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Case Report

Genetically Proven Retroperitoneal Fetus-in-Fetu Successfully Excised in a Neonate

Bir Yenidoğanda Genetik Olarak Kanıtlanmış Retroperitoneal Fetus-in-Fetu'nun Başarılı Eksizyonu

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ABSTRACT

Background: Fetus in fetu (FIF) is an exceptionally rare congenital anomaly, often difficult to distinguish from fetiform teratoma. We report a genetically proven retroperitoneal FIF in a neonate and review the literature.

Case Presentation: A term female infant presented with a prenatal retroperitoneal cystic mass. Postnatal imaging demonstrated calcifications suggestive of vertebral structures, although teratoma remained in the differential diagnosis. Serum tumor markers showed markedly elevated alpha-fetoprotein (AFP) and normal beta-human chorionic gonadotropin (β-hCG). Complete excision at 2 months revealed a sac containing a fetiform mass with scalp. Histology identified only mature tissues (glial tissue, choroid plexus, retinal pigment epithelium, dental alveoli, lamellar bone with hematopoiesis), without immature elements. Genetic testing by quantitative fluorescent PCR confirmed a diallelic profile identical to the host (46,XX), establishing the diagnosis of FIF. AFP normalized within 6 months, and the infant remained asymptomatic at 18 months.

Discussion: Imaging, particularly CT and MRI, is essential for diagnosis and surgical planning, though distinction from teratoma can remain uncertain. Histology may suggest FIF but is not always definitive. Genetic identity between host and mass provides diagnostic certainty, resolving the long-standing controversy with fetiform teratoma. Our review confirms approximately 250 cases reported to date, with ~80% retroperitoneal and excellent outcomes following complete resection.

Conclusion: FIF should be considered in neonates with retroperitoneal masses. Genetic analysis is crucial when pathology is inconclusive, ensuring diagnostic accuracy and guiding follow-up.

Keywords: *Newborn, Genetic Testing, Fetus Abnormalities, Retroperitoneal Neoplasms, Monozygotic twinning*

ÖZET

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Başvuru: 12 aylık kız hasta, apne ve siyanoz ile seyreden solunum güçlüğü epizodu sonrası başvurdu. Ebeveynler, hasta uyanana kadar 20 saniye göğüs kompresyonu uyguladı. Bu, son 10 ay içinde yaşadığı üçüncü apne epizodudur. Ebeveynler ayrıca 2 aylıkken başlayan kronik bifazik stridor tanımlamaktadırlar. Stridor pozisyonel değildir veya yemek yeme ile ilişkili değildir, ancak hasta olduğunda kötüleşir. Beslenmeden sonra kusma yoktur ve stertor yoktur.

Fizik Muayene: Ateş 36,2°C, kalp hızı 140 atım/dakika, kan basıncı 119/77 mmHg, solunum hızı 30 nefes/dakika, SpO2 oda havasında %98. İyi görünümlü, hafif konjesyon ve steteskop olmadan duyulabilen bifazik stridor mevcut.

Değerlendirme: Solunum paneli rinovirüs için pozitif, bu virus 3 hafta önce önceki apneik olay sonrasında da pozitifti. Akciğer grafisi normal. Konuşma-dil patoloğu tarafından yapılan değerlendirmede aspirasyon bulgusu saptanmadı. Video EEG normaldi. EKG sinüs taşikardisi gösterdi. Göğüs BT anjiyografisi, sağ brakiyosefalik (innominat) arterin trakea üzerinden geçtiği yerde trakeada belirgin kompresyon ortaya koydu.

Tanı: Hastaya bronkoskopi yapıldı ve yaklaşık %90 obstrüksiyon ile trakeal kompresyon gösteren trakeomalazi saptandı, bu innominat arter kompresyon sendromu (IACS) tanısı ile uyumluydu. Bu hasta innominat arter reimplantasyonu geçirdi ve ameliyat sonrası bronkoskopi trakeal kompresyonda belirgin düzelme gösterdi. Bir ay sonra apneik olaylarla başvurdu ve tekrar bronkoskopi posterior duvar prolapsusu ile trakeomalazi gösterdi. Daha sonra posterior trakeopeksi yapıldı ve ardından yapılan bronkoskopi kollaps veya dinamik kompresyon göstermedi.

Tartışma: İnnominat arter trakea kompresyonu bifazik stridor, solunum arresti ve büyüme geriliğine neden olabilir. Kompresyon derecesi asemptomatikten ciddi obstrüksiyona kadar değişebilir. Solunum yolu enfeksiyonları sıklıkla stridora neden olur ve IACS gibi nadir bir durum için şüphe endeksini etkileyebilir. Yaşamı tehdit eden apneik olaylarla başvuran çocuklarda cerrahi müdahale gereklidir.

Keywords: *kulak burun boğaz, kardiyoloji, trakeal kompresyon*

INTRODUCTION

Fetus in fetu (FIF) is an exceptionally rare embryological anomaly, in which a fetiform mass develops within its host [1, 2]. Classically, it is defined by a calcified vertebral axis with rudimentary organs or limbs [3]. Although this criterion has been considered essential, cases without identifiable vertebrae have been reported, where limbs with innervated muscles provided indirect evidence of a rudimentary spinal axis [4]; thus, absence of visible vertebrae does not exclude FIF [5].

Its incidence is estimated at roughly 1:500 000 live births, with slight male predominance [5-7]. About 80 % are retroperitoneal [2, 5, 8] -probably reflecting vitelline drainage into the superior mesenteric artery [1, 9] - although skull, scrotum, sacrum, oral cavity and adrenal gland have also been reported [10]

Two main origins are debated [6, 11]: the "teratoma theory", considering FIF as an extreme form of well-differentiated teratoma, and the "identical-twin theory", which defines it as a parasitic monozygotic twin [4]. According to the latter, an underdeveloped twin becomes encapsulated in its sibling through a persistent vitelline circulation [1,2]. This arises from unequal division of the inner cell mass, leaving a smaller cluster incorporated into the embryo, generating a vestigial remnant [11,12]. A family history of twin pregnancy may support this mechanism [4], and most parasitic twins are anencephalic [11,13].

Diagnosis relies on imaging, but calcified bone is absent in up to 20% [2]. Ultrasound may mimic teratoma (complex, mixed, amorphous echogenic mass with poorly defined solid and cystic components) [6, 14]; while computed tomography (CT) and magnetic resonance imaging (MRI) better define anatomy and surgical relationships [1, 8, 14].

Tumor markers such as alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β-hCG) may aid differential diagnosis. Treatment is complete surgical excision, with histology required to exclude immature elements [2, 5]. Given the significant histological overlap between FIF and teratomas, genetic studies are also essential for a definitive diagnosis [8, 15]. Prognosis is excellent after total excision [2], with AFP normalization [16] and rare recurrence if resection is complete [6, 8].

CASE REPORT

We report a full-term female newborn (38+0 weeks, 3130 grams, Apgar 9/10), the fifth child of a mother with gestational diabetes. Notably, her obstetric history included a previous preterm twin gestation that ended in neonatal death of both infants. At 29 weeks an obstetric ultrasound revealed a thin-walled, heterogeneous and avascular cystic lesion in the upper left fetal abdomen. Fetal MRI confirmed a fluid sac containing a solid component with bone-like structures, strongly suggesting FIF.

Post-natal radiograph showed irregular calcifications. Ultrasound confirmed an avascular 41×36 mm cystic lesion with thin walls containing an internal solid structure with linear hyperechogenic images resembling vertebral structures (*Figure 1*). Serum markers showed normal β-hCG (4 mUI/mL), but markedly elevated AFP (136.299 ng/mL). MRI did not reveal well-defined fetal anatomical structures, raising suspicion for teratoma as the more likely diagnosis, although FIF could not be definitively excluded. CT revealed a left hypochondrial mass containing fluid, fat, and calcifications, compatible with a teratomatous lesion (*Figure 2*).

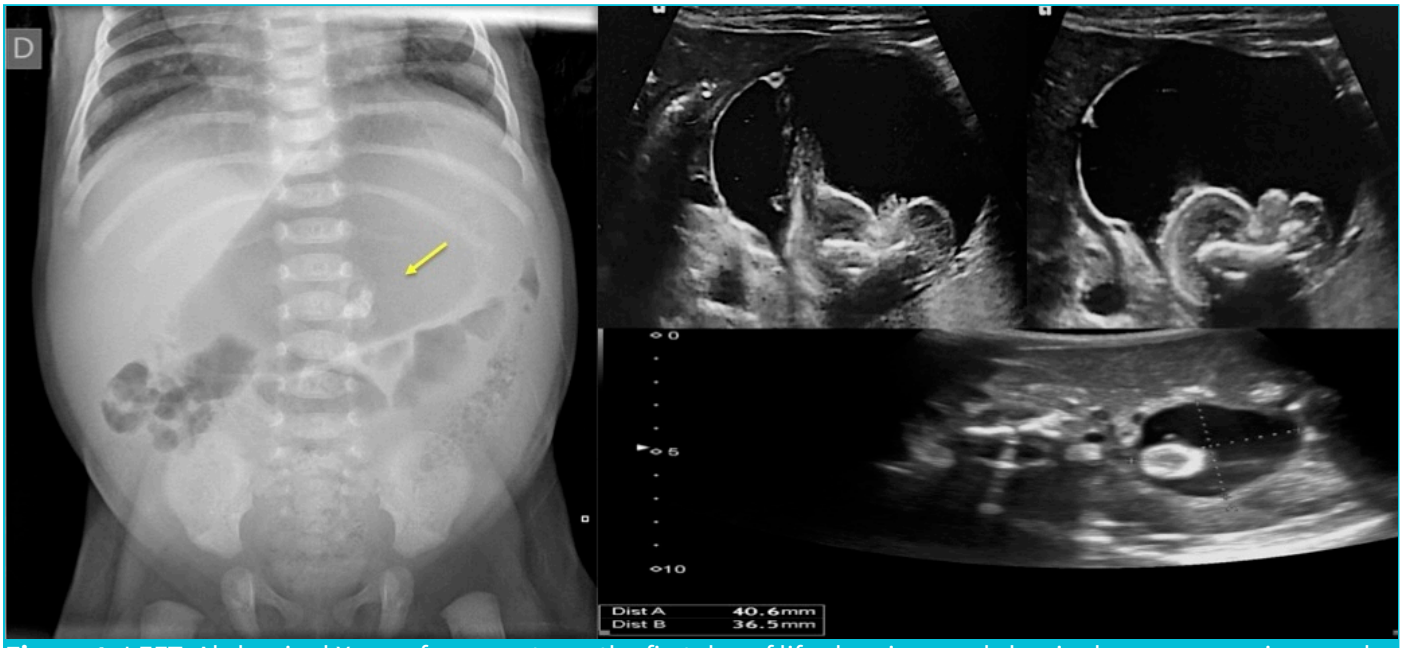

Figure 1. LEFT: Abdominal X-ray of a neonate on the first day of life showing an abdominal mass occupying nearly the entire left hypochondrium. Within it, coarse amorphous calcification is visible, with no clearly defined anatomy (arrow). RIGHT: Abdominal ultrasound performed in a neonate with a prenatal diagnosis of an intra-abdominal cyst, showing a cystic image measuring 40.6 × 36.5 mm in the mesogastric-right flank region. Internal calcifications are observed, the largest being a rounded one measuring 14 × 22 mm. A solid structure is seen inside, with linear echoes and posterior acoustic shadowing suggestive of a vertebral column, raising fetus in fetu as the leading diagnosis.

Surgical excision at 2 months removed a sac-like 7 × 2.3 × 2 cm cyst containing a 2.3 × 1.8 × 1.5 cm fetiform mass with a cephalic pole covered by scalp (*Figure 3*). The postoperative course was uneventful, and AFP normalized by 6 months.

Histology showed keratinizing squamous epithelium, hairy skin with subcutaneous tissue, mature glial tissue, choroid plexuses, retinal pigment, Isolated serous glands and occasional ciliated columnar respiratory-type epithelium. The area with bony consistency consisted of lamellar bone trabeculae with foci of hematopoiesis and mature cartilage. No immature elements were found.

Histopathological analysis concluded that the findings were suggestive of a highly differentiated mature cystic teratoma of fetiform type, without being able to rule out FIF, thus indicating the need for genetic studies, that showed the presence of a dialelic profile identical to the host (46, XX), confirming monozygotic origin and establishing a definitive diagnosis of FIF.

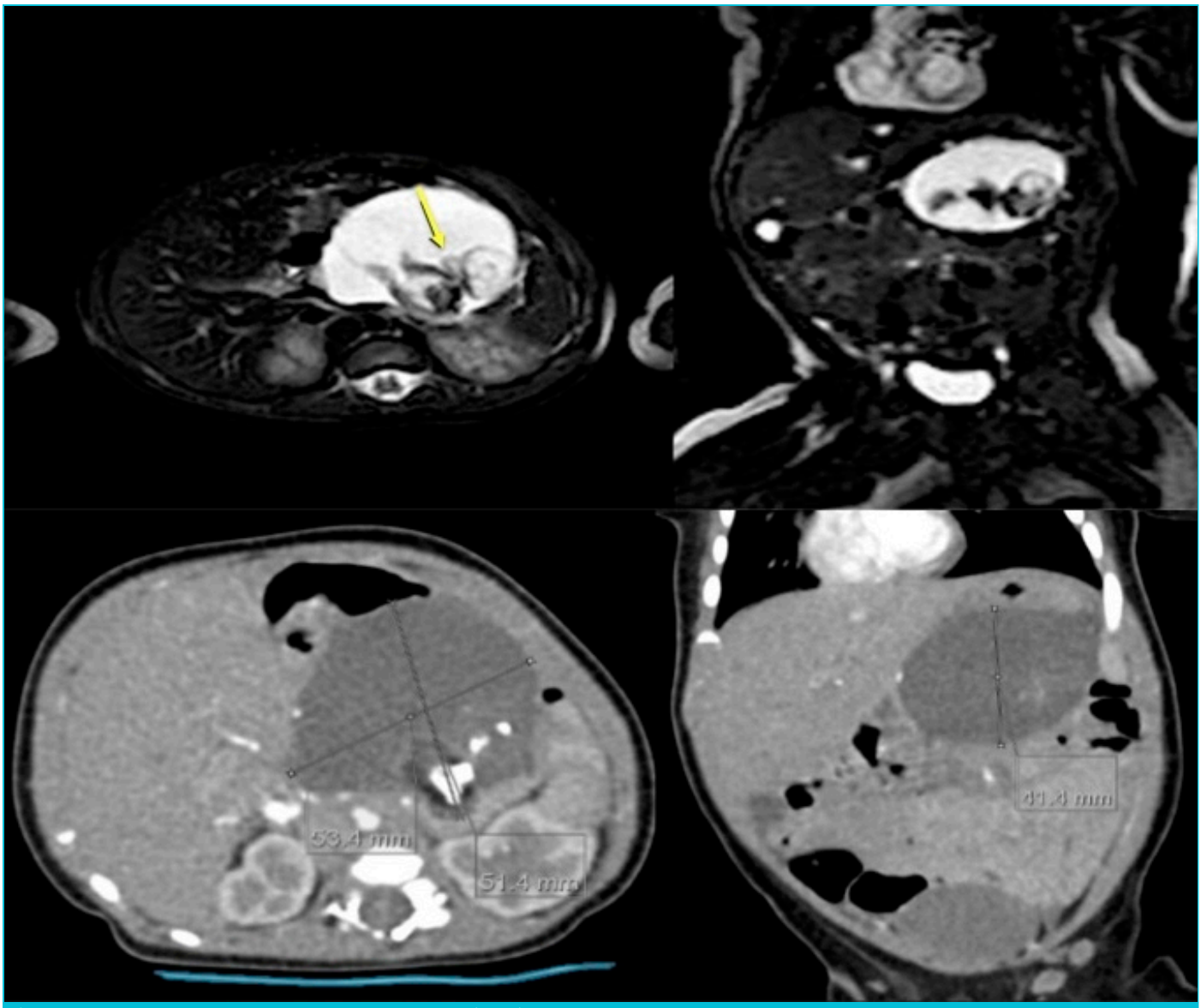

Figure 2. TOP: Magnetic Resonance Imaging (MRI) showing a complex abdominal mass with a predominantly cystic component located high in the retroperitoneum, occupying almost the entire left hypochondrium. Inside, there is a soft tissue area with a lobulated, heterogeneous appearance, containing foci of calcification and macroscopic fat (arrow). The findings suggest a teratoma, as no clearly defined fetal anatomical structures are identified, although fetus in fetu cannot be definitively ruled out. BOTTOM: Computed Tomography (CT) scan showing a well-defined mass in the left hypochondrium, measuring 53.4 mm in transverse diameter, 51.4 mm in oblique diameter, and 41.4 mm in craniocaudal diameter. Macroscopically, three types of tissue can be distinguished, the majority being homogeneously hypoattenuating, consistent with fluid. In the posterior aspect, a small area of fat and calcification is identified, vaguely resembling the morphology of a vertebra. On the medial wall, at the interface with the hepatic parenchyma, a hyperdense spot is observed, which may correspond to a small focus of calcification.

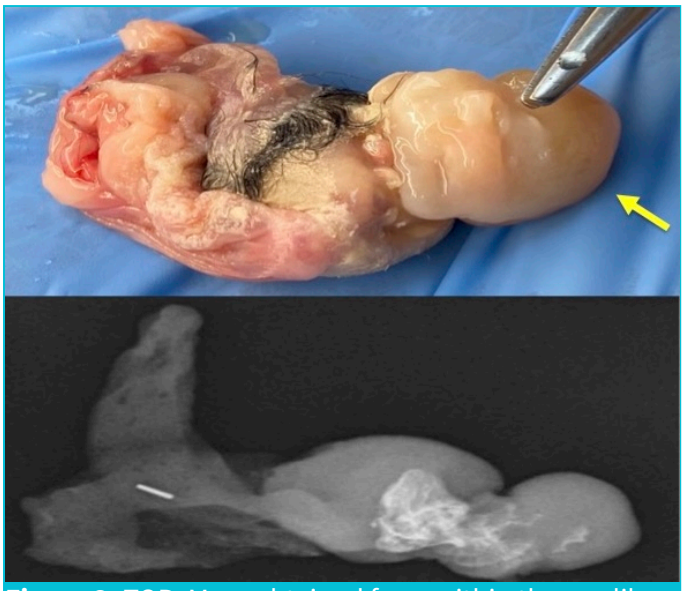

Figure 3. TOP: Mass obtained from within the sac-like formation after surgical resection in a 2-month-old infant with a prior diagnostic suspicion of fetus in fetu. A cephalic pole with scalp tissue was identified (arrow). BOTTOM: X-ray of the extracted mass showing calcifications suggestive of ossification, although they do not have a morphology resembling normal bones.

DISCUSSION

Fetus in fetu is extraordinarily rare, and the scarcity of published cases limits the development of standardized diagnostic and therapeutic criteria [2, 6]. Three major reviews illustrate its features. Hoeffel et al. (2000) [5] published the first series including 87 cases, mostly presented with an abdominal mass (70%) with retroperitoneal location (80%). Only one of the 88 reviewed cases showed recurrence after resection. Later, in 2015, Prescher et al. [11] reviewed 95 cases over a 15-year period, confirming male predominance, frequent retroperitoneal location (72%), high rates of anencephaly and excellent prognosis of patients following surgical intervention (97%). Palo et al. (2024) [2] published the most extensive systematic review to date, including 249 cases, again emphasizing retroperitoneal predominance, a finding consistent with both our case and the two previous reviews.

A distinctive feature of our case was the high level of diagnostic suspicion from the very first prenatal ultrasound. In the review by Palo et al., approximately 75% of reported cases were not initially suspected to be FIF [2]. Even when considered, distinguishing FIF from teratoma remains challenging because of overlapping radiological findings [6]; indeed, in our patient, diagnostic uncertainty persisted despite comprehensive CT and MRI evaluations. We agree with the literature in that both computed tomography (CT) and magnetic resonance imaging (MRI) play a fundamental role in the preoperative assessment of such complex cases [14]. These modalities provide superior spatial resolution and allow a more accurate definition of the relationship between the mass and adjacent organs, thereby optimizing surgical planning [11]. In our case, CT and MRI proved fundamental in guiding the operative strategy.

Some authors advocate testing AFP and β-hCG pre-operatively because elevated values have been described [1, 6]; but no consistent association with FIF has been established [2]. In our case, AFP was markedly elevated while β-hCG remained normal, a pattern previously reported.

Histopathology remains the cornerstone for diagnosis [2,10,17]. In our specimen, multiple mature tissues were present, including glial tissue-described as the second most frequent after gastrointestinal elements [2,11]-but findings alone were insufficient to confirm FIF. Genetic analysis was therefore required to establish a conclusive diagnosis. The distinction between FIF and mature teratoma has been the subject of intense debate. De Lagausie et al. [18] suggested that FIF and teratomas are not two absolute entities but rather represent the same pathological phenomenon at different stages of differentiation and maturation, with probable overlap between them [11, 13]. In this regard, zygosity analysis has been proposed as a useful tool to differentiate both entities: whereas teratomas are typically homozygous, FIF would be genetically identical to the host [13, 15]. The study by Miura et al. [19] demonstrated that host and mass share the same genotype across all loci studied. In our case, genetic analysis revealed a diallelic pattern and a normal 46, XX karyotype. The identical diallelic profile of the mass and its host rules out teratoma and confirms its origin as a true fetus in fetu.

Finally, some authors propose that a family history of twin gestation may indirectly support the twinning theory [4]. This detail is particularly relevant in our case, as the patient's mother had previously carried a twin pregnancy, suggesting a predisposition to abnormal twinning phenomena.

Overall, this case underscores the importance of a multidisciplinary approach-integrating neonatology,

radiology, pediatric surgery, pathology, and genetics-to reach diagnostic certainty and ensure optimal outcomes in such rare and challenging conditions.

CONCLUSION

Fetus in fetu is an exceptional embryological anomaly that poses major diagnostic challenges due to its clinical, radiological, and histopathological overlap with fetiform teratomas. Our case highlights that advanced imaging can strongly suggest the diagnosis but may not be conclusive. Ultimately, genetic analysis proving identical allelic profiles between the mass and the host is decisive, ruling out teratoma and establishing FIF with certainty. This case adds to the limited literature and reinforces the importance of a multidisciplinary approach, combining clinical, radiological, pathological, surgical, and molecular expertise to ensure accurate diagnosis and excellent outcomes.

Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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