel was reminiscent of the so-called “fetiform teratoma,” although the remainder of the tissues do not show fetiform features. Postoperatively, the patient had an uneventful course and was discharged on postoperative day (POD) 11.

Discussion

Differentiating “normal” mature cystic teratomas from fetiform teratomas is challenging. If the tumor meets the criteria for teratoma and exhibits highly organized organ-like features, it is classified as a FT. In comparison, FIF is understood to be an actual fetus turned non-viable mass inside of the viable fetus.

The most commonly accepted hypothesis is the parasitic twin theory, which describes abnormal embryogenesis of monozygotic diamniotic monochorionic twins of unequal sizes. The smaller fetus is incorporated into the larger fetus via an unknown mechanism. Failure of normal growth of the smaller fetus has been thought to be caused by insufficient blood supply or inherent defects of the encased twin [3,10]. Another potential mechanism is a persistent anastomosis of the vitelline circulation, which causes the smaller fetus to merge with the larger fetus during the second and third weeks of development [3,10].

The fetiform teratoma theory was originally put forth by R. A. Willis and stated that FIF is an extremely differentiated

teratoma, surpassing fetiform criteria to instead generate an actual fetus. This suggests that these entities exist on a spectrum rather than exhibiting 2 distinct disease processes. FIF would thus have a similar pathogenesis with all teratomas, while exhibiting astoundingly different results [3,10,11].

Based on the popular parasitic twin theory, a theoretic, albeit arbitrary, distinction has historically been used to distinguish FIF from FT: the presence of a vertebral column or notochord [3,5,10,12]. The presence of vertebral bodies in FIF signifies that the fetus has undergone gastrulation, which indirectly reflects its derivation – the primitive streak developing during the third week in a normal embryo [12].

There are several other characteristics that can help distinguish FT from FIF. FIF is a more rare phenomenon, occurring in 1: 500 000 births [12]. FIF is almost always retroperitoneal, whereas FT can be found all over the body, and are more commonly midline, as discussed previously [8,12]. FIF tends to present earlier, in the early neonatal period, as a large abdominal mass, whereas FT often presents in older females ages 9-65 years, most commonly arising from the ovaries, like other teratomas [7,8,13].

FIF tends to arise more commonly in males, whereas FT tends to arise more commonly in females, from the ovaries [10]. In FIF, the lower limbs tend to be more developed than the upper limbs [7,8]. FIF tends to be suspended by a single pedicle, lending support to the persistent vitelline duct theory, inside of an encapsulated, well-defined, sac-like structure of the amniotic sac remnant, something not seen with FT [5,10].

Distinguishing between FT and FIF has important prognostic and management implications. FIF is considered to be completely benign, with only 1 recorded case of malignant

transformation, whereas teratomas of all types have a ~10% chance of malignant conversion [12]. Thus, the recommendation for all FT is often surgical removal or at least close follow-up to prevent future malignancy, whereas no such recommendation exists for FIF [12].

Our case highlights many of the often confusing clinical and diagnostic dilemmas associated with distinguishing these entities. The unique features of this case include the presence of FT in a newborn male, which no previous records have demonstrated, as well as the location within the retroperitoneum, which is more typical of FIF. Although large cartilage structures and bone tissue were present, no identifiable vertebral column was seen. There were multiple different tissue types, including nervous, cardiac, and bone, with a fully-formed duplicated intestine, signifying a high degree of organization. Unfortunately, no genetic studies were performed on these

specimens to assess zygosity, which likely would have served as a nice “tie-breaker” to solidify one diagnosis over the other. In this case, the diagnosis of FT seems more fitting, despite containing a fully developed, duplicated intestine, as the organization of the intestine was an outlier compared with the rest of the mass.

Conclusions

This case is unique due to the presentation of FT in a newborn male, and the retroperitoneal location and presence of a duplicated intestine, which is more typical of FIF. These diagnostic overlaps provided an opportunity to discuss the challenges of distinguishing these 2 entities and their important differences in both prognosis and management.

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