Original Research Article

Ovarian ectopic pregnancy: a case report with review of literature

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Abstract

Background: Ectopic pregnancyis a major health issue in reproductive age group female. Incidence of primary ovarian ectopic pregnancy as mentioned in literature of India is variable from 0.001% to 0.014% of normal pregnancies.Only 0.15% to 3.0% of all ectopic pregnancy occurs in ovary and it is 2nd m/c site of ectopic pregnancy after fallopian tube. Annual incidence ofextra uterine cavity pregnancyis rising over past 3 yrs. **Aim and Objective:** Aim of this review article is basically to describe a case of ovarian pregnancy and to study by a review of literature, the clinical sign &symptoms, diagnostic criteria and management of particular pathlogy accordingly, promote conservative surgical management. CASE-Here we report a case of 28 years old women, G5P3L3A1, presented to our hospital withlower abdomen pain with one and half month pregnancy with clinical feature of shock. Diagnosis was confirmed by transvaginal ultrasound, patient was prepared & taken for laparotomy in view of ruptured ovarianectopic pregnancy. Her intraoperative findings were 200 cc hemoperitoneum present, salpingo-oophorectomydone on Rt side. Tubal ligation done on left side by modified pomeroy method. Postoperative period was uneventful. Her histopathological report shows ovarian tissue in wall of gestation sac. **Conclusion:** According to spigelbergcriteria,it is a diagnostic challenge to obstetrician. Diagnosis can be missed radiologically and intraopertively. It Should be suspectedinpatients presented with rupturedec topic pregnancy, ultrasound features suggestive of normal b/lfallopian tubewith hemoperitoneum with breached ovarian surface. Conservative surgical approach is preferred, Now days Medical management is preferred for unruptured ectopic pregnancy. Confirmation of ovarian pregnancy done only after histopathologicalreport

Keywords: Ectopic pregnancy, Laprotomy, Salpingoophorectomy,Methotrexate

Introduction

The Incidence of ectopic pregnancy is 1.2 -1.4%. Incidence of primaryovarian ectopic pregnancy as mentioned in literature of India is variable from 0.001% to 0.014% of normal pregnancies. Only 0.15% to 3.0% of all ectopic pregnancy occurs in ovary and it is 2nd m/c site of ectopic pregnancy after fallopian tube [1]. Extra-iterine pregnancy or ectopic ovarian pregnancy a greek word originated from “EKTOPOS” which means out of place. Ektopos refer toimplantation of blastocyst outside of uterine cavity [1]. Primary ovarian ectopic pregnancy is very rare clinical presentation of extrauterinepregnancy & very dangerous life-threatening emergency if not diagnosed timely. Fallopian tube is most common site of ectopic pregnancy, comprises to 95% of total ectopic pregnancies. Incidence increasing with ART proceduresand IUCD insertion. Ovarian pregnancy is gestational sac implantation in the ovary.First case of ovarian pregnancy is reported by St. Maurice in 1689. Its diagnosis is very difficult & based on clinical diagnosis, intraoperative finding and on histo-pathological report. Definite management of ruptured ovarian pregnancy is surgery. Approximately 75% pregnancies terminate in early gestation 12.5% patients terminates in the second trimester & 12.5% patients reached till term. Ovarian pregnancyin 1624, suggested first by Mercerus[2,3].

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Incidence of ectopic pregnancy is-

1. Tubal pregnancy- 90-95.5%
2. Ovary-1.5- 3%
3. Abdomen-1.3%
4. Cervical -0.15%
5. Heterotopic 1-2%
6. Caesarean -6%
7. Interstitial -2.5%

Case Report

-28 years old female, she is $G_5P_3L_3A_1$ presented to our NIMS hospital emergency with complaints of amenorrhea of one and ½ months corresponds to 6 weeks and 3 days of gestation. According to patient her previous menstrual history was normal. There was no history of PID, ART procedure, Infertility treatment, Tuberculosis. Onher examination, vitals were BP-90/60 mm of Hg, PR-110 /min, clinical features suggestive of haemorrhagic shock were present. On P/A soft distension present and tenderness in RIF.P/V examinationrevealed –uterusmobile and non-tender, cervical motion tenderness present, 2.8x2.8 cm adnexal mass felt in right fornix.Patient investigated, her UPT +ve, Hb% 8gm, TLC 10,600/cumm, rest hemogram was normal, USG findingswere uterine cavity Empty & bulky ET-19 mm, 2.8x2.8 cm with out fetal pole, freefluid was present in POD.

Figure-1: Ultrasound showing ovauran ectopic pregnancy

Our provisional diagnosis was ruptured ectopic pregnancy & patient was prepared for laparotomy, her intraoperative findings-

- ✓ Hemoperitoneum of 200 cc was present
- ✓ Uteruswas bulky
- ✓ B/L fallopian tubes normal &left ovary normal
- ✓ Rt ovary enlarged with 2.8 ×2.8 cm size adnexal mass in situ, bluish red in color with bleeding frombreached ovarian surface.

Right salpingo-ooporectomy done.Left side tubal ligation done by modified pomeroy's method and tissue sent for histopathologicalexamination. Her postoperative period was uneventful. Her histopathological report shows corpus luteum with trophoblastic villi in the ovarian tissue.Histopathological report of her D&C tissueshowsabsence of villous or fetal tissue.

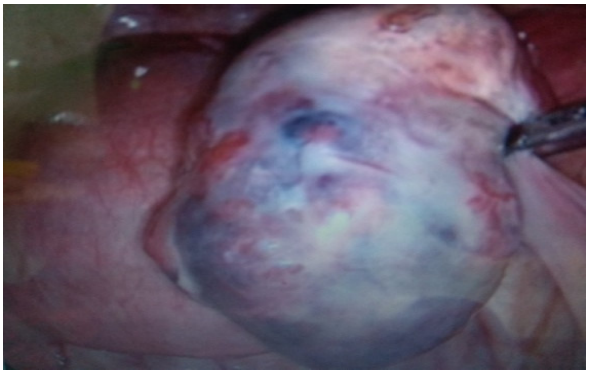

Figure 2: Intraoperative finding showing ovarian pregnancy

Histopathology report & her intraoperativefindings were satisfied with the spigelberg criteria. Her immediate and long term postoperative course was uneventful .Patient followed up in OPD after 1 week of surgery. Her serial β hcg was on D5 -500miu/ml, D12 -30miu/ml, D19- undetectable.

Discussion and Review of Literature

Clinical presentation of primary ovarian ectopic pregnancy is variable. This is a life-threatening emergency. Etiology of ovarian ectopic pregnancy still remain obscure. A study done by goyal et. al concluded that incidence of ovarian pregnancy is 4.8% of all pregnancies. 94% patients diagnosed in first trimester, in 11% cases preoperatively diagnosed only [3,4]. Increase incidence with ART procedures [due to increase progesterone from corpus luteum, ovarian hyper vascularity due to hyper stimulation], PID, previous pelvic surgery, PCOD, fibroid uterus. IUCD is found in 15-32% of patients of non ovarian ectopic pregnancy. 60-92% of patient of ovarian ectopic pregnancy. Grimes et. al studied 24 case of ovarian pregnancy & concluded greater then 50% cases had infertility or failed ART(4,5).

Cigarette smoking also interferewith tubal motility and ovum pickup. There is usually delay in diagnosis because Gestation sac of ovarian ectopic pregnancy in ultrasound mimic to haemorrhagic cyst of ovary, corpus luteal cyst, endometrioma of ovary. Diagnosis confirmed by TVS and CT scan. Ovarian pregnancy carries higherriskof morbidity and mortality then tubal pregnancies because ovarian pregnancy located at the most vascularised site of female pelvis. Uteroovarian anastomosis of blood vessels eroded by developing chorionic villi, leads to severe haemorrhage and patient went into haemorrhagic shock [6,7].

Ovarian ectopic pregnancies diagnosed intraoperatively &histo-pathologically fewexceptions according to **spigelberg criteria**. ovarian ectopic pregnancy should be differentiated from ampullary /infundibulam tubal pregnancy, in these cases ovaries may involve secondarily after tubal abortion or rupture [8].

Criteria includes:

1. Gestation sac should occupy the normal position of the ovary.
2. Gestation sac and uterus connected with each other by utero-ovarian ligament.
3. Affected side fallopian tube with its fimbria should be intact andseparate from ovary.
4. Ovarian tissue (tunica albugenia) must be present in the specimen or in the wall of gestational sac.
5. Empty uterine cavity and evidence of amniotic cavity within follicle.

3D ultrasound (TVS) help to differentiate from haemorrhagic corpus luteal cyst (8).Diagnostic features of ovarian pregnancy are-.

Sensitivity is 85%-92% and specificity is 99.98%

1. Double echogenic ring found within hypoechoic latero-uterine mass&echogenecity of ring is more then ovary itself (inhomogenous mass). Wideechogenic ring with an internal echolucent areas on superficial ovarian surface are also found.
2. Gestational sac found very adjacent to the ovary.
3. All around mass follicles & corpus luteum is present as a part of ovarian cortex.
4. Empty uterine cavity & free fluid in peritoneal caviy.(mild fluid in pod is physiological)
5. Ovarian ectopic pregnancywill move with ovary on pressure applied with transvaginal probe.

Gestation sac visualizedby trans-abdominal scan at β-hCG discriminatory zone ≥6500miu/ml in 1981.Discriminatory zone for Transvaginal ultrasound upto 1000 to 2000 miu/ml. Com shock et. al studied ultrasonographic appearance of ovarian ectopic pregnancy and they concluded ovarian pregnancyis rarely identified correctlyby sonographyandit is evenvery difficultto diagnose intra operatively [8,9]. Ectopic pregnancy may coexist with an intrauterine pregnancy but it is very rare with incidence 1/40000, diagnosis is very difficult. It is common with assisted conception. Benauereaf et. al suggested that transducer frequency from 7MHZ to 10MHZ is helpfulin improving diagnostic accuracy [9].

Ovarianectopic pregnancy classifiedinto two types –

1. Intrafollicular pregnancy- In this ovum trapped inside the follicle, mature ovum not picked up or expelled from its follicle. Sperm fertilizethe egg after entering into follicle various theories are given for explanation

- Hormonal causes
- Thickened tunica albugenia of the ovary
- Defect in ovum pick up due to inadequate fimbria on ovarian surface

2. Extra follicular pregnancy-mature ovum fertilized outside of ovary, implant on ovariansurfacebecause of endometrial decidual reaction.

Fe why potheses suggested, Inflammatory thickened tunica albugenia and malfunctioning of tubes. Interference of release of mature ovum from follicle.

The sign and symptom of primary ovarian pregnancy are very similar to tubal ectopic pregnancy. Very difficult to differentiate clinically from chocolate cyst, haemorrhagic cyst, tubal pregnancy.

Trophoblastic cells invade theovarian tissue on6th day, followed by the invasion of the ovarian artery. Although ovarian pregnancies rupture by the 40th gestational day, reports of those progressing into the 3rd trimester even to live births have been established.

Most of primary ectopic pregnancy usually ruptured in first trimester of pregnancy. Recurrent ectopic pregnancy is not reported yet, in contrast totubal pregnancy, 15% recurrence noted in primigravidapatients. A study done by Savita et al. according to them out of 104 patients only 94 patients had ectopic proved by histopathology and remaininghad either haemorrhagic cyst or corpus lutealhematoma. Out of 94 patients only four hadovarian pregnancy who fulfilled spigelberg criteria.

Future fertility after surgery is unaffected- Goyal et al.done aretrospectivecross – sectional study onovarian pregnancy at Government medical college & hospital Chandigarh, they studied risk factor, incidence, diagnosis and management of ovarian pregnancy [3,10].

Table No- 1: Risk factor for ovarian pregnancy.

S. No	Age	POG-weeks	O/H	Past history	USG finding	Management
1	22	9 wk	G4P2L2A1	IUCD-3yr	FF in POD	Excision of sac& B/L salpingectomy
2	24	-	G1	1*infertility	FF in POD	Excision of sac& B/L salpingectomy
3	25	7wk	G5P2L2A2	IUCD-2yr	Bhcg-2000	Excision of sac& B/L salpingectomy
4	26	Nil	P4L4	IUCD-5yr	4×4cm,adnexal	Rtoopherectomy
5	23	36wk	G3P2L2	MTP	Placenta previa	Laprotomy with Exicion of placenta delivery of baby and oophectomy
6	34	8wk	G3P1L1A1	--	FF in POD,βhcg-1800	Excision of sac ,repair
7	23	9wk	G2A1	--	Lt adnexal mass, FF +	Lt oopherectomy
8	36	6wk	G4P3L3	IUCD-5yr	Ltovarian G. Sac, βhcg-2000	Excision of sac
9	25	7wk	G1	Infertility	FF in POD	Excision of sac
10	7	Nil	P3L3	--	Rt adnexal mass βhcg-3000	Excision of sac & repair

A study done by Savita et al. They concluded out of 4 patient 3 patient had history of risk factor like IUCD was present.

Management- Expectant management-Success rate is 48%-100%.
Inclusion criteria –

- Asymptomatic women with stable vitals
- B-hCG<1000miu/ml
- Ultrasound findings –Size ≤ 2cm and GA < 6 weeks, Cardiac activity absent, YoIk sac and fetal polealso absent, Free fluid in pouch ofdouglas<100CC.
- Serum progesterone level <3.1 ng/ml
- Cooperative patient willing for follow up

These patients followed twice weeklyon Day 3,7.

1. If β-hcg fall >50% within a week,continue expectantmanagement
2. If β-hcg fall <50% within a week, consider medical /surgical management.

It is most useful when initial β-hCGlevel is ≤1000 iu/l with unruptured ectopic pregnancy. Success rate is b/w 50-80%. According to a prospective observational study, 118 patients are on expectant management out of them 88% recovered successfully. They hadβ-hCG ≤ 200 mIU/mL andpatients with β-hCG level≥ 2000 mIU/ml only 26% recovered. Favorable factors for success of expectant management areserum β-hCG level≤200, gestational age ≤ 6 weeks & progesterone level below 10 nmol/L.

Expectant management to be stoppedif the patient is having if the β-hCG level increases or Persistantly increasing abdominal pain. To avoid rupture of ectopic pregnancy,Patient should instructto avoid vigorous physical activity sexual activity & pelvic examination.

Medical Management- Mittal et. al first-time used injection methotrexate directly into gestational sac of ovary [11]. Kudo et. alreported first successful use of methotrexate in ovarian pregnancy. Gabbur et al. Done a retrospective analysis on MTXuse in unruptured ovarian ectopicand concluded that after single MTX injectionon D7 β-hcg levels only, predict aneed of surgery or successful treatmentnot Day 4 β hcg level [10,11].

Patient selection is very important. Methotrexate is antagonist of folic acid that impairs cellreplication & DNA synthesis. In 1982 first time used for medical management and mode of action by killing rapidly dividing cytotrophoblasts cells at implantation [11,12].

Table No-2: Contraindication of Meth trexate treatment in ectopic pregnancy.

Absolute	Relative
i. Hypersensitivity ii. Thrombocytopenia(< 1 lac/µl) iii. Liver dysfunction >2 fold. Alcoholic liver diz. iv. Pulmonary and peptic ulcer disease v. Hematological dysfunction with bone marrow depression TLC < 1500/µl vi. Heterotopic pregnancy vii. Ruptured ectopic pregnancy viii. Lactating mothers ix. Moderate to severe anemia x. creatinine clearance < 50 mL per minute per 1.73 m^2 .	i. B-hCG>5000miu/ml ii. Ectopic mass > 4 cm iii. Fetal cardiac activity present iv. Poor complaint patient

Patient should instruct to stop taking prenatal vitamins, Alcohol, nonsteroidal anti-inflammatory drugs & avoid excessive sunlight (to avoid MTX induced dermatitis) and folate supplementation, as folate will counteract action of injection methotrexate.Rh status of patient must be known to determine further need of immunoglobin therpy in Rh negative patient. A meta-analysison single and multiple dose regimens done by Barnhart et al. They concluded multidose regimen is more effective (90 %) then single dose (80%) [13,14,15].

If β hCG is ≥ 5000 treatment failure rate is 40%. If 15% decrease occurs b/w Day 4 and Day 7, β-hCG levelsmonitored weekly tillreach zero. This will takeat least five to sevenweeks.

Single dose of methotreaxate- Levin et al. done a study and concluded, out of 69 women of study group 45 patient was treated successfuly withsingle dose of injection methotrexate. before single dose of methotrexategood predictorsof successful treatment are-

If β-hCG level≤ 1600 iu/landincrease ≤14%, in a day or 24 hr.

Single dose regimen associatedleast side effects.

Table No.- 3: Single dose of methotrexate treatment protocol.

	0	4	7
1. Investigations	Bhcg, CBC,ABOrh LFT,RFT	Bhcg	Bhcg
2. Medical management	Methotreaxate in dose of 50mg/m^2 of body surface area is given by IM route	Methotreaxate in dose of 50mg/m^2 of body surface area is given by IM route	i. If Decrease in βhcg>15% between from day 4 to day 7. Moniter βhcg weekly till zero. ii. If βhcg decrease< 15% between day 4 to day 7 give methotreaxate

Two dose regime of methotrexate of ectopic pregnancy- Branhart was only one whofirst described "Double dose regimen". Hossam et al. concluded that double dose protocol is better then single dose regimen [16,17].

Table No-4: Multiple dose of methotrexate treatment protocol.

	0	4	7	11	14
Investigation Medical managment	CBC, ABoRh, LFT, RFT, βhcg Methotreaxate in dose of 50mg/m^2 of body surface area is given by IM route.	Bhcg Methotreaxate in dose of 50mg/m^2 of body surface area is given by IM route.	Bhcg If Decrease in βhcg>15% between from day 4 to day 7. Moniter βhcg weekly till zero. If βhcg decrease< 15% between day 4 to day 7. givemethotreaxate.	Bhcg If Decrease in βhcg>15% between from day 7 to day 11. Moniter βhcg weekly till zero. If βhcg decrease< 15% between day 7 to day 11. givemethotreaxate	Bhcg If Decrease in βhcg>15% between from day 11 to day 14. Moniter βhcg weekly till zero. If βhcg decrease< 15% between day 11 to day 14 Refer to surgery

Multiple dose regime of methotrexate in ectopic pregnancy- Krik et al. concluded that multiple dose regimen is more effective then singe and double dose protocol with sensitivity 94%, specificity 86% [1,17,18].

Table No-5: Double dose of methotrexate treatment protocol.

	1	2	3	4	5	6	7	8
Investigations	CBC,AB, Rh, RFT LFT,β Hcg		β hcg		β hcg		β hcg	
Medical management	Methotrexate to be given by 1mg/kg by IM route	Leucovorin to be given by 0.1mg/kg by IM route	If Decrease in βhcg>15% between from day 1 to day 3. Moniter β hcg weekly till zero. If βhcg decrease< 15% between day 1 to day 3. Give methotreaxate.	LEU	If Decrease in βhcg>15% between from day 3 to day 5. Moniter βhcg weekly till zero. If βhcg decrease< 15% between day 3 to day 5. Give methotreaxate.	LEU	If Decrease in βhcg>15% between from day 5 to day 7. Moniter βhcg weekly till zero. If βhcg decrease< 15% between day 5 to day 7. Give methotreaxate.	LEU

Sucess rate of treatment with β- hCG ≤1000miu/ml is 87% . Failure rate is 40 % with level ≥5000miu/ml.

Surgical Management- Primary management of Ovarian ectopic pregnancy is surgical. According to 3 prospective randomized trial laparoscopic approach is superior then laparotomy in view of less blood loss & pain, shorter hospital stays and there is no significant difference in recurrence, subsequent intrauterine pregnancy [17,18]. Laparoscopic surgery has become preferred method & gold standard nowdays. Conservative surgical technique like ovarian wedge resection, enucleation are also in trend now days. 80% cases managedby conservative management and radical oophorectomy done in 13% cases only. John et al. Was performed first laparotomy for ovarian ectopic pregnancy in 1759. In 1884 Robert et al. Ligatedbleeding blood vessels first time during laparotomy [4]. Shapiro and Adler introducedfirst time a laparoscopic approach in 1973 [20,21]. According to Cochrane review 2007, there is no significant difference b/w systematic methotrexate and conservative surgeryif β -hCG level ≤1500miu/ml. Corpus lutealcystectomy for trophoblast, curettage of trophoblast by coagulation and hemostatic suture of the bed.These are totally conservative surgeries. In case of advanced ectopic pregnancyoophorectomy or ovariectomy [22,23,24]. Recurrence ofovarian pregnancy in literature till now. Only single case reported has been reported in contrast to tubal ectopic pregnancyrecurrence rate isup to 15 % [25-29].

Conclusion and Perspective

According to spigelberg criteria,it is a diagnostic challenge to obstetrician. diagnosis can be missed radiologically, intraoperatively. Ovarian pregnancy canoccur evenin Nulliparous female without risk factors like IUCD, PID, ART. Now days Medical management with single dose of Methotrexate is very successful for unruptured ovarian pregnancy. Should be suspected inpatients presented with rupturedectopic pregnancy, ultrasound features suggestive of normal b/lfallopian tube with hemo-peritoneum with breached ovarian surface. Conservative surgical approach is preferred. Confirmation of ovarian pregnancy done only after histo-pathologicalreport.

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