J Ped Surg Case Reports 3 (2015) 554–562

Contents lists available at ScienceDirect

Journal of Pediatric Surgery CASE REPORTS

journal homepage: www.jpscasereports.com

Fetus in fetu: Review of the literature over the past 15 years

Lindsey M. Prescher [a], William J. Butler [a], Tyler A. Vachon [b], Marion C. Henry [a], Thomas Latendresse [c], Romeo C. Ignacio Jr. [a,*]

[a] Department of General Surgery, Naval Medical Center San Diego, 34800 Bob Wilson Drive, San Diego, CA, USA
[b] Department of Radiology, Naval Medical Center San Diego, 34800 Bob Wilson Drive, San Diego, CA, USA
[c] Department of Anesthesiology, Naval Medical Center San Diego, 34800 Bob Wilson Drive, San Diego, CA, USA

ARTICLE INFO

Article history:
Received 13 September 2015
Accepted 11 October 2015

Key words:
Fetus in fetu
Retroperitoneal tumor
Teratoma
Abdominal mass

ABSTRACT

Fetus in Fetu (FIF) is a rare congenital anomaly in which a malformed parasitic twin is found within the body of a living child or adult. In this case report, an 18 month-old male child presented with a large abdominal mass and failure to thrive. Imaging studies confirmed the presence of a large retroperitoneal fetus in fetu with significant mass effect of the adjacent structures. A surgical resection was performed and pathology confirmed the diagnosis. These rare cases have become more frequently reported and a review of the literature for the past 15 years will describe the demographics, updated genetic findings, pathology and outcomes of this unusual tumor. Recent findings will also discuss an infrequent association with teratomas that may warrant a longer follow-up for surveillance of malignancy.

Fetus in fetu is a rare anomaly of embryogenesis in which a malformed parasitic twin is found within the body of the normally developed host [1]. The majority of cases appear in infancy with an incidence reported at 1 in 500,000 births [2]. In most cases, the parasitic twin is anencephalic and usually contains a vertebral column and budding limbs. The upper limbs are less developed than lower limbs, and are usually located in the abdomen of the autosite [3]. The monozygotic diamniotic twin is quite similar to a mature teratoma; however, a key difference from fetus in fetu is a mature teratoma has an independent growth ability and malignant potential [4]. Diagnosis is often made preoperatively with ultrasonography, plain radiography, computed tomography (CT) or magnetic resonance imaging (MRI). Histopathologic findings confirm the diagnosis, and the recommended treatment is complete excision. We report one case of FIF, located in the retroperitoneum of a male child. An extensive review of the literature is performed to discuss some of its characteristics not noted in earlier reports, general differentiation from teratomas and potential need for long-term follow-up.

1. Case report

During a humanitarian mission in Southeast Asia, an 18 month-old male toddler, noticeably small for his age, presented with a distended abdomen and failure to thrive. Mother first noted the abdominal mass at approximately 8 months of age, and she stated that the mass had been gradually increasing in size. The child was the youngest of four children born at term to a gravida six mother. The patient's antenatal history was unremarkable. There was no history of maternal illness, exposure to radiation, or drug intake during pregnancy and both parents denied a family history of twining or congenital malformations.

Further examination of the child revealed a cachectic, malnourished child. A relatively fixed, firm and non-tender mass in the right lower quadrant was palpated on abdominal exam. The mass measured approximately 14 × 9 × 9 cm in size (Fig. 1). No organomegaly was observed and the only other abnormality on physical exam was a right undescended testicle. Secondary to limited laboratory resources on the hospital ship, the only blood tests obtained included a complete blood count and a basic metabolic panel, both of which were found to be within normal limits. A referral to host nation hospitals was unsuccessful due to the limited capabilities.

Initial imaging with plain abdominal films revealed irregular calcifications in the right lower quadrant and although a non-obstructed bowel gas pattern was appreciated, slight displacement of bowel loops to the left of the abdomen was noted. Follow up

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

* Corresponding author. Department of General Surgery, Division of Pediatric Surgery, Naval Medical Center San Diego, 34800 Bob Wilson Drive, San Diego, CA 92134, USA. Tel.: +1 619 453 6926; fax: +1 619 532 7673.
E-mail address: romeo.c.ignacio.mil@mail.mil (R.C. Ignacio).

2213-5766/Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
http://dx.doi.org/10.1016/j.epsc.2015.10.006

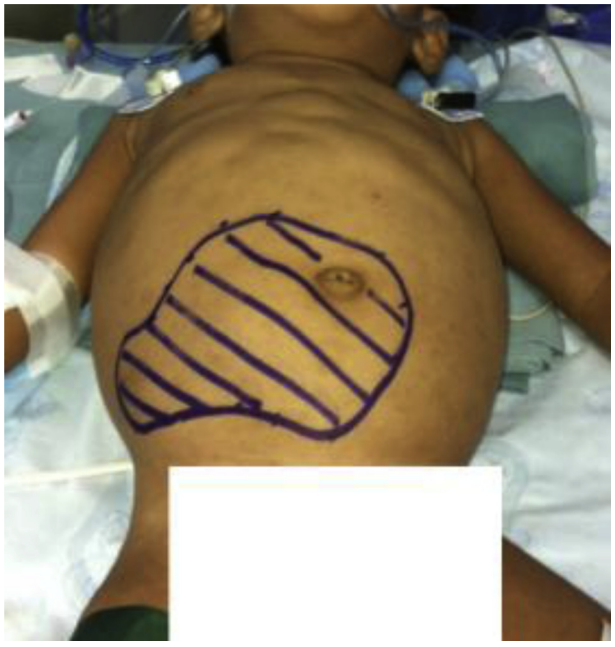

Fig. 1. Intraoperative image of patient with the palpable mass outlined. The mass measured approximately 14 × 9 × 9 cm in size.

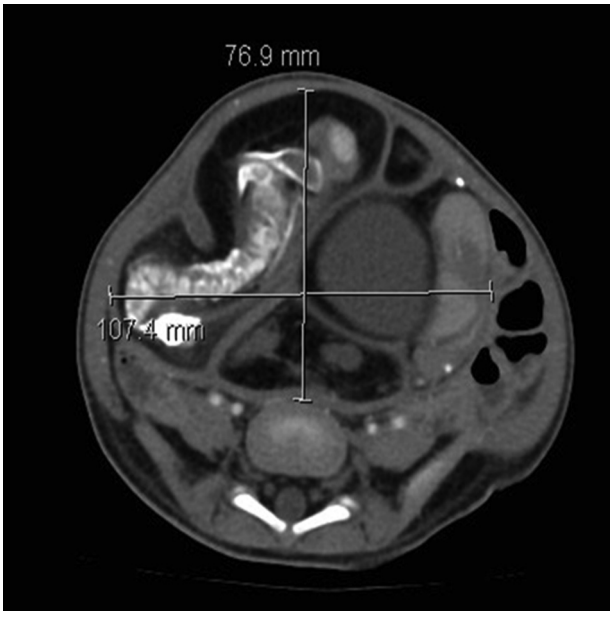

Fig. 3. Axial image of contrast-enhanced CT scan demonstrated a developed rudimentary skeleton with large soft tissue and cystic structures measuring 10.7 × 7.7 cm within the abdomen. The mass measured 11.9 cm in the coronal plane and extended deep in the pelvis.

ultrasound evaluation demonstrated a large heterogeneous, complex solid and cystic mass (Fig. 2). There were areas of increased echogenicity, which corresponded with calcifications on plain films. A contrast enhanced CT of the abdomen and pelvis greatly improved evaluation of the mass, and an axial skeleton was appreciated within the enhancing soft tissue mass (Fig. 3). While no cranial vault was appreciated, a vertebral column and pelvic girdle were identified as well as possible lower extremity buds. These were further characterized with maximum intensity projection images and post processed to provide a 3-D rotating model (Fig. 4). Finally, a CT angiogram was performed to identify any prominent vascularity. This was done to assess the feasibility of completing the operation on board the ship. The largest feeding vessel appeared to arise inferiorly from the patient's left common iliac artery and bifurcation while several smaller, less than 2 mm, vessels were visualized along the right and left lateral margins.

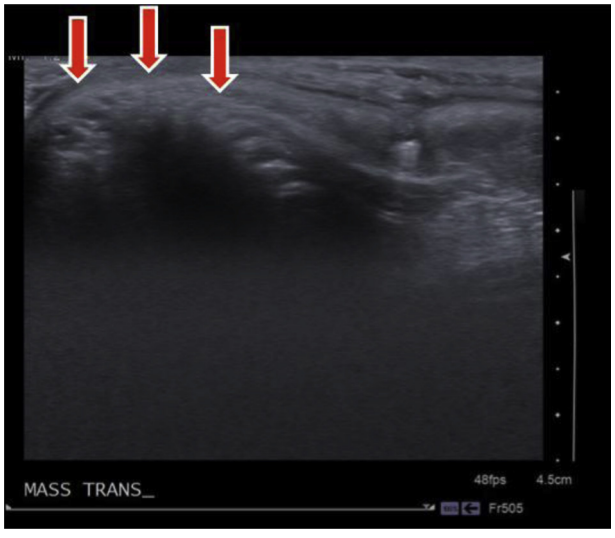

Fig. 2. Ultrasound image of fetus in fetu with calcifications and heterogenous echogenicity suggestive of a vertebra associated with soft tissue mass.

An elective laparotomy was performed with a low transverse incision. A well-encapsulated, partially cystic retroperitoneal mass was found. The mass had displaced the right ureter and cord structures anteriorly resulting in an undescended right testicle (Fig. 5). The mass encompassed the majority of the abdomen and displaced the bladder anteriorly and superiorly as it extended down toward the pelvis. Three well-defined vascular pedicles were identified supplying the mass, and the mass was removed en bloc. Further pathologic review revealed a skin-covered heterogeneous mass of soft tissue with bone and cartilage resembling a vertebral column and pelvic bone structures (Fig. 6). Within the soft tissue were scattered areas of benign colonic mucosa, as well as rare lymph nodes. No other major tissue structures and no malignancies were identified. The gross and histologic features were consistent with an anencephalic fetus in fetu, with the mass corresponding to an incompletely developed twin fetus. The procedure was complicated by a 2 mm prostatic urethral injury, where the mass was adherent to the urethra, requiring a primary repair and prolonged bladder catheterization. The postoperative period was uneventful and the catheter was removed after two weeks without further complications.

2. Discussion

Fetus in fetu, first described by Johann Friedrich Meckel, is the malformed or parasitic monozygotic diamniotic twin that is found inside the body of a living child or sometimes in an adult. The pathogenesis is still largely unknown; but during the ventral folding of trilaminar embryonic cyst (2nd and 3rd weeks of development), the diamniotic monochorionic twin is included within its host [5]. The inclusion in the sister embryo is speculated to be because of a persistent anastomosis of the vitelline circulation during development [6]. It is thought to result from unequal division of the totipotent inner cell mass of the developing blastocyst,

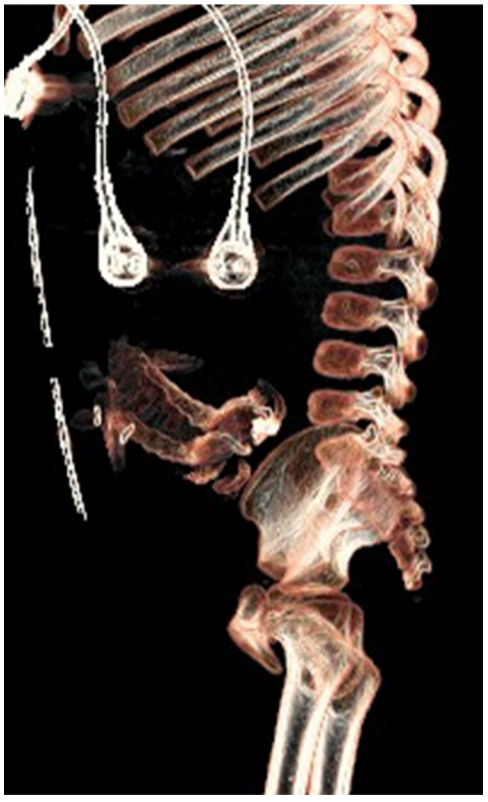

Fig. 4. Three-dimensional reformats showed spatial relationship between child's lumbar spine and pelvis with visualized portion of the axial skeleton of the fetus in fetu.

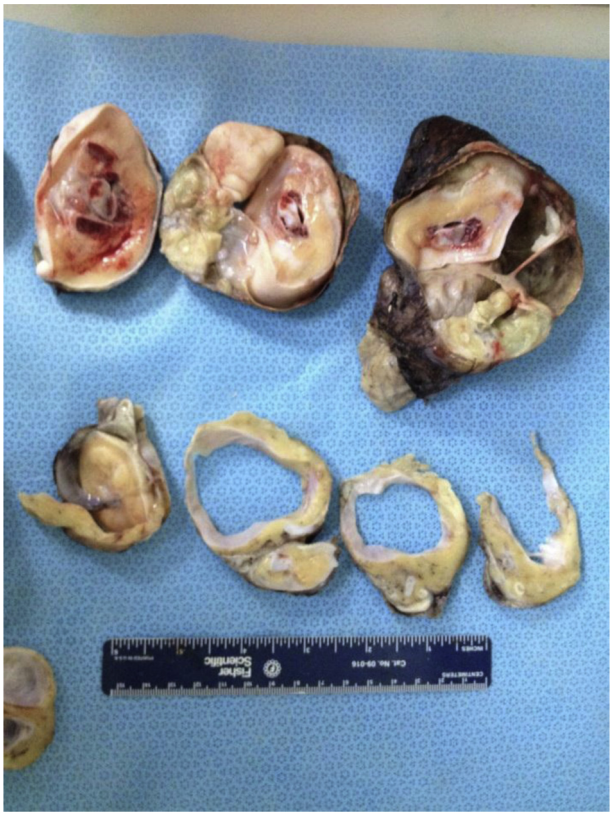

Fig. 6. Pathology specimen of retroperitoneal mass revealed a heterogenous fetus in fetu with bone and cartilage resembling a vertebral and pelvic bone structures.

causing a small cell mass within a maturing sister embryo. This ultimately results in a vestigial remnant, or fetus in fetu [7].

Clinical and pathologic features can be discussed while considering the differential diagnoses. In an infant with an abdominal mass showing diffuse calcifications or ossifications on ultrasonography, the differential diagnoses include neuroblastoma, FIF, meconium pseudocyst, and teratoma [8]. Congenital neuroblastoma, the most common neoplasm in the neonate, usually presents with further involvement of skin, liver, or bone. Teratomas rarely arise in the retroperitoneum, comprising less than 5% of retroperitoneal masses, compared to FIF, which are most often observed in the retroperitoneal location [9]. However, there is no debate that teratomas are far more common than FIF. Pathologically, FIF is highly differentiated tissue about a vertebral skeleton, whereas teratomas are discordant congregations of pleuripotential cells (from more than 1 germ layer) without systemic organization [10]. Pneumoperitoneum, ascites and calcifications with a family history of cystic fibrosis are suggestive of a meconium pseudocyst with peritonitis [11]. In general, intra-abdominal fetus in fetu is usually suspended by a single pedicle within a complete sac containing fluid. Besides the vertebral column, structures commonly found in fetus-in-fetu include dermal, limb, gastrointestinal, and portions of the central nervous system [12]. Less commonly noted are the gonads, adrenal glands, heart, and a primitive respiratory unit.

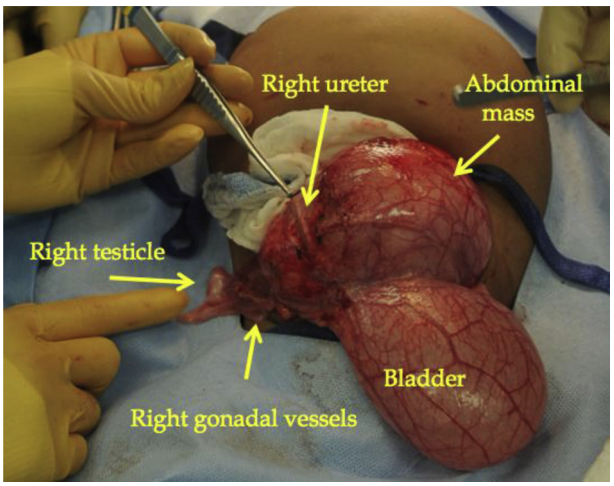

Fig. 5. Intraoperative photo demonstrating the large retroperitoneal mass displacing the bladder and ureter. The right testicle was intraabdominal in location.

With the advances in ultrasonography, one can associate early diagnosis with improved patient outcomes [8]. However, ultrasound sometimes is not confirmatory and as discussed often leads to a wide differential diagnosis. With the increased use of CT and MRI, the capability of narrowing to a single diagnosis has greatly improved [13]. Upon review of the radiologic literature, there is only one case with 3-D reconstruction demonstrating the fetus-in-fetu rare phenomenon. The argument for accurate pre-operative diagnosis by utilization of multidetector CT technology in fetus-in-fetu can be made when assessing the surgical planning required for such complex cases. Advanced imaging can provide improved resolution and unique insight into the spatial relationship of the mass with its surrounding structures [14], thus improving the surgeon's ability to create a more informed operative plan. In our case, considering the limited operative capabilities aboard the hospital ship, pre-operative 3D imaging (Fig. 4) was imperative in the decision making process.

Surgical treatment for fetus-in-fetu is curative since it is currently considered a benign disease. The main indication for

Table 1
Summary review of data for fetus in fetu case reports/series published between 1999 and 2013.

Case	Patient age at Dx	Sex	Location	Presentation	# of fetuses	Vert. column present (at least half) (+/−)	# fetal limbs	CNS present (+/−)	Other findings	Fetal size & weight	Genetic analysis	Preop diagnosis	Patient prognosis/ outcome
Kumar (1999)	3 mo	M	RP	Abdominal mass	1	+	3	−	None reported	135 g 15 × 20 cm	DNA match	Imperforate anus/ Abd mass	Good after surgery
Shin (1999)	6 d	M	Right Scrotum	Right scrotal swelling	1	+	4	+	None reported	60 g 5 cm	None reported	Scrotal mass	NR
Magnus (1999)	5 d	F	Intrahepatic	Liver abnormality on PN U/S in 2nd trimester	2	+	Nodule 3 has 2	Nodule 3 has spinal cord	Nodule 1: mature teratoma	Nodule 2 & 3: 3 cm	None reported	Fetus in fetu	Good after surgery
Shrivastava (1999)	27 yr	M	RP	RUQ mass	1	+	NR	−	None reported	20 × 18 cm	None reported	Dermoid cyst	Good after surgery
Patankar (2000)	16 yr	M	RP	Upper Abd mass	1	+	2	NR	Blood supply from AA	2000 g 30 cm	Not done	Fetus in fetu	NR
Patankar (2000)	3 yr	F	RP	LUQ mass	1	+	2	−	None reported	500 g	Not done	Fetus in fetu	NR
Al-Zaiem (2000)	2 wk	M	RP	Abd mass	1	−	4	+	None reported	11 × 12 × 15 cm	None reported	Fetus in fetu	Good after surgery
Hoeffel (2000)	19 mo	F	RP	RUQ mass	1	+	4	−	Blood supply from SMA	20 × 8 × 5 cm	None reported	Fetus in fetu	Good after surgery
Khadaroo (2000)	1 d (36WGA)	F	RP	Abd mass, bowel obstruction	1	+	10	+	Polyhydramnios	95 g	Karyotype and DNA analysis	Meconium peritonitis	Ileus and DIC postop, eventual disch with good prognosis
Awasthi (2001)	30 yr	M	RP	Abd mass, constipation, pain	1	+	4	None reported	Blood supply from AA	1500 g 26 × 12 × 15 cm	Not done	Fetus in fetu	Good after surgery
Federici (2001)	8 mo	M	RP	Abd mass	1	+	4	−	Blood supply from iliac bifurcation	650 g 14 × 9 × 9 cm	None reported	Fetus in fetu	Good after surgery
Ianniruberto (2001)	17 WGA	NR	Intracranial	Intracranial mass on PN U/S	1	+	4	−	FIF had active heartbeat initially. Host with multiple defects	40 mm	None reported	Fetus in fetu	Spont. Abortion at 18 WGA
Jones (2001)	34 WGA	M	RP	S at ?WGA/S at 34 wks	1	+	4	+	Blood supply from SMA	36 g	None reported	Fetus in fetu	Good after surgery
Massad (2001)	27	M	RP	Dysphagia	1	+	4	+	Blood supply from right inferior adrenal artery	14 cm long 754 g	Karyotype: normal 46XY	Teratoma	Good after surgery
Mills (2001) & Gllbert-Barness (2003)	38 WGA	F	RP	S at ?WGA/S at 38 wks	1	+	4	−	Blood supply from SMA. second mass with skin & single bone resembling vertebrae. At 2 yrs, presented with mature cystic teratoma	10 × 8 × 2 cm 50 g	DNA analysis	Fetus in fetu	Good after surgery
Nagar (2001)	2 yrs	M	NR	Abd mass, distention, emesis	1	NR	NR	NR		10 × 8 × 8 cm	NR	NR	NR
Nastanski (2001)	1 d	F	RP	S at ?WGA/S at 21wks	1	+	2	+	Blood supply from aorta	10 × 7 × 5.5 cm	None reported	Unclear	Good after surgery
Hong (2002)	2 d (37 WGA)	M	RP	S at ?WGA/S	1	+	4	NR	Blood supply from right renal artery. Separate 3 cm indeterminate mass (FIF vs teratoma)	7 cm 185 g	None reported	Fetus in fetu	NR
Lee (2002)	1 d (35 WGA)	M	Pelvic	Abd distention	1	+	2	−	Patient: 47XY +21	3.6 × 2.1 × 3.1 cm	Karyotype: 47XY +21	Fetus in fetu	Good after surgery
Wagner (2002)	3 mo	M	RP	Abdominal mass	1	+	2	+	None reported	NR	None reported	Fetus in fetu	NR
Iyer (2003)	1 d (37WGA)	M	RP	S at ?WGA/S at 37 WGA Abd distention on day 1	2	a: + b: +	a: at least 3 b: at least 2	−	Blood supply from left renal artery (both).	a: 18 cm L 130 g b: 8 cm L 50 g	None reported	Fetus in fetu	NR
Mohta (2003)	2 mo	M	RP	S at ?WGA/S at 32 WGA	1	+	4	−	Maternal serum AFP high	9 × 4 × 6 cm	None reported	Teratoma	NR

(*continued on next page*)

Table 1 (*continued*)

Case	Patient age at Dx	Sex	Location	Presentation	# of fetuses	Vert. column present (at least half) (+/−)	# fetal limbs	CNS present (+/−)	Other findings	Fetal size & weight	Genetic analysis	Preop diagnosis	Patient prognosis/ outcome
Sharma (2003)	4 mo	F	RP	Rapidly enlarging Abd mass	1	+	3	−	Blood supply from SMA	360 g	None reported	Fetus in fetu	NR
Sinha (2003)	18 mo	F	Right subhepatic	Slow growing Abd mass	1	+	NR	+	Vertebral column not seen on radiographs	20 × 15 cm	None reported	Fetus in fetu	NR
Varanelli (2003)	2 d (39 WGA)	M	RP	Palpable Abd mass at birth	1	+	4	−		7.2 × 4.5 × 9.3 cm	None reported	Fetus in fetu vs teratoma	Good after surgery
Aoki (2004)	1 d (36 WGA)	M	Mediastinum	Chest mass on PN U/S at 33WGA	1	+	3	+	Blood supply from intercostal artery	3.5 × 4.3 × 3 cm 19.8 g	None reported	Fetus in fetu	Good after surgery
Beaudoin (2004)	10 d (30 WGA)		Mediastinum	Paracardiac mass on PN U/S at 21 WGA	1	+	4	−		6.5 × 6 × 2 cm 23 g	None reported	Teratoma	Good after surgery
Brand (2004)	1 d (38 WGA)	M	RP	S at ?WGA/S at 26WGA	1	+	4	+	Blood supply from left iliac artery.	7 × 6 × 3 cm	Uniparental isodisomy of chromosome 14/ 15	Teratoma	Good after surgery
Kapoor (2004)	1 d (29.5 WGA)	M	Oropharyngeal	Mass on PN U/S	1	−	at least 2	+	Polyhydramnios, elements suggestive of yolk sac carcinoma	16 × 12.5 × 6 cm 371 g	None reported	Fetus in fetu	NR
Borges (2005) & Woodard (2006)	1 d (37WGA)	F	Left neck	Neck mass on PN U/S at 29 WGA	1	+	2	+	Absence of Left Carotid and Jugular Veins	5 × 6 × 7 cm	NR	Fetus in Fetu	Failed extub led to trach. Did well after
Bozilow (2005)	2.5 yr	M	RP	2–3 days Abd pain and emesis	1	+	4	+		12 × 5 cm	NR	Fetus in fetu	Good after surgery
Bozilow (2005)	11 d	M	RP	Abd mass at birth	1	+	2	−	Blood supply from iliac vessels	NR	NR	NR	Good after surgery
Chua (2005)	1 d (37WGA)	M	RP	Abd mass on PN U/ S at31 WGA	1	+	3	+	Blood supply from presacral plexus	4.5 × 2.5 × 2.5 cm 20 g	Karyotype (same as host)	Fetus in fetu	Good after surgery
House (2005)	1 d (37WGA)	NR	NR	Abd Mass on PN U/ S at 21 WGA	1	+	NR	NR	Blood supply from abdominal aorta	NR	NR	Fetus in fetu	NR
Kahloul (2005)	1 d	F	RP	Abd mass/ distention at birth	1	+	4	+		9 × 6 × 5.5 cm	NR	Teratoma	Bowel obstruct. At 3yrs, but ok after
Lee (2005)	39 yr	M	Intraperitoneal	Abd discomfort	1	Unclear	at least 2	NR		NR	NR	Fetus in fetu	Surgery not done
Neto (2005)	12 yr	F	Left lung	Cough (was being treated for TB)	1	+	NR	−		275 g	NR	NR	Good after surgery
Wada (2005)	4 mo	F	RP	Abd mass	2	a: + b: +	a: 4 b: 0	a: + b: +	Vasc connections to lumbar artery and IVC	Whole mass 8 × 6 × 4 cm	PCR–> both are XX	Fetus in fetu	Good after surgery
Higgins (2006)	10 mo	M	RP	Abd distention/ mass	1	+	3	+		10 × 12.5 × 11 cm 916 g	DNA allele profile	NR	NR
Higgins (2006)	1 d (37 WGA)	M	RP	Abd mass on PN U/ S at 20 WGA	1	None reported	None reported	−	1st PN U/S: twins. Repeat at 20 WGA: single fetus with Abd mass	5 × 4.5 × 3 cm	Cytogenetic testing inconclusive	Teratoma	NR
Kajbafzadeh (2006)	6 mo	M	RP	Abd mass	1	+	4	−	Blood supply from left renal artery	500 g	NR	Fetus in fetu	Good after surgery
Miura (2006) & Saito (2007)	35 WGA	M	RP	Abd mass on PN U/ S at 25 WGA	2	a: + b: +	a: 4 b: 4	a: + b: +	Blood supply from aorta	a: 8 × 5.5 × 4 cm b: 6 × 5.5 × 3 cm	Karyotype & STR matched	Fetus in fetu	Initial heart failure, but full recovery
Miura (2006) & Saito (2007)	21 WGA	M	Intracranial	Intracranial mass on PN U/S at 19WGA	1	+	Present but, number NR	−	6 fetiform masses also present	6 cm	Microsatellite markers; methylation specific PCR	Teratoma	Preg terminated at 21 WGA
Tiwari (2006)	(PN)	M	RP	Abd mass on PN U/ S at WGA	1	+	2	+		5.5 × 3 × 2.5 cm	NR	Fetus in fetu	NR
Aslanabadi (2007)	1 d (36WGA)	M	Oropharyngeal	Mass in oral cavity at birth	1	+	1	+	U/S at 20 wks didn't show any abnormalities.	14 × 9 × 5.5 cm 400 g	NR	NR	Good after surgery
Coolen (2007)	30 WGA	M	RP	Pelvic mass on PN U/S at 28 WGA	1	+	4	+	Blood supply from SMA	9.5 × 7.1 × 4 cm	NR	Fetus in fetu	NR

Garces-Inigo (2007)	6 d	M	RP	Abd mass on PN U/S	1	NR	NR	NR		NR	NR	NR	NR
Hui (2007)	10 d (39 WGA)	M	RP	Abd mass on PN U/S at 25 WGA	1	–	1	+		3 × 4 × 4 cm	NR	FIF vs teratoma (MRI at 30 WGA)	Good after surgery
Kaufman (2007)	2 yrs	M	RP	Postprandial Abd pain and bloody stools	1	None Reported	1	–	Mass invaded cecum and ascending colon	12 × 15 cm	NR	NR	Good after surgery
Mohan (2007)	3 yrs	M	RP	Progressive Abd distention	1	+	4	+		14 × 5 × 4.5 cm 1700 g	NR	Teratoma	Good after surgery
Sharma (2007)	36 yrs	M	RP	Abd swelling/discomfort	1	+	4	–	None	27 cm	NR	Fetus in fetu	Good after surgery
Abdur-Rahman (2008)	6 mo	F	RP	Lumbar mass	1	+	1	–		20 × 20 cm	NR	Fetus in fetu	Good after surgery
Balogun (2008)	3 mo	F	RP	Abd swelling/poor weight gain	1	–	1	+	Blood supply from left renal	12 × 12 cm	NR	Mesenteric cyst	Good after surgery
Chang (2008)	2 d (37 WGA)	F	RP	Abd mass on PN U/S at 20 WGA	1	–	3	+		NR	NR	Unclear	Good after surgery
Escobar (2008)	2 wks	F	RP	Abd mass	1	+	4	+		5 × 4.7 × 3.1 cm 49.9 g	Karyotype	Teratoma	NR
Gerber (2008)	30 WGA	F	9 intraperitoneal, 2 RP	Abd mass on PN U/S at 21 wks	11	a: + b: + c: + d: + e: – f: – g: + h: + i: + j: + k: –	a: 4 b: 4 c: 2 d: 2 e: 0 f: 0 g: 4 h: 4 i: 4 j: 2 k: 2	a: +	Fetal hydrops, left ovarian teratoma		Karyotype	Fetus in fetu	Surgery on day 2, death on day 34
Heuer (2008)	6 yr	F	Extracranial	Right temporo-occipital swelling	NR	NR	NR	NR	NR	NR	NR	NR	NR
Karaman (2008)	10 d	F	RP	Abd mass	1	+	3	+		10 × 7 × 6 cm	NR	NR	Good after surgery
Karaman (2008)	28 d	M	Pelvic	Buttocks lump	1	–	2	–		8 × 8 cm	NR	NR	Good after surgery
Khalifa (2008)	2 mo	F	RP	Abd mass at birth	1	+	3	–		12 × 10 × 8 cm 250 g	NR	Wilm's tumor	Good after surgery
Kim (2008)	4 mo	M	Intracranial	Setting sun sign of the eyes	1	Notochord	4	+		12 cm diameter	STR genotyping	Teratoma	Needed shunt, but did well after
Marnet (2008)	15 mo	M	Intracranial	Hydrocephalus on PN U/S at 36 WGA	1	–	NR	NR		NR	NR	Epidermoid cyst	Good after surgery
Santos (2008)	9 d	M	RP					+					
Tofigh (2008)	4 yrs	M	RP	Asymptomatic Abd mass	1	+	4	–		NR	NR	Fetus in Fetu	Good after surgery
Arlikar (2009)	2 yrs	M	RP	Enlarging Abd mass	1	–	1	–		20 × 18 cm	NR	Teratoma vs FIF	Good after surgery
Arlikar (2009)	4 mo	F	RP	Asymptomatic Abd mass	1	–	At least 2	–		NR	NR	Teratoma	Good after surgery
Bouyahia (2009)	18 d	F	RP	Abd mass on PN U/S at 25 WGA	1	+	4	+		6 × 5 cm 90 g	NR	Teratoma	Good after surgery
Daga (2009)	20 yr	M	RP	Abd pain/distention	2	a: + b: +	a: At least 2 b: 2	None reported		NR	NR	Fetus in fetu	Good after surgery
Joshi (2009)	6 mo	F	RP	Abd mass × 2 mo	1	NR	At least 2	None reported		NR	NR	Fetus in fetu	Good after surgery
Louati (2009)	1 d	F	RP	Abd mass on PN U/S	1	+	1	+		4.5 × 4.2 × 3.5 cm	NR	Fetus in fetu	NR
Louati (2009)	3 d	NR	RP	Abd Mass at birth	1	NR	NR	None reported		10 cm L	NR	NR	NR
Pourang (2009)	2 d	F	RP	Abd mass, bilious emesis, and feeding intol.	2	a: + b: +	a: 4 b: 4	a: + b: +	3rd mass: immature teratoma	a: 20 × 5 × 3 cm 150 g b: 16 cm L 100 g	NR	Teratoma vs FIF	Good after surgery
Vasani (2009)	14 mo	F	RP	Asymptomatic Abd mass	1	+	NR	NR		NR	NR	Fetus in fetu	Good after surgery
Gangopadhyay (2010)	10 wks	M	RP	Abd distention/emesis for 1 mo	2	a: + b: +	Present, but unclear# for both	+	Blood supply from AA	20 × 8 × 5 cm	NR	Fetus in fetu	Good after surgery
Gupta (2010)	9 yrs	M	RP	3 mo dull Abd pain	1	+	4	+	Blood supply from AA	12 × 10 × 10 cm 600 g	None reported	Fetus in fetu	Good after surgery
Gupta (2010)	18 mo	M	RP	Abd swelling	1	+	4	–	Blood Supply from AA	10 × 8 × 7 cm 800 g	None reported	Fetus in fetu	Good after surgery
Singh (2010)	3 mo	M	RP	Abd distention, emesis	1	+	NR	+		9 × 8 × 6 cm	None reported	NR	Good after surgery

(*continued on next page*)

Table 1 (*continued*)

Case	Patient age at Dx	Sex	Location	Presentation	# of fetuses	Vert. column present (at least half) (+/−)	# fetal limbs	CNS present (+/−)	Other findings	Fetal size & weight	Genetic analysis	Preop diagnosis	Patient prognosis/ outcome
Varga (2010) & Cingel (2012)	2 d	M	Mediastinum	Intrathoracic mass on PN U/S at 36 wks	1	+	NR	+		4.2 × 2.4 × 2.3 cm	NR	Teratoma, hamartoma, neuroblastoma or FIF	Good after surgery
Agrawal (2011)	4.5 mo	F	RP	Abd mass	1	+	3	NR		18 × 10 × 9 cm 480 g	None reported	Teratoma	Good after surgery
Bajaj (2011)	1 d	M	Oropharyngeal	Mass seen at birth	NR	NR	NR	NR		9 × 7 × 5 cm 300 g	None reported	NR	NR
Gunaydin (2011)	1 d (38WGA)	M	RP	Abd mass on PN U/S at 32 wks	1	+	4	−		10 × 10 × 7 cm	None reported	Fetus in fetu	Good after surgery
Gunaydin (2011)	3.5 yrs	M	Mediastinum	Recurrent resp infections	1	+	NR	Unclear		8 cm L	None reported	Teratoma vs FIF	Good after surgery
Kim (2011)	5 d	F	RP	Abd mass/ascites. presumed meconium peritonitis on PN U/S	1	−	1	NR		15 × 9 × 5 cm	None reported	Teratoma	NR
Mercy (2011)	2 d	F	RP	Abd distention	1	+	5	+		9 × 8 × 4.5 cm 184 g	DNA analysis	Meconium peritonitis	NEC, resp support, discharge at 5 wks. Repeat surgery at 6 mo for residual tissue.
Mohta (2011)	4 mo	M	RP	Abd mass	1	−	1	+	Blood supply from SMA	15 × 10 × 8 cm	None reported	Teratoma	Good after surgery
Parashari (2011)	14 yr	F	RP	Abd swelling, ache, emesis	1	+	4	NR	Blood supply from AA	15 cm L 1000 g	Not done	Fetus in fetu	Good after surgery
Rai (2011)	6 wks	M	RP	Abd mass, emesis	2	a: + b: +	a: 4 b: 1	a: − b: −	Blood supply from AA, venous drainage to IVC	a: 250 g b: 180 g	None reported	Fetus in fetu	Good after surgery
Savelli (2011)	18 d	F	RP	Abd mass on PN U/S at 25 WGA	1	+	4	+		7 × 6 × 3 cm	None reported	Teratoma vs FIF	Good after surgery
Dutta (2012)	19 d	F	RP	Abd mass	1	+	4	NR		11 × 9 × 8 cm	None reported	Fetus in fetu	NR
Gan (2012)	2 yrs	M	RP	Abd mass	1	+	2	NR		10 × 10 × 3.5 cm	None reported	Fetus in fetu	Good after surgery
Hoogendoorn (2012)	11 yr	M	RP	Swelling in right upper Abd since birth	1	+	4	NR		9 × 6 × 12 cm	Zygote study = monozygous	Fetus in fetu	NR
Huddle (2012)	1 d	F	Intracranial	Dilated lateral ventricles on PN U/S at 37 WGA	2	a: + b: +	a: 4 b: 4	a: − b: −		17 × 13 × 2.4 cm 230 g (aggregate)	FISH, SNP microarray, & karyotype matched	Fetus in fetu	At 1 yr had poor muscle tone and needed shunt
Kurdi (2012)	4 d	M	RP	Abd mass on PN U/S at 29 WGA	1	+	4	+	Blood supply from femoral artery	11 × 9 × 7 cm 460 g	None reported	Fetus in fetu	NR
Mustafa (2012)	4 mo	M	RP	Abd mass	1	+	4	NR		13.75 × 12.5 × 6.25 cm 500 g	None reported	Fetus in fetu	Good after surgery
Peng (2012)	11 yr	F	Back	Back mass	1	NR	1	NR		NR	None reported	Fetus in fetu	NR
Sun (2012)	3.5 mo	M	RP	Abd mass	1	+	4	NR		10 × 8.5 × 7 cm	None reported	Fetus in fetu	Good after surgery

WGA = Weeks gestational age, PN = Prenatal, NR = Not reported.

resection is to prevent or palliate symptoms of an intra-abdominal mass. The most frequent symptoms reported are distension, palpable mass, emesis, poor feeding, jaundice, and/or dyspnea [15]. However, there have been isolated cases of malignancy following resection of a FIF, prompting some surgeons to recommend complete resection on a more urgent basis followed by postoperative surveillance of tumor markers for 2 years [16]. These tumor markers would include alpha-fetoprotein (AFP) and human chorionic gonadotropin hormone (HCG). There has been some controversy about the differentiation of FIF from teratomas. Some reports describe a "pseudofetu" or a sacrococcygeal teratoma without a vertebral column, but with rudimentary organs that again argue the possibility of pathologic overlap [17]. In essence, both of these entities may present with different degrees of spinal dysgenesis or residual posterior enteric remnants secondary to early focal disturbance of endodermal-ectodermal differentiation [18]. It is not difficult to ascertain why the continued pathological controversy exists when discussing differentiation of FIF from a mature or well-organized teratoma.

In 2000, a literature review of all previous cases of FIF was performed that described some general characteristics. However, since that time frequent prenatal testing, advances in imaging technology, new genetic testing and updates in pathologic evaluations have led to more frequent publications of this congenital anomaly [2]. We have reviewed 95 cases published in the literature since 1999 to update this information and compared these with our own case. Highlighted features of this condition are portrayed in (Table 1). Of the 95 articles of FIF reported, 58 (63%) were male and 34 (37%) were female with 3 cases in which the sex could not be identified. A single fetus was seen in 89% percent of the case reports with the most common location being the retroperitoneum (72%), and one unusual case where 11 fetuses where identified in a single patient. Less frequent sites were intracranial, chest, mouth or neck. A vertebral column was identified in 76%, with 1 case revealing only a notochord. Based on reviewed literature, most FIF masses are acardiac and anencephalic. However intestinal, neural, pulmonary, gonadal, pancreatic, and adrenal tissue are often present. In our review we found 40 (55%) fetuses had evidence of central nervous tissue, 61% had gastrointestinal tissue, and 36% had evidence of genitourinary development. A substantial number of fetuses (35%) were identified on prenatal imaging, with 50% identified within the first month of life, and 75% within the first 2 years of life. Five cases involved an associated teratoma found at time of diagnosis or operation, and one case coincided with a yolk sac carcinoma. In comparison to the 2000 article by Hoeffel et al. we found a significant increase in prenatal diagnosis but interestingly a decrease in total number of cases diagnosed prior to 18 months of age. In our review, of those reported, 97% had a good prognosis after surgery (27 cases did not report on post surgical status or prognosis). For the two cases without good prognosis, one patient was alive at one year but with poor muscle tone and ventriculoperitoneal shunt requirement, and the other died on postoperative day 32 from complications associated with fetal hydrops. For those not operated on, one was terminated at 21 WGA, one resulted in spontaneous abortion at 18 WGA, and one did not have surgery due to parental choice.

As previously stated, most cases present as an abdominal mass during the first year of life. However, some reports of FIF in adults as old as 36 years of age have been reported [19]. Despite the overall health seen with these rare cases of FIF in adults, the importance in early diagnosis can be relayed through the increased morbidity seen in the majority of patients diagnosed at a later stage in development. With our patient, failure to thrive, cryptorchidism, and likely development delay can all be partially or completely contributable to his tumor. In today's technologically advanced world, prenatal diagnosis is on the rise. In 2001, only five cases were reported as being detected prenatally in comparison to the 35% we found in our review [2]. Diagnosis with US was first reported by Nicolini et al. [20]. Most reports prior to 1980 showed that a preoperative diagnosis of FIF was made in only 16.7% of cases.

In the past decade, increasing description of the genetic features of FIF have also have been identified. In all reports, the karyotype of the FIF is identical to that of the host fetus or infant [21]. Molecular genetic analysis using 10 STR (short tandem repeat) markers has also shown that the genotypes of the FIF mass and the host infant are heterozygous and identical. These findings confirm that the FIF originates from a premeiotic stem cell [22].

Looking again at the pathological controversy behind FIF, according to Willis in 1935, the 'features distinguishing a fetus-in-fetu from a highly differentiated teratoma are as follows: (1) There must be a separate spinal column, which demonstrates that the fetus has passed through a primary stage after gastrulation, involving formation of the neural tube, metamerization, and symmetrical development around this axis; and (2) the organs must have developed in a synchronized manner so that all have achieved the same degree of maturation [23].' Our review demonstrated that approximately 25% of case reports had no vertebral column identified, which reveals the lack of consistency in diagnosing FIF. More recently Gonzalez-Crussi further defined FIF as, 'any structure in which the fetal form is in a very high development of organogenesis' and linked it 'to the presence of a vertebral axis' [24]. However, reports of simultaneous or sequential FIF and teratoma are becoming more frequent, and whenever karyotyping and blood grouping have been performed, the results have been identical in the affected infant and the fetus-in-fetu or teratoma [25].

Currently, it appears that FIF and teratoma are not two distinct entities, but rather two aspects of the same pathology at different stages of maturation. Current treatment guidelines stress the importance of differentiating a mature teratoma from FIF because there is up to a 10% malignancy rate with retroperitoneal teratomas, implying the necessity of follow up [26,27]. With the recent literature reviewed and our findings of coinciding tumors, we raise the argument that treatment guidelines should be identical for both conditions. Treatment of choice would therefore involve complete resection of the tumor and monitoring of alpha-fetoprotein levels because of the risk of malignant recurrence. The occurrence of a subsequent teratoma is not unprecedented. Hopkins et al. [16] reported on a five-day-old boy who was found to have a retroperitoneal FIF and who later developed a right abdominal mass which proved to be a teratoma with malignant components requiring chemotherapy. Also Gilbert-Barness E et al. [11] reported the third known instance of FIF associated with a benign teratoma at age one. Although rare, these cases emphasize the consideration for potential long-term follow-up for surveillance to avoid any missed malignancy that may develop after surgical resection.

3. Conclusion

Fetus-in-fetu is currently classified as a benign condition; however, controversy continues regarding its future malignant potential or association. When mass compression becomes significant, as in our case, the child or adult can suffer from poor growth or development, infections, and even lack of organ function. With surgical treatment, normal anatomy and physiology can be restored and the malignant potential excised. With the ability of tumor marker surveillance and advances in radiographic technology, genetic testing and pathologic reviews, physicians must consider the potential for a minimum of 2 year follow up to avoid a missed malignancy. Surgical outcomes are reportedly good following

excision, but further data collection is required for long term results.

Disclosures

No financial relationships or sponsors are associated with this report and all authors declare that there are no conflicts of interests.

Informed consent

Informed consent was obtained from the mother of the child prior to their inclusion in the study. All details that would disclose the identity of the subject were omitted in the study.

Acknowledgments

This case was performed during Pacific Partnership 2012 humanitarian mission onboard the USNS (United States Naval Ship) MERCY. IRB and U.S. Navy PAO approval was obtained prior to the publication of this manuscript.

References

[1] Arlikar JD, Mane SB, Dhende NP, Sanghavi Y, Valand AG, Butale PR. Fetus in fetu: two case reports and review of literature. Pediatr Surg Int 2009;25:289–92.
[2] Hoeffel CC, Nguyen KQ, Phan HT, Truong NH, Nguyen TS, Tran TT, et al. Fetus in fetu: a case report and literature review. Pediatrics 2000;105:1335–44.
[3] Escobar MA, Rossman JE, Caty MG. Fetus-in-fetu: report of a case and a review of the literature. J Pediatr Surg 2008;43:943–6.
[4] Spencer R. Parasitic conjoined twins: external, internal (fetuses in fetu and teratomas), and detached (acardiacs). Clin Anat 2001;14:428–44.
[5] Gunaydin M, Celik FC, Tander B, Bozkurter AT, Sullu Y, Baris S, et al. Two cases of fetus in fetu. J Pediatr Surg 2011;46:e9–12.
[6] George V, Khanna M, Dutta T. Fetus in fetu. J Pediatr Surg 1983;18:288–9.
[7] Knox AJ, Webb AJ. The clinical features and treatment of fetus in fetu: two case reports and a review of the literature. J Pediatr Surg 1975;10:483–9.
[8] Hing A, Corteville J, Foglia RP, Bliss Jr DP, Donis-Keller H, Dowton SB. Fetus in fetu: molecular analysis of a fetiform mass. Am J Med Genet 1993;47:333–41.
[9] Grosfeld JL, Stepita DS, Nance WE, Palmer CG. Fetus-in-fetu: an ususual cause for abdominal mass in infancy. Ann Surg 1974;180:80–4.
[10] Khadaroo RG, Evans MG, Honore LH, Bhargava R, Phillipos E. Fetus-in-fetu presenting as cystic meconium peritonitis: diagnosis, pathology, and surgical management. J Pediatr Surg 2000;35:721–3.
[11] Gilbert-Barness E, Opitz JM, Debich-Spicer D, Mueller T, Arnold SR, Quintero R. Fetus-in-fetu form of monozygotic twinning with retroperitoneal teratoma. Am J Med Genet A 2003;120A:406–12.
[12] Phatak. Fetus-in-fetu: a case report. Indian J Radiol Image 2003;13:93–4.
[13] Patankar T, Fatterpekar GM, Prasad S, Maniyar A, Mukherji SK. Fetus in fetu: CT appearance – report of two cases. Radiology 2000;214:735–7.
[14] Hong SS, Goo HW, Jung MR, Kim HJ, Kim EA, Kim KS, et al. Fetus in fetu: three-dimensional imaging using multidetector CT. AJR Am J Roentgenol 2002;179:1481–3.
[15] Eng HL, Chuang JH, Lee TY, Chen WJ. Fetus in fetu: a case report and review of the literature. J Pediatr Surg 1989;24:296–9.
[16] Hopkins KL, Dickson PK, Ball TI, Ricketts RR, O'Shea PA, Abramowsky CR. Fetus-in-fetu with malignant recurrence. J Pediatr Surg 1997;32:1476–9.
[17] Gude D, Rayudu BR, Bansal D, Sashidhar C. Revisiting fetus-in-fetu. Ann Saudi Med 2012;32:427–9.
[18] Bentley JF, Smith JR. Developmental posterior enteric remnants and spinal malformations: the split notochord syndrome. Arch Dis Child 1960;35:76–86.
[19] Sharma N, Verma P, Pathak P. 27 cm fetus in fetu presenting in a 36-year-old man: report of a rare case and brief review of literature. Indian J Surg 2007;69:155–7.
[20] Nicolini U, Dell'Agnola CA, Ferrazzi E, Motta G. Ultrasonic prenatal diagnosis of fetus in fetu. J Clin Ultrasound 1983;11:321–2.
[21] Chua JH, Chui CH, Sai Prasad TR, Jabcobsen AS, Meenakshi A, Hwang WS. Fetus-in-fetu in the pelvis: report of a case and literature review. Ann Acad Med Singapore 2005;34:646–9.
[22] Kim JW, Park SH, Park SS, Wang KC, Cho BK, Kim SY, et al. Fetus-in-fetu in the cranium of a 4-month-old boy: histopathology and short tandem repeat polymorphism- based genotyping. Case report. J Neurosurg Pediatr 2008;1:410–4.
[23] de Lagausie P, de Napoli Cocci S, Stempfle N, Truong QD, Vuillard E, Ferkadji L, et al. Highly differentiated teratoma and fetus-in-fetu: a single pathology? J Pediatr Surg 1997;32:115–6.
[24] Mills P, Bornick PW, Morales WJ, Allen M, Gilbert-Barness E, Johnson PK, et al. Ultrasound prenatal diagnosis of fetus in fetu. Ultrasound Obstet Gynecol 2001;18:69–71.
[25] Boyce MJ, Lockyer JW, Wood CB. Foetus in foetu: serological assessment of monozygotic origin by automated analysis. J Clin Pathol 1972;25:793–8.
[26] Lewis RH. Foetus in Toetu and the retroperitoneal teratoma. Arch Dis Child 1961;36:220–6.
[27] Lord JM. Intra-abdominal foetus in foetu. J Pathol Bacteriol 1956;72:627–41.