Case series

Heterotopic pregnancy: Five case reports diagnosed in 2021

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ABSTRACT

Introduction and importance: Heterotopic pregnancy is the occurrence of pregnancies in at least two different implantation sites in the same time. The diagnosis is one of the most difficult of the gynecological emergencies. In 2021 this pathology still underdiagnosed and remains unknown by physicians. Most patients are admitted in critical stage.

Cases presentations: We reported 5 cases of heterotopic pregnancies in symptomatic women admitted from January 2021 to December 2021, in maternity department, mother and child hospital Abderrahim Harouchi, Ibn Rochd University Hospital of Casablanca. The frequency of this pathology in our hospital in 2021 is about 10% of ectopic pregnancies (5/52 cases of ectopic pregnancies). All the cases were received in critical phase of the pathology (vascular collapsus or hemodynamic shock). The mean diagnostic was suspected in gray scale ultrasound that show an intrauterine pregnancy associated with adnexal mass corresponding to hematosalpinx or gestational sac in the uterine tubes with medium to high abundance hemoperitoneum. All of our cases were treated by laparotomy in emergency after resuscitation measures.

Clinical discussion: The existence of intrauterine pregnancy does not exclude an ectopic pregnancy and often confuses the physician who consults the patient in early stage of symptoms. The clinical symptomatology is often related to a threatened or ongoing abortion, the diagnosis of heterotopic pregnancy is usually made in the stage of hemoperitoneum secondary to a rupture of the ectopic pregnancy. The standard treatment is conservative surgery, preferably by laparoscopy. The manipulation of the uterus must be careful to preserve the intra uterine pregnancy. Laparotomy retains its indications especially in forms with hemorrhagic shock. The abortion is not rare after surgery. A progestin treatment is always indicated.

Conclusion: The diagnosis of heterotopic pregnancy should not be delayed by the discovery of an intra-uterine gestational sac in symptomatic women and the adnexa must be systematically examined in the first trimester sonographic exam. The Diagnosis is often difficult and management should be initiated as soon as possible given the risk of maternal mortality.

1. Introduction and importance

Heterotopic pregnancy (HP) is the occurrence of an intrafallopian pregnancy and an ectopic pregnancy (EP) simultaneously, whatever its location [1]. The most common ectopic pregnancies are located in the fallopian tubes. Abdominal location increases the risk of maternal mortality up to 90 times higher than a normal IUP [2]. The diagnosis of a heterotopic pregnancy is still underdiagnosed and difficult. The presence of the intrauterine pregnancy at the sonographic exam can make confusion to the physician. The main treatment consists of removing the ectopic pregnancy, while preserving the IUP, that make the second challenge after diagnoses.

We report 5 cases of heterotopic pregnancy, diagnosed all of them in our maternity service, hospital mother and child Abderrahim Harouchi, university hospital of Casablanca between January and December 2021. All of them were complicated by a large hemoperitoneum with vascular collapse. This pathology constitutes in this year 10% of all ectopic pregnancies (52 cases). Those cases reports have been reported in line with the SCARE 2020 criteria [3].

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2. Cases presentations

For comparative approach of the cases, we aim to resume our cases in tables (Tables 1-4).

3. Clinical discussion

Heterotopic pregnancy is a rare form of twin pregnancy, defined by the coexistence of an ectopic and intracural pregnancy. It was described for the first time by DUVERNET at 1708 [4].

The frequency increased with the avancement of assisted reproductive techniques (ART), especially the frequency of use of ovulation inducer. The incidence is estimated at 1/30000 when associated with spontaneous pregnancy, above 1/100 when associated with in vitro fertilization, and 1/900 when using clomiphene citrate [5-7].

In 2021, the frequency of this pathology in our maternity was about 10% of all ectopic pregnancies (52 cases). One of them was induced with clomiphene citrate.

The mechanical or functional fallopian tube factors are the same ones for the ectopic pregnancies (endometriosis, peritoneal adhesions, infections, pelvic inflammation...). Multiple embryo transfers in ART techniques are also associated with high risk of heterotopic pregnancies [8].

The diagnosis of heterotopic pregnancy remains one of the greatest challenges of the gynecological emergencies. It is often delayed due to the early visualization of an intracural sac, that confused the physician, with late detection of adnexal abnormalities. Also the clinical symptoms are often related to an ongoing abortion.

The most common symptoms include abdominal pain, vaginal bleeding, peritoneal irritation and uterine enlargement, making the diagnostic easier [9,10]. Otherwise, the symptoms can be misleading when we had isolated abdominal pain associated with intracural pregnancy. This situation is very dangerous, and the evolution can be towards rupture of the ectopic pregnancy or even maternal shock.

In our five cases, diagnosis was delayed at minimal 7 days, after symptoms declaration, going to 23 days. All of them was diagnosed at advanced stage with vascular collapse.

The diagnostic is based on suprapubic and transvaginal ultrasound by specifying the presence and the vitality of the intracural pregnancy and the site of the ectopic pregnancy. Although, the sensitivity of ultrasound can vary from 26.3% to 92.4% [11]. Often, the presence of an intracural pregnancy leads to difficulties of interpretation, especially in the youngest pregnancies that can make confusion to inexperimented physician. In 2 cases the adnexal mass was interpreted as an ruptured hemorrhagic cyst.

The echographic signs that allow to confirm the diagnosis are the presence of intracural gestational sac associated with heterogenous adnexal mass corresponding to hematosalpinx or the visualization of latero-uterine mass surrounded by an echogenic trophoblastic halo, sometimes containing an embryon. The presence of hemoperitoneum supports the diagnostic [12,13].

In the above reported clinical cases, both intracural and ectopic pregnancies were visualized by ultrasound, 3 with hematosalpinx and 2 with evolutive ectopic pregnancies with embryo outside the uterine cavity. Hemoperitoneum was large in 4 cases.

The treatment of heterotopic pregnancies consists of intervening as early as possible on the ectopic pregnancy, respect the intracural one, preserve patient fertility, and avoid the recurrence.

Laparoscopy should be performed as the first line treatment, especially in case of uncertain diagnosis [14]. It has the advantage of avoiding the risk of uterine manipulation to preserve the intracural pregnancy, compared to laparotomy, which can cause uterine irritability and postoperative spontaneous abortion.

Urgent Laparotomy is recommended in cases of hemodynamic instability or large hemoperitoneum like in our cases. Manipulation of the uterus should be minimal [15].

Salpingectomy was performed in all our cases because of anatomical damage following the rupture in 4 of them and the deep implantation of the trophoblast in the case of the abdominal pregnancy.

For asymptomatic, hemodynamically stable patients and no evolutive ectopic pregnancy, expectant management can be suggested Intramuscular injection of Methotrexate maybe an alternative only if the intracural pregnancy is not progressive [16].

A progestin therapy can be associated to avoid post-operative abortion. A 800 mg of Micronized progesterone was administered to four of our patients with intracural active pregnancies. One of them had spontaneous abortion 1 week later versus 3 with evolutive pregnancies. We report a second spontaneous abortion in our series without any
hormonal treatment, but the evolution of the pregnancy was uncertain. The prognosis of the Heterotopic pregnancy depends on the early diagnoses and treatment [17]. Precisely treated, 30 to 75% of intra-uterine pregnancies progress to term [18]. The complications are the result of late diagnosis, they are often hemorrhagic. In our cases, all of our patients had a severe anemia, 4 of them was transfused with red cell blood, 2 had elevated creatinine level and was admitted in intensive care unit.

Take away points:
1- The exam of adnexa must be systematic in the first sonographic exam for pregnancy in all patients.
2- Detailed history and physical examination are importance to explore all risk factors related to heterotopic pregnancy.
3- The presence of intra uterine pregnancy doesn’t make optional the exam of adnex, especially if the patient reports symptoms or ectopic pregnancy risk factors.
4- The delayed diagnoses limit the possibility of conservative treatment and can be responsible of secondary infertility.

4. Conclusion
The frequency of heterotopic pregnancy has increased in recent years, with the emergence of medically assisted procreation. The diagnosis is often difficult. The presence of any symptoms or ectopic pregnancies risk factors, associated with intrauterine pregnancy must lead the physician to miniciously screen of the adnexas to research any abnormalities. The standard treatment is conservative surgery, preferably by laparoscopy. However, treatment by laparotomy is not uncommon.

Table 1
Summary of clinical features of the five cases.

| Profile                          | Case 1       | Case 2       | Case 3       | Case 4       | Case 5       |
|----------------------------------|--------------|--------------|--------------|--------------|--------------|
| Age (years)                      | 40           | 38           | 36           | 28           | 32           |
| Parity                           | 5            | 2            | 0            | 0            | 3            |
| Pathological medical or surgical history | No           | 2 cesarean sections | 2 spontaneous miscarriage | Repeated genital infections | No           |
| Contraception                    | Micro-progessative pills | Intra-uterine contraceptive device | No | No | No           |
| Smoking exposition               | No           | No           | No           | No           | No           |
| History of ectopic pregnancy     | No           | No           | No           | Right ectopic pregnancy 6 months ago treated with methotrexate | No           |
| Induced or spontaneous pregnancy | Spontaneous  | Spontaneous  | Citrate clomiphene induced pregnancy | Spontaneous | Spontaneous  |
| Interval between beginning of symptoms and diagnostic (days) | 10            | 23           | 7            | 12           | 15           |

Table 2
Summary of sonographic (suspubic and transvaginal) and biological features of the five cases.

| Profile                          | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|----------------------------------|--------|--------|--------|--------|--------|
| Sonographic parameters           |        |        |        |        |        |
| Intrauterine pregnancy           |        |        |        |        |        |
| Active intrauterine pregnancy    |        |        |        |        |        |
| of 7 weeks and 5 days of gestation according to Crown-rump length (CRL) (Fig. A) |        |        |        |        |        |
| Ectopic pregnancy                |        |        |        |        |        |
| Left uterine hematosalpinx       |        |        |        |        |        |
| measuring 45 mm without any embryo structure (Fig. A) |        |        |        |        |        |
| Hemoperitoneum                   | Large  | Large  |        |        |        |
| Biological parameters            |        |        |        |        |        |
| Hemoglobin (g/dl)                | 6.9    | 8.1    | 5.4    | 5.2    | 8.7    |
| Platelets (ele/mm$^3$)           | 308,000| 156,000| 203,000| 120,000| 150,000|
| Hematocrit (%)                   | 20     | 28     | 29.1   | 18     | 25     |
| Prothrombin level (%)            | 60     | 90     | 79     | 52     | 71     |
| Creatinine (g/dl)                | 4.8    | 5.6    | 14     | 17     | 12     |
Through these case reports, we brought to light the importance correlation of the clinical symptoms, and all risk factors in order to make the diagnosis as early as possible.

**Patient consent**

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patients.

**Ethical approval**

I declare on my honor that the ethical approval has been exempted by my establishment.

**Table 3**

Summary of management features of the five cases.

| Profile                        | Case 1                  | Case 2                  | Case 3                  | Case 4                  | Case 5                  |
|--------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Anesthetic management          | General                 | General                 | General                 | General                 | General                 |
| Anesthesia mode                | General                 | ALR                     | General                 | General                 | General                 |
| Red blood cells                | 2                       | No                      | 3                       | 3                       | 1                       |
| Transfusion (unit)             |                         |                         |                         |                         |                         |
| ICU admission                  | No                      | No                      | Yes (1 day)             | Yes (3 days)            | No                      |
| Surgical approach             | Laparotomy (vascular    | Laparotomy (vascular    | Laparotomy (vascular    | Laparotomy (hemorrhagic | Laparotomy (vascular    |
| collapse)                      | collapse)               | collapse)               | collapse)               | choc)                   | collapse)               |
| Intra-operative finding        |                         |                         |                         |                         |                         |
| Hemoperitoneum (ml)            | 1000 ml                 | 600 ml                  | 1000 ml                 | 1500 ml                 | 700 ml                  |
| Localisation of the ectopic pregnancy | Ruptured ectopic pregnancy in left ampullar fallopian tube (Fig. D1) | Ruptured ectopic pregnancy in left ampullar fallopian tube | Abdominal ectopic pregnancy with trophoblastic implantation in the abdominal side of the left ampullar fallopian tube an intact gestational sac with embryo floating in intraperitoneal cavity. (Fig. C) | Ruptured ectopic pregnancy in right isthmic fallopian tube | Ruptured ectopic pregnancy in left ampullar fallopian tube (Fig. D2) |
| Anatomical conditions of the fallopian tube | Damaged                | Damaged                 | Damaged                 | Damaged                 | Damaged                 |
| Predisposing anatomical cause  | No                      | Multiple peritoneal adhesions | No                      | Multiple peritoneal adhesions (chlamydia infection sequels). | No                      |
| Treatment                      | Left salpingectomy      | Left salpingectomy      | Left salpingectomy      | Right salpingectomy     | Left salpingectomy      |

**Table 4**

Summary of post-operative management and evolution features of the five cases.

| Profile                        | Case 1                  | Case 2                  | Case 3                  | Case 4                  | Case 5                  |
|--------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Post-operative management      | Vaginal progesterone    | Vaginal progesterone    | Vaginal progesterone    | No vaginal progesterone | Systematic vaginal progesterone 800 mg/day (4 weeks) |
| Evolution                      | 800 mg/day              | 800 mg/day              | 800 mg/day              |                         |                         |
| Abortion 1 week later          | Normal evolution of the IUP | Abortion 1 week later | Normal evolution of the IUP | Spontaneous miscarriage 2 days later | Normal evolution of the IUP |

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**Author contribution**

Lamrissi Amine: Corresponding author writing the paper and operating surgeon
Antaky Redouane: writing the paper and operating surgeon
Mourabbih mariam: writing the paper
Jalal Mohamed: study concept
Fichtali Karima: study concept
Bouhya Said: correction of the paper and operating surgeon.
Guarantor
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Declaration of competing interest
The authors declare having no conflicts of interest for this article.

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Fig. C. Intra operative finding of the heterotopic abdominal pregnancy: the localisation of the ectopic pregnancy in the abdominal side of the fallopian tube with the presence of a gestational sac with embryo floating in the peritoneal cavity (C2).

Fig. D. Intraoperative finding of ectopic pregnancy in the left ampullar tube associated with large hemoperitoneum.