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Case Series

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Single-center experience of fetus in fetu: A case series

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KEYWORDS

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ABSTRACT

Background: Fetus in fetu is a rare congenital malformation resulting from abnormal embryogenesis in a monochorionic diamniotic twinning gestation. This study aimed to document our experience with this anomaly in a developing country.

Methods: This retrospective analysis covers cases of fetus in fetu diagnosed at our institution between 1999 and 2023. Patients presenting with an intracorporeal mass containing a vertebral column and an appropriate arrangement of organs and limbs around the axis were included in the study.

Results: Five female patients with fetus in fetu were identified. The timing of diagnosis varied from incidental antenatal ultrasound discovery to postnatal abdominal mass presentation. The initial diagnosis involved radiological and serological investigations, confirmed by histopathology after surgical excision. The mean age at the time of surgery was 44 days. All patients underwent complete excision of the fetal mass, resulting in excellent postoperative outcomes and no recurrences.

Conclusion: Fetus in fetu is a pediatric rarity and must be distinguished from a teratoma mass, which carries a high malignant potential. Histological and genetic studies may contribute to understanding the pathogenesis and etiology of the disease.

INTRODUCTION

Fetus in fetu (FIF) is a rare congenital malformation secondary to abnormal embryogenesis in a monochorionic diamniotic twinning gestation [1]. Although it is currently classified as part of the mature teratoma spectrum by the World Health Organization, it has been implied to have a different pathogenesis and to be the consequence of aberrant inclusion of small totipotent inner cell mass within the healthy twin during the ventral folding of the trilaminar embryonic disc [2].

The first description dates back to the late 18th century, with less than 200 cases reported in the literature so far [2]. Due to the low incidence rate, it remains a pathological curiosity with an unclear etiology to this day. Diagnosis is either made by antenatal ultrasonography (USS) or as an incidental discovery of an asymptomatic abdominal mass [3]. Multidisciplinary prenatal and/or postnatal counseling helps in planning the management and follow-up care. Due to the embryological similarities, differentiating a FIF from a teratoma is challenging, and the final diagnosis is confirmed by histopathology.

Given the rarity of this pathology, the literature is limited to case reports and small case series of FIF. Herein, we present our experience with five cases of abdominal FIF.

METHODS

We conducted a retrospective analysis of cases with FIF presenting at our medical center from 1999 to 2023. The diagnosis was based on radiological and histopathological examination.

Inclusion criteria comprised cases with histopathological findings of the amniotic sac and the presence of a vertebral column with an appropriate arrangement of other organs or limbs around the axis.

Clinical data were retrieved from patient records and included age, sex, timing and type of clinical presentation, diagnostic workup, operative findings, histopathology findings, and postoperative outcomes.

The study was approved by the institutional ethical board and conducted per the Declaration of Helsinki [4].

RESULTS

A total of five FIF cases were identified over the 24-year interval. All cases were female, born from normal pregnancies at full term, and had normal birth weights. There was no family history of congenital malformations, twin pregnancies, or consanguinity, and no history of medication use during pregnancy.

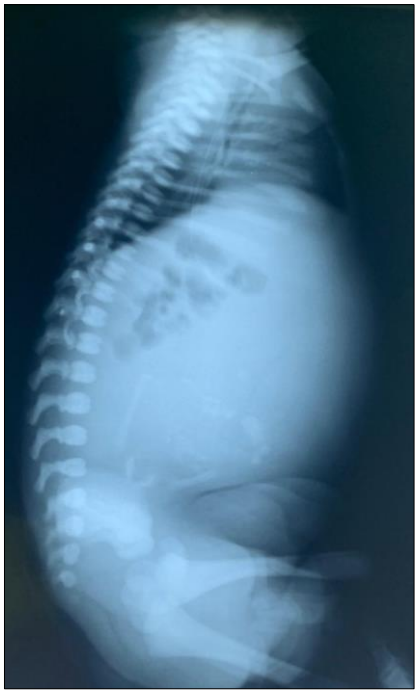

Figure 1: Plain X-ray showing a soft tissue mass with a well-formed vertebral body and limb bones.

A summary of clinical data and diagnostic workup for each FIF case is presented in Table 1. The antenatal diagnosis was made in three cases (60%), with the detection of a fetal mass in two cases and a pseudocyst in one. The median gestation period at the time of diagnosis was 36 weeks (range: 35-37). Patients diagnosed after birth presented with abdominal bulging and a palpable abdominal mass. There was no clinical dysmorphia and no associated anomalies.

After birth, the diagnostic workup of all neonates included an ultrasound (USS), whereas two neonates had X-rays (Fig. 1), four had computed tomography (CT) (Fig. 2), and one had magnetic resonance imaging (MRI). The features noted by radiological studies were a heterogeneous abdominal mass containing a patchy distribution of fat, intact bones, and soft tissue. These masses were well-limited, displacing the adjacent organs, located in the upper retroperitoneum in three cases and intraperitoneal in two cases, with a median size of 6.9 cm (range: 3.5-10 cm). However, the preoperative workup failed to identify the lesion origin and the correct source of blood supply. Three patients had a well-formed vertebral column indicating FIF preoperatively, whereas two neonates had a suspected teratoma diagnosis. Given the differential diagnosis, preoperative serum alpha-fetoprotein (AFP) and beta human chorionic gonadotropin levels (BHCG) were performed in three cases, which confirmed normal values (Table 1).

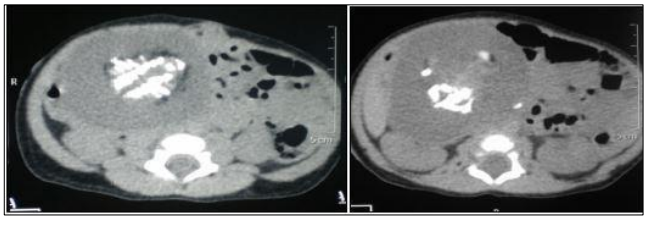

Figure 2: Non-contrast computed tomography imaging showing a solid cystic mass displacing the adjacent organs with the presence of well-formed bones, vertebral column (a), and ribs (b).

All patients underwent elective laparotomy at an average age of 44 days (range: 2-120 days). Given the presence of a distinct membrane, the mass was well-separated from surrounding structures, investing vessels were divided, and in-toto excision with an intact capsule was achieved in all cases. Each sac contained only one fetus (Fig. 3). Further abdominal exploration did not detect any additional pathology. Recovery was uneventful in all but one patient who presented with postoperative adhesional bowel obstruction after 45 days, which required surgical reintervention.

The diagnosis of FIF was confirmed by postoperative histopathological examination of specimens. Gross examination revealed the presence of an amniotic external sac, skin, an axis vertebral column, and a variable number of limbs with a human-like spatial orientation. Histopathological examination identified cutaneous epithelium and fully developed organ systems, with the gastrointestinal system being the most commonly identified internal organ system. There was no evidence of immature elements.

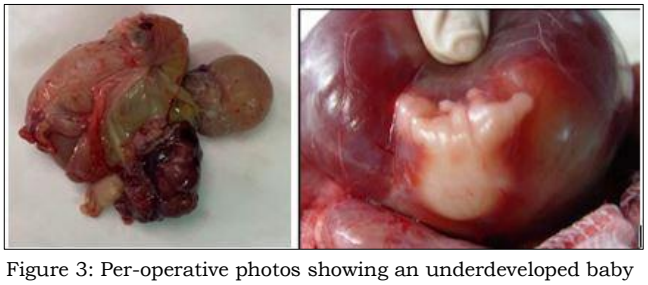

Figure 3: Per-operative photos showing an underdeveloped baby weighing approximately 450 g and containing rudimentary limbs, intestine, and brain. We can identify a foot floating within the amniotic sac.

All patients were followed up clinically, biologically (via tumor markers), and radiologically (via USS) until three years of age. They were all doing well by the last consultation with no sign of recurrence.

Table 1: Clinical data and diagnostic workup of patients with abdominal FIF

Case n° and year	Sex	Diagnosis time	USS findings	CT or MRI findings	Serology	Location	Size (cm)	Age at surgery (days)	Outcome
1 1999	F	Antenatal/ 36 weeks of gestation	Cystic mass with echogenic fatty content and limbs suggesting a teratoma	CT confirmed the diagnosis of teratoma	AFP +BHCG: NL	Retroperitoneal-lower abdomen	5	95	Favorable
2 2008	F	Postnatal/ 1st day of birth	Large heterogeneous cystic mass with non specific calcifications suggesting a teratoma	CT consisted with the diagnosis of teratoma	AFP +BHCG: NL	Intraperitoneal – upper abdomen	9	3	Adhesional bowel obstruction requiring another surgery →Favorable
3 2012	F	Postnatal/ 1st day of birth	Large heterogeneous cystic mass with no calcifications suggesting a teratoma	CT showed an encapsulated mass with vertebral-like structure consisting with FIF	-	Retroperitoneal – upper abdomen	7.5	2	Favorable
4 2017	F	Antenatal/ 35 weeks of gestation	Heterogeneous cystic mass with the presence of limbs suggesting teratoma	CT showed an encapsulated mass with vertebral-like structure and long bone formation suggesting FIF	-	Retroperitoneal-upper abdomen	3.5	120	Favorable
5 2021	F	Antenatal/ 37 weeks of gestation	Large cystic heterogeneous mass with the presence of limbs, vertebral-like structure and well-identified organs suggesting FIF	MRI consisted with FIF	-	Intraperitoneal-lower abdomen	10	2	Favorable

AFP: alpha-fetoprotein; BHCG: beta human chorionic gonadotropin; CT: computed tomography; MRI: magnetic resonance imaging; NL: normal; USS: ultrasonography

DISCUSSION

FIF is a rare pediatric tumor that affects 1 in 500,000 live births [3]. Though it was first described around 1800, the definition criteria differ. While Willis required the development of a vertebral axis [5], Gonzalez-Crussi proposed a wider definition that requires highly developed organogenesis organized around a vertical axis [6]. In recent years, Spencer suggested that FIF has one or more of the following characteristics [7]: (1) enclosed within a well-developed sac, (2) partially or completely covered by normal skin, (3) the presence of grossly recognizable anatomical parts, and (4) attachment to the host by a pedicle containing few relatively large blood vessels. This definition encompasses cases with highly developed organogenesis even in the absence of a vertebral axis. Our reported cases fully meet the required criteria.

Some authors claim a male predominance [8] of FIF, while others claim an equal distribution [9], whereas our cases were exclusively female. Perhaps this phenomenon of solely female patients could be a coincidence or partially explained by observations that teratomas arise more often from the ovaries, hence it would be logical for FIF to be more prevalent in females [9]. The timing of diagnosis is most

commonly reported during the first 18 months of life [10]. Late diagnosis of FIF is extremely rare, with the oldest documented patient being 47 years old [11]. Antenatal USS has been reported to detect 15% of cases [12]; however, with the advancement of antenatal imaging and fetal MRI, early diagnosis has been increasing. In our cohort, diagnosis was made antenatally in three (60%) cases, whereas two had normal prenatal imaging and were diagnosed on the first day of life.

Diagnosis after birth depends on the size and location of the mass. The most common location is the abdominal cavity due to the close anastomosis of the fetus to the vitelline circulation, with 80% of cases located in the upper retroperitoneum [13]. Three (60%) of our cases had the common retroperitoneal site of FIF, whereas two cases had lower intra-abdominal masses. Case reports have described other sites of FIF, including the skull [14], oral cavity [15], neck [16], posterior mediastinum [17], rectum [18], and scrotum or undescended testis [19].

The majority of patients with abdominal location present with an abdominal lump, with the size of the mass ranging from 4 to 24.5 cm in the literature [10]. It is primarily related to the origin of its vascular attachment with poor correlation to the degree of organogenesis. Larger fetuses present distinct vascular connections to the host. In our series, the smallest mass was 3.5 cm and the largest was 10 cm, and vascular supplies were secondary to the sac's attachments to the host's abdominal wall. Usually, as in our case series, a solitary fetal mass is present; however, few case reports have described multiple fetoid forms with up to 11 masses [20,21].

Imaging remains crucial in the diagnostic process; however, it accounts for only 16.7% of preoperative diagnosis [20]. Plain X-ray can depict a well-formed vertebral axis, although in some cases the spinal column may be underdeveloped and dysplastic, rendering it indistinguishable even by pathology [7]. All of our cases had well-formed vertebral and skeletal elements, but only two were identified by plain X-ray. Detailed imaging such as USS, MRI, and CT aid in the identification of multiple highly organized structures and symmetrical arrangement of limbs. As ultrasound and MRI lack ionizing radiation, these imaging tests should be the modalities of choice for FIF cases [22]. In our cohort, ultrasound assisted in the detection of heterogeneous abdominal masses by identifying the presence of fat and soft tissues, as well as the presence of well-formed limbs in three cases and well-formed vertebral columns in one. MRI is an expensive imaging test and requires general anesthesia. This imaging modality was conducted in only one patient and assisted in establishing the correct diagnosis, whereas a CT scan was used to diagnose the remaining four patients. However, it provided the correct preoperative diagnosis in only two patients.

Differential diagnosis usually includes teratoma and meconium pseudocyst [23]. The presence of classic eggshell calcifications and the absence of bony structures straightforwardly distinguish a meconium pseudocyst. Distinguishing a teratoma from FIF is more complex, particularly as these entities share many similarities, such as the presence of well-differentiated tissues, bone, and skin appendages [13]. Some authors consider both entities as a spectrum of the same pathology and argue that FIF may lack a spinal column and teratomas may be highly organogenic [23]. However, it is imperative to acknowledge that a teratoma correlates with a 10% malignancy rate. Serum AFP and ƁHCG analysis can help differentiate malignant teratoma or the presence of chorionic tissues within the mass [24]. However, despite imaging and serology, making a definitive diagnosis preoperatively is difficult, and in most cases, it is confirmed by postoperative histopathological examination and genotyping studies. In two of our cases, fetal masses were initially identified as teratomas, whereas histopathology confirmed FIF diagnosis. Postoperative histopathological examination identifies the vertebral column, recognizable anatomic parts, and organs with an orderly arrangement including skin coverage and the external fibrous capsule. In our series, histology was critical in confirming the presence of the skin and the external amniotic capsule as well as identifying the symmetric arrangement of the fetoid organs with respect to the vertebral axis, thus establishing the diagnosis.

In rare cases, histopathology may be insufficient, and molecular karyotyping and genetic analysis aid in distinguishing FIF from teratoma by confirming the monozygotic twin origin [22]. So far only a few cases have been studied genetically according to published literature [8,23,25]. In our series, genetic analysis could not have been utilized due to its unavailability in the country. Additionally, histopathological findings are important for guidance in determining an appropriate follow-up protocol. Close clinical, radiological, and serological monitoring is required in cases with immature elements or incomplete resection [13,26]. Authors recommend monthly serology for the first year followed by bimonthly serology for the second year [27]. Imaging should be performed three, six, twelve, and twenty-four months postoperatively [19]. In the absence of risk factors, however, recommendations are less stringent.

Although FIF is a benign condition, the treatment of choice is complete surgical resection to relieve any obstruction and prevent further compression of adjacent organs. Additionally, bleeding, infection, and

pleuroperitoneal inflammation have occurred as complications of FIF [28]. Resection is commonly straightforward due to the presence of a separating sac. Conversely, surrounding adhesions, formed after leakage or inflammation, are prone to make surgical excision more difficult. Two case reports found in the literature describe common bile duct damage of the host, intraoperatively misdiagnosed due to intense inflammation, with one of the cases resulting in demise [29]. Therefore, caution should be maintained throughout fetal mass dissection to prevent lesions of the capsule and adjacent structures [22]. There have been two reports of recurrence and malignant transformation attributed to the presence of residual immature tissue in the surrounding membrane; therefore, total resection is mandatory with the included surrounding sac [13,25]. In our cohort, postoperative surveillance revealed no recurrence; however, one case of postoperative adhesional bowel obstruction required a surgical reintervention.

CONCLUSION

FIF is a rare entity with an unknown etiology and is often misdiagnosed as a malignant teratoma. As treatment and prognosis are vastly different, and with the risk of malignancy recurrence, meticulous resection and postoperative supervision are required. Our case series additionally provides knowledge of a small number of published cases on the diagnosis, management, and follow-up of FIF.

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