

Management of extra-tubal and rare ectopic pregnancies: case series and review of current literature

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Abstract

Objective Management of extra-tubal ectopic gestations remains an inadequately explored clinical field due to the rarity of the presentations. We present a synopsis of the management highlighted by our personal case series.

Method A literature search was conducted through PubMed and Medline databases. We reviewed all cases presenting with extra-tubal nidations in our institute, including seven interstitial, two cervical, three ovarian and two abdominal pregnancies.

Result The advances in minimal access techniques and imaging modalities have resulted in novel fertility preserving endoscopic procedures. All except one of the patients were treated by endoscopic procedures, including a novel procedure for evacuation of cornual ectopics.

Conclusion A high index of suspicion is essential, combined with meticulous review of clinical findings and imaging modalities to make an accurate diagnosis. Treatment with the least invasive method, either by minimal access techniques, non-invasive radiological procedures or medical treatment should be encouraged.

Keywords Ectopic gestation · Pregnancy · Endoscopy

Introduction

Ectopic pregnancy remains one of the most common causes of pregnancy related deaths with a rate of 1.8/1,000 ectopic pregnancies [20]. Between 1991 and 1993 it accounted for 9% of all maternal deaths in the USA [14]. The incidence of the disease has risen sixfold over the past 25 years, and has risen to 11/1,000 pregnancies in 2000–2002 [4].

Extra-tubal nidations of ectopic pregnancies are rare. But they could be life threatening and prone to torrential bleeding as the sites of nidation are usually of increased vascularity. Additionally, the atypical clinical presentation and equivocal investigations, lead to delayed diagnosis. This is amply illustrated by the The confidential enquiry into maternal and child health 2002 (CEMACH 2002) finding that, in all the four cornual pregnancies, which contributed to the maternal mortality, the diagnosis was made only after rupture [4].

We present 2 years experience of extra-tubally sited ectopic gestations in our Early Pregnancy Assessment and Treatment Unit. In the period 2002 to date, we diagnosed and managed 14 unusually sited ectopics including seven interstitial/cornual, two cervical, three ovarian and two abdominal pregnancies. Additionally, we managed two bilateral tubal ectopic gestations occurring in spontaneous conceptions. We have developed novel methods of treatment using minimal access techniques and all our patients were treated by fertility preserving procedures.

Diagnoses and management of these unusual ectopic gestations are clinically challenging and the treatment options have traditionally involved major surgical procedures, which affect future fertility. We present this review underlined by our personal series to raise awareness of these rare presentations, which require a high degree of suspicion from the investigating clinician, and also to highlight

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the recent advances in fertility preserving less morbid treatments.

Cases

Interstitial/cornual pregnancies

Seven interstitial pregnancies were diagnosed and treated from 2002 to date. The maternal age at presentation varied between 25 and 37 years. The presentations were between 9 and 12 weeks, usually with bleeding PV (per vaginum) and lower abdominal pain. The lowest level of serum beta HCG (human chorionic gonadotrophin) was 10,905 IU/l and the highest was 20,650 IU/l with an average level of 14,874 IU/l. Five out of the seven patients revealed a significant gynaecologic history. Laparoscopy and dye test showing blocked tube, recurrent miscarriages in two patients and bicornuate uterus on scan in two patients were present. Diagnosis was made by ultrasound scan examination which showed a high sensitivity, the correct diagnosis being made in six out of the seven patients (Fig. 1).

A novel method of surgical treatment was developed and successfully performed [22]. Laparoscopic and ultrasound guided trans-cervical evacuation of the ectopic gestation was performed in five of our patients. Laparoscopic excision of right cornual ectopic pregnancy was performed in one patient, and one patient was managed conservatively as repeated hormonal levels indicated a failing pregnancy. Histology confirmed products of conception in all the surgically treated patients (Fig. 2).

Cervical pregnancies

Two cervical pregnancies were diagnosed and treated from 2002 to date. Both patients presented at 6 weeks gestation

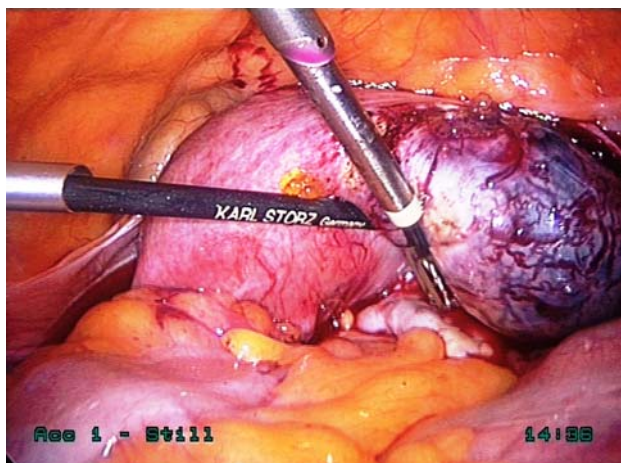


Fig. 1 Laparoscopic view of a right cornual ectopic pregnancy

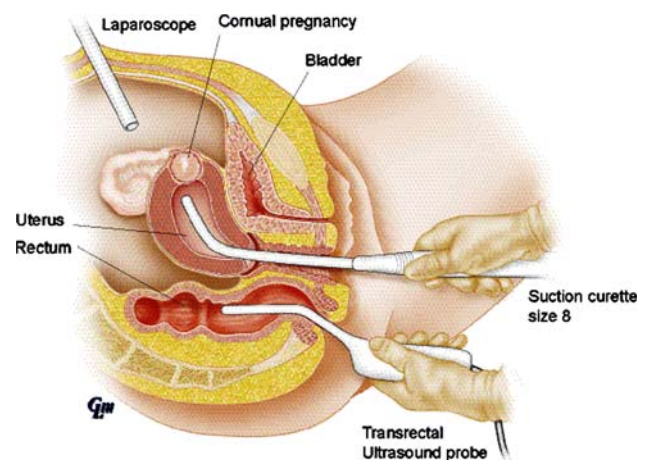


Fig. 2 Schematic diagram of the Laparoscopic and ultrasound-guided transcervical evacuation of cornual ectopic pregnancy. Transrectal ultrasound and laparoscopy are performed simultaneously and the ectopic pregnancy evacuated through transcervical suction curettage

with painless bleeding PV. One of the conceptions was spontaneous and the other was by IVF (in vitro fertilization). Gynaecologic history was non-significant in both the patients.

Scans revealed gestation sacs with viable singleton fetus sited just below the level of the internal os. Serum beta HCG levels at presentation were 20,985 and 22,368 IU/l. (Fig. 3)

Both the cases were managed by bilateral ligation of the descending branch of uterine artery followed by cervical dilatation and suction evacuation of the ectopic. Histology confirmed products of conception in both cases (Fig. 4).

Ovarian pregnancies

Three ovarian pregnancies were diagnosed and treated from 2002 to date. Significantly all three patients presented prior



Fig. 3 Cervical ectopic pregnancy: transvaginal scan image showing intracervical gestational sac below the closed internal cervical os

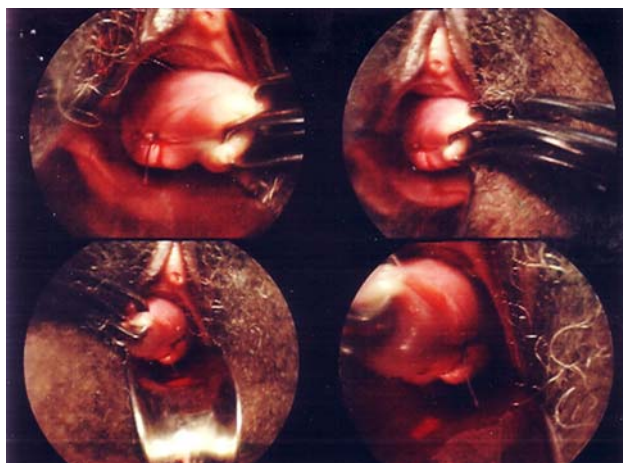


Fig. 4 Ligation of bilateral descending branch of the uterine artery is performed to decrease the risk of bleeding during curettage of the cervical ectopic pregnancy

to missing the menstrual period, 10, 11 and 17 days after the last menstrual period. All the cases were spontaneous conceptions and presented with severe lower abdominal pains. Scans in all three patients failed to make the correct diagnoses and provisional diagnoses of ovarian cysts were made. Serum beta HCG levels at presentation were at the lower levels of 533, 614 and 333 IU/l. Excision of a right ovarian ectopic by laparotomy was performed in one of the patients due to haemodynamic deterioration. Intra-operatively the diagnosis of a bleeding right corpus luteum was made.

Laparoscopic removal of ovarian ectopic pregnancies was performed in the other two cases and intra-operatively the diagnosis of ovarian ectopic was made in both of the cases. Histology confirmed trophoblastic tissue in the ovarian tissue in all the cases establishing the diagnoses of ovarian ectopic pregnancy (Fig. 5).

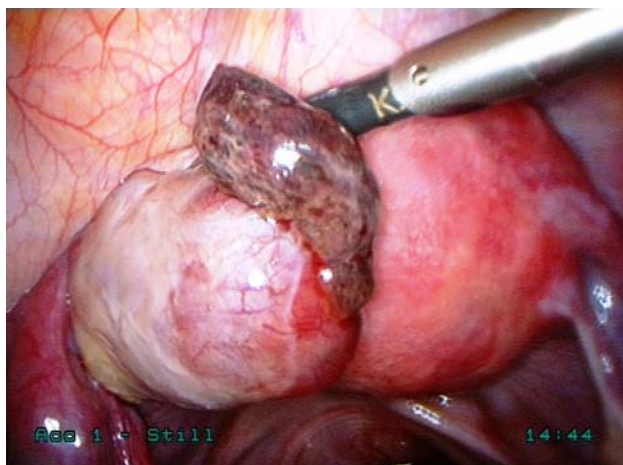


Fig. 5 Laparoscopic view of a left ovarian ectopic pregnancy

Abdominal pregnancies

Two abdominal pregnancies were diagnosed and treated from 2002 to date. Both cases presented at 6 weeks gestation with low back pain and spotting PV. Scan in both patients showed a collection of echoes in the cul de sac. The first patient had a coil in situ when she fell pregnant, which had been removed 3 days prior to admission. Serum beta HCG at presentation was 1,802 IU/l. Laparoscopy revealed gestational tissue on the left pelvic side wall, which was evacuated laparoscopically. Laparoscopy in the second patient revealed gestational sac and products of conception in the cul de sac and attached to colonic serosa. Bilateral tubes and uterus was normal. The ectopic was removed laparoscopically. Histology in both cases confirmed chorionic villi and established the diagnoses of abdominal pregnancy.

Bilateral tubal pregnancies

Two bilateral tubal ectopic pregnancies were diagnosed and treated from 2002 to date. Both patients presented with spontaneous conceptions at 6–7 weeks gestations with lower abdominal pain. Serum beta HCG levels at presentation were 11,330 and 572 IU/l.

At laparoscopy in both cases, bilateral tubal pregnancies were revealed with both sides unruptured. Salpingectomy was performed on the right side and a linear salpingostomy with evacuation of the ectopic was performed on the left side in both our patients. Histology in both cases confirmed chorionic villi in both tubes and established the diagnoses of bilateral tubal ectopic pregnancy (Fig. 6).

Method

A literature search was conducted through Pubmed and Medline databases. We Identified MeSH terms by using PubMed's MeSH Browser and entered qualifications requiring that all retrieved citations be written in English, and restricted to major topic headings. Due to the large number of recall, subheadings were used to limit the search and focus on extra-tubal sites. Individual searches were also performed on the known extra-tubal sites of gestation.

Discussion

The literature search and also our experience has highlighted that a meticulous clinical history and examination is imperative in the diagnosis of extra-tubal ectopic pregnancies as well as tubal ectopic pregnancies. Risk factors appear to be similar for both extra-tubal and tubal ectopic

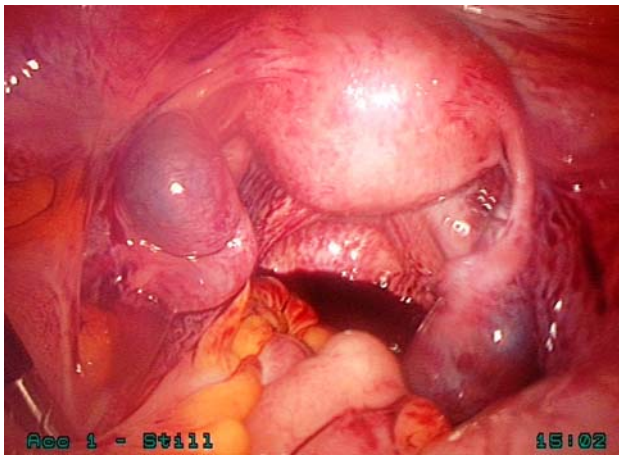


Fig. 6 Laparoscopic view of bilateral tubal ectopic pregnancies

gestations. The clinician must exhibit a high index of suspicion as most of the patients present atypically and clinical deterioration could be rapid (Table 1).

Interstitial/cornual pregnancies

Interstitial/cornual pregnancies account for 2–6% of all ectopic pregnancies, with an incidence of 1 in 2,500–5,000 live births and a mortality rate of 2–2.5% [4]. Presentation is usually delayed due to the distensibility of the myometrium and patients present between 9 and 12 weeks with abdominal pain, amenorrhea and abnormal vaginal bleeding. No cardinal risk factor has been identified, but significantly 25–40% of patients have had a previous salpingectomy [18]. In our series of patients the majority presented with significant previous gynaecologic history of damaged tubes, recurrent miscarriages and also bicornuate uterus in two of the patients.

Ultrasound scanning provides the diagnosis in the majority (75%) of cases, but the diagnosis is rendered difficult due to similarity between an interstitial site and an eccentrically sited intrauterine gestation. In our unit, ultrasound scans diagnosed six out of seven patients correctly. Magnetic Resonance Imaging (MRI) scans have been used with greater accuracy in cases presenting diagnostic difficulties on scan.

With the recent advances in sensitive diagnostic modalities and high-resolution scans, earlier diagnosis has become possible. This has resulted in the surge of newer conservative means of treatment which are fertility preserving and associated with lesser morbidity. They involve injection of the implantation site with methotrexate, prostaglandin or KCL and also systemic methotrexate injections. Developments in minimal access techniques have resulted in novel methods of treatment. Laparoscopic and ultrasound-guided vaginal evacuation has been successfully performed [22],

Table 1 Table of comparison of clinical presentation, diagnosis and treatment of the various extra-tubal sites of ectopic pregnancy

Sites of ectopic	Cornual	Cervical	Ovarian	Abdominal	Bilateral tubal
Incidence	1 in 2,500–5,000 live births	1 in 2,500 to 1 in 12,422	0.15–3.2%	1 in 2,200 to 1 in 10,200	1 in 725 to 1 in 1,580
Gestational age	9–12 weeks	6 weeks	4–6 weeks	1 ^o –1st trimester, 2 ^o –2nd trimester	6–7 weeks
Significant risk factor	Damaged tubes, previous salpingectomy in 25–40%	Previous curettage in 70%	Intrauterine contraceptive device	Pelvic inflammatory disease, infertility	Tubal disease
Major symptoms	Abdominal pain amenorrhea, abnormal vaginal bleeding	Painless PV bleeding, globular distended cervix	Abdominal pain amenorrhea, intra-abdominal bleed in 30%	Abdominal pain amenorrhea	Abdominal pain amenorrhea, abnormal vag bleeding
Approximate median HCG	15,000 IU/l	21,000 IU/l	500 IU	1,000 IU/l	800 IU/l
Preoperative diagnosis	Ultrasound diagnosis in 75%	3D power Doppler ultrasound, MRI	Ultrasound—only in 25%	Diagnosis usually intra-operative	Diagnosis usually intra-operative
Fertility preserving treatments	Injection of site or IM methotrexate, hysteroscopic or laparoscopic resection	Injection of site with KCL/methotrexate curettage with ligation	Laparoscopic resection IM methotrexate	1 ^o laparoscopic removal, 2 ^o laparotomy	Laparoscopic treatment

and laparoscopic resection with or without endoloop and encircling suture method has been performed. Laparoscopic vasopressin injection, cauterization of ascending uterine vessels and fibrin glue application has been performed to stem the profuse bleeding which can occur intra-operatively [13]. Hysteroscopic suction evacuation of the implanted site has been described [12] and the success rate of resection is increased after systemic methotrexate treatment. Non-invasive methods have been recently developed. Ultrasound guided transvaginal or transabdominal injection of KCL has been employed successfully to destroy the ectopic gestation [5].

Five of our seven patients were treated by the novel method of laparoscopic and ultrasound guided vaginal evacuation [22]. This results in preservation of future fertility as risk of hysterectomy is lessened. Furthermore the vaginal evacuation eradicates the need for future deliveries by cesarean section, as the uterine musculature is not incised into. Conservative management of one of our patients highlights the concept that a failing pregnancy irrespective of the site can be managed non-interventionally. In such a situation close monitoring is necessary with 24 h rapid access of the hospital services by the patient.

Cervical pregnancies

The incidence of cervical ectopic pregnancy is 0.15% and a common predisposing factor seems to be prior dilatation and curettage present in up to 70% of patients [18]. Patients usually present with painless vaginal bleeding and the cervix is usually found to be enlarged, globular or distended as it was in our series of two patients. Ultrasound scans delineate the cervical nidation, and recently MRI scans and three-dimensional power Doppler ultrasounds have been used to increase the diagnostic accuracy. Both our patients were diagnosed by ultrasound scans.

Traditionally, cervical ectopic pregnancy has been treated by hysterectomy and is still the procedure of choice in advanced pregnancies and life-threatening haemorrhage. Systemic methotrexate treatment has been successfully used and has a failure rate of 5%. The failure rate rises to 10% if the gestational age is greater than 6 weeks, the mass is greater than 3.5 cm and fetal cardiac activity is present [19]. Prostaglandin or the progesterone antagonist RU-486 has been used concomitantly with methotrexate increasing the success rate and also preoperatively to decrease the vascularity [19].

Conservative surgical management includes curettage with balloon tamponade [8], and hysteroscopic resection with a resectoscope [9]. Ultrasound-guided administration of KCL intra-amniotically followed by systemic administration of methotrexate has been performed successfully [11]. Non-invasive methods of ultrasound-guided transcervical

aspiration of the gestational sac and ultrasound-guided transvaginal or transabdominal injection of KCL have been employed successfully to destroy the ectopic gestation [5]. Torrential intra-operative haemorrhage is not uncommon during cervical ectopic surgical treatment. Lateral cervical suturing of the cervical vessels, cervical cerclage [19], bilateral internal iliac artery ligation [15] and uterine artery embolization used on its own and preoperatively prior to dilatation and curettage has aided the decrease in the risk of massive haemorrhage.

In our series, bilateral ligation of the descending branch of uterine artery served to control the haemorrhage during evacuation of the pregnancy. Ultrasound-guided transvaginal injection of KCL into the sac was performed in one of the patients prior to the evacuation to destroy the conceptus. Thus treatment by major surgical procedures was avoided minimizing morbidity and preserving fertility.

Ovarian pregnancies

The incidence of ovarian pregnancy is 0.15–3.2% and they account for less than 3% of all ectopic gestations. Clinical presentation is similar to tubal ectopic pregnancies with amenorrhea, abdominal pain and intra-abdominal bleeding, which may be severe, and can occur in up to 30% of patients [18]. Traditionally, diagnosis was made intra-operatively only in a quarter of the patients. In our series, ultrasound scan failed to diagnose an ovarian ectopic in all our patients. Intra-operatively the correct diagnosis was made only in two of the patients, while in the other a diagnosis of bleeding corpus luteal cyst was given.

Laparotomy has been replaced by laparoscopic resection or ablation as the preferred mode of treatment and systemic methotrexate treatment has been tried successfully.

Abdominal pregnancies

Approximately 1–3% of ectopic pregnancies are peritoneal implantations and the incidence ranges from 1 in 2,200 to 1 in 10,200 pregnancies [1]. The fetal mortality rate is very high and varies from 30–95% with fetal abnormalities in 30–100% of fetuses born alive. Maternal mortality can be as high as 20% in advanced abdominal pregnancies.

Diagnosis of abdominal pregnancies is difficult and is usually made intra-operatively. Ultrasound scan is occasionally successful with the finding of an empty uterus low in the pelvis. Both of our patients were not diagnosed preoperatively with the imaging techniques.

Management is mostly surgical and should be immediate as the risk of haemorrhage is high. Preoperative arterial embolization decreases the vascularity and the risks of bleeding. Angiographic embolization of internal, iliac, hypogastric or uterine artery has been tried with variable

results. Primary abdominal pregnancy usually presents in the first trimester and can be removed laparoscopically with minimal patient morbidity, as was the case with both the patients in our series. Secondary abdominal pregnancies are usually advanced at presentation and require an open procedure.

Surgical removal of the placenta requires careful analysis of the vascular attachments and the risk of bleeding [1]. Occasionally, removal of organs might be necessary to achieve haemostasis, i.e., bowel resection, subtotal hysterectomy. The medical anti-shock garment (MAST suit) placed around the abdomen has been successfully used to stem intractable haemorrhage. If the placenta is firmly attached with no significant bleeding, it can be left in situ after trimming the cord and membranes. Postoperative treatment with systemic methotrexate has been used to assist the involution process. Follow-up of placental involution should be with imaging modalities and by serial beta HCG levels and may take years to complete.

Bilateral tubal pregnancies

The incidence of spontaneous bilateral ectopic pregnancy has been reported between 1/725 and 1/1,580 pregnancies [21]. The first published report was by Bledsoe in 1918 [3]. Histology from both our cases showed chorionic villi in samples from both tubes, thus fulfilling the Norris criteria [16]. Bilateral ectopic pregnancies bear no distinguishing feature from unilateral ectopics, regarding clinical presentation or hormonal levels and the diagnosis is usually missed preoperatively [21]. Laparoscopic treatment offers the best option for conserving future fertility, as well as reducing operative morbidity. In both our patients we were able to conserve the lesser-damaged tube by a linear salpingotomy and evacuation of the pregnancy. Salpingectomy of the worst damaged tube prevents a future potential ectopic pregnancy. These case reports also underscore the clinical concept that finding evidence of bleeding from one tube does not preclude other pathology and a thorough examination of the pelvis is necessary.

Other unusual sites

The co-existence of an intrauterine and an ectopic pregnancy is classed as a heterotrophic pregnancy and the incidence is 1:3–4,000 pregnancies [18]. Heterotrophic pregnancies present diagnostic conundrums due to equivocal diagnostic results and treatment dilemmas due to patients desire to conserve the viable intrauterine pregnancy. Traditionally, laparotomy and recently laparoscopy has been the treatment choices. A recent case report details local injection of low dose methotrexate following aspiration of the cornual pregnancy, which destroyed the ectopic

gestation and allowed the intrauterine pregnancy to continue [17]. The rising incidence of cesarean sections has resulted in the changing profile of scar ectopic pregnancies from very rare to rare. Diagnosis is usually by ultrasound scans and recently MRI scans have been used with increased diagnostic accuracy. Traditionally, laparotomy and hysterotomy with excision of the implantation site has been employed as the main treatment. Laparoscopic ligation of uterine vessels followed by resection of the ectopic pregnancy mass has been performed [23]. Successful conservative management has been described by systemic methotrexate treatment [7]. Excision with a resectoscope under laparoscopic and ultrasound guidance has been reported recently. Non-invasive methods of ultrasound-guided transvaginal or transabdominal injection of KCL has been employed successfully to destroy the ectopic gestation [5].

Pregnancy of a rudimentary horn of the uterus is very rare with an incidence of 1 in 100,000 to 1 in 150,000. Chances of rupture are very high, in the region of 70% and maternal mortality is approximately 0.5%. Ultrasound and MRI scanning are the usual modalities of diagnosis. Surgical removal of the horn is usually required as most cases rupture in the first or second trimester. Laparoscopic removal has been described and decreases the immediate and long-term surgical morbidity [24].

Intramurally sited ectopic pregnancy is one of the rarest form of ectopic pregnancy, constitutes less than 1% of all ectopics and the diagnosis is almost always made intra-operatively. Patients usually present with clinical findings of rupture uterus between 11 and 30 weeks of gestation. Thirty-three cases have been reported so far, and the treatment is invariably surgical resection [10]. A single case report of successful expectant management has been reported where the pregnancy failed spontaneously [2].

Retroperitoneal site of ectopic is exceptionally rare with only four cases in the literature. In all the cases diagnosis was made intra-operatively and excision of the mass was the treatment performed [6].

Case reports of other unusually sited ectopic pregnancies abound. Caecal pregnancy causing massive bleeding per rectum, ectopic gestation beneath the serosa of the anterior abdominal wall, angular pregnancies at the uterine cornua and medial to the round ligament, intra-ligamentary pregnancies and pregnancy in an inguinal herniorrhaphy scar have all been described. Diagnosis is invariably made intra-operatively and surgical excision remains the treatment of choice.

Conclusion

The rising incidence of pelvic inflammatory disease and infertility treatments has been concomitant with the rise in

the incidence of ectopic pregnancies. In addition to tubal ectopics, the incidences of extra-tubal sites of ectopic nidations are becoming more frequent. An awareness of the presentation and management is essential as even though the incidence is rare they could be life threatening. Diagnostic challenges are the norm as the presentation is usually atypical. The treatment of these gestations can prove difficult. Systemic methotrexate and the usual surgical techniques have a high failure rate. Earlier diagnosis has facilitated treatment with more conservative and non-invasive methods. The burgeoning of recent innovative conservative treatment methods evidences this.

Insufficient evidence exists to recommend one single ideal management option and the decision should be a consensus of the presentation, surgeon's skills, available techniques, patient preference and the need to preserve future fertility. A high index of suspicion combined with careful review of clinical findings and imaging modalities and coupled with treatment with the least invasive method will go far towards lessening the high morbidity and mortality rate.

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