Research Paper

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HISTOPATHOLOGICAL CHANGES IN FALLOPIAN TUBES IN ECTOPIC TUBAL PREGNANCY: AN OBSERVATIONAL STUDY

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ABSTRACT

Background: The incidence of ectopic tubal pregnancy varies from 1 in 300 to 1 in 150 pregnancies. Tubal pregnancy may terminate by tubal abortion or tubal rupture, contributing significantly to maternal morbidity and mortality. Keeping in view the high rate of tubal pregnancy and highly variable incidence of pathological changes in the tube, this work was planned to study the morphological alterations in fallopian tube histology in ectopic tubal gestation and to identify the pathological conditions most frequently associated with it. **Methods:** The 6 year study (5years- retrospective and one year– prospective) included 220 histologically proven cases of ectopic tubal pregnancy diagnosed in the Department of Pathology, Government Medical College, Jammu. For the prospective study, formalin-fixed gross specimens were routinely processed and stained with H&E. Retrospective analysis was done by retrieving the slides of the diagnosed cases of tubal ectopic pregnancy from archives of Histopathology Section of the Department of Pathology, Government Medical College, Jammu. The sections from fallopian tubes with tubal pregnancy were examined microscopically for the evaluation of associated morphological features like haemorrhage, edema, acute/chronic/granulomatous/inflammation, perforation/rupture, extent of wall invasion by chorionic villi, necrosis, fibrosis, luminal contents, decidualised stroma, salpingitis isthmica nodosa, walthard cell nests, inclusion cysts, neoplasia and any congenital anomaly. **Results:** Out of 220 cases studied, majority of ectopic tubal pregnancies were on right side and presented at less than 8 weeks of gestation. Approximately three-fourth of the cases were encountered in females aged 18-32 years. The most frequent and consistent observation was the presence of an inflammatory infiltrate in the tubal wall seen in 203 out of 220 cases. Based on the morphological alterations observed on microscopy, the pathological conditions associated with the ectopic tubal gestation were classified as chronic salpingitis (53.18%), acute on chronic salpingitis (15.45%), acute salpingitis (12.73%), follicular salpingitis (5%), granulomatous salpingitis (0.45%), salpingitis isthmica nodosa (10%), walthard cell nests (6.82%) and inclusion cysts (0.90%). **Conclusion:** The study highlights that inflammation of tubes i.e. salpingitis is the most common pathological condition associated with tubal ectopic pregnancy followed by the salpingitis isthmica nodosa.

KEYWORDS

Ectopic tubal pregnancy, fallopian tube, chronic salpingitis, salpingitis isthmica nodosa.

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INTRODUCTION

Ectopic pregnancy is the term applied when embryonic implantation occurs outside the uterus. About 1% of all pregnancies are noticed in an ectopic location with implantation not occurring inside of the uterus. Of these ectopic pregnancies 98% occur in the fallopian tube.1,2,3 In tubal pregnancy the gestational sac is completely made up of tubal tissue, with no participation from the ovarian or intraligamentary tissues.4 The incidence of tubal pregnancy varies from 1 in 300 to 1 in 150 pregnancies. Because of unfavourable environment, early interruption of pregnancy is inevitable within 6-8 weeks. Tubal pregnancy may terminate by tubal abortion or tubal rupture, contributing significantly to maternal morbidity and mortality.5 Risk factors for ectopic pregnancy are prior ectopic pregnancy, prior tubal surgery or infection, smoking (>20 cigarettes/day), pelvic in ammatory disease, multiple spontaneous abortions(>3), increasing age (>40 years), prior medically induced abortion, infertility (>1 year), multiple sexual partners (>5), and previous intrauterine contraceptive device (IUD) use.6,7 Ectopic pregnancy also occurs as the consequence of chronic salpingitis, which leads to inflammatory destruction of the lining folds and retention of the ovum.2,8 Congenital tubal abnormalities, functional tubal disturbances, and salpingitis isthmica nodosa are responsible for a minority of the cases.9 Keeping in view the high rate of tubal pregnancy and highly variable incidence of pathological changes in the tube, this work was planned to study morphological alterations in fallopian tube histology in ectopic tubal gestation and to identify the pathological conditions most frequently associated with ectopic tubal pregnancy.

MATERIAL AND METHODS:

The 6 year study (5years- retrospective and one year– prospective) included 220 histologically proven cases of ectopic tubal pregnancy diagnosed in the Department of Pathology, Government Medical College, Jammu.

Inclusion criteria – Histologically proven ectopic tubal gestation with presence of one or more of the following features in sections from the fallopian tube:

Foetal parts (embryo), chorionic villi or syncytiotrophoblast cells.
Exclusion criteria – Absence of all of the abovementioned features.

For the prospective study, after noting down the clinical details from the patient's case record, a detailed gross examination was conducted with regard to the nature of the specimen, size, site of tubal pregnancy, tubal ligation, presence of an intra-uterine device (IUD). The formaline-fixed salpingectomy or salpingo-oophorectomy specimens were routinely processed and stained with H&E stain for histopathological analysis. Retrospective analysis was done by retrieving the case records, grossing notes and slides of the diagnosed cases of tubal ectopic pregnancy from archives of Histopathology Section of the Department of Pathology, Government Medical College, Jammu. The sections from fallopian tubes with tubal pregnancy were examined microscopically for the evaluation of associated morphological features like haemorrhage, edema, acute/chronic/granulomatous/inflammation, perforation/rupture, extent of tubal wall invasion by chorionic villi, necrosis, fibrosis, luminal contents, decidualised stroma, salpingitis isthmica nodosa, walthard cell nests, inclusion cysts, neoplasia and any congenital anomaly.

RESULTS

Out of 220cases studied, majority of ectopic tubal gestations were

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observed in multigravida females (40.90% and 21.82% were gravida 2 and 3 respectively, primigravidae were 15.45%), and most (55.45%) presented at less than 8 weeks of gestation. Approximately three-fourth of the cases were encountered in females aged 18-32 years when the females are likely to be sexually most active and productive. Around 28 cases (12.73%) had previous history of surgeries and 15 cases (6.82%) had previous history of ectopic pregnancy. Right fallopian tube was more frequently involved (59.55%) than the left and at presentation 143 out of 220 tubal pregnancies (65%) were ruptured as against 77 (35%) unruptured ones.

On gross examination an overwhelming majority of the specimens were salpingectomies comprising of 213 cases (96.81%). The rest were the tuboovarian masses (TO mass) or salpingoophorectomies accounting for a meagre 7 cases (3.18%).Tubal ligation or evidence of an intrauterine contraceptive device were not observed in any of the cases on gross examination. Within the fallopian tube, the ampulla was the preferred site for ectopic gestation accounting for approximately three-fourth of the cases (73.64%). Fimbrial end (21.36%) and cornua (interstitial) (5%) were a distant second and third respectively (Fig:1). The specimens ranged from 2cm to 5.5cm in size. Grossly the tissue was hemorrhagic and edematous in all cases (Fig:2). A well-formed embryo was identified in 3 cases (1.36%) grossly as well as histologically.

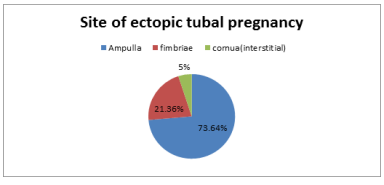

Fig:1

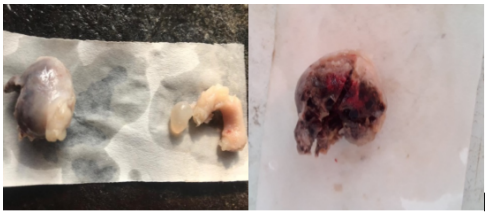

Fig 2: Grossly oedematous and haemorrhagic tubal tissue

The associated morphological alterations in the fallopian tube in cases of ectopic tubal gestation were studied in detail on microscopic examination (Table 1).

Table 1: The distribution of different microscopic morphological alterations in fallopian tube in ectopic tubal gestation.

S.no.	Morphological alterations	No. of cases (N=220)	Percentage (%)
1.	Hemorrhage	220	100
2.	Edema	220	100
3.	Inflammatory infiltrate		
	Chronic (pred. lymphocytes)	140	63.64
	Mixed	34	15.45
	Acute (pred. neutrophils)	28	12.73
	Granulomatous	1	0.45
4.	Necrosis	142	64.55
5.	Fibrosis	78	35.45
6.	Extent of tubal wall invasion by villi		
	Upto smooth muscle	77	35.00
	Upto serosa	143	65.00
7.	Cellular luminal contents	85	38.64
8.	Decidualised stroma	110	50.00
9.	Walthard cell nests	15	6.82
10.	Inclusion cysts	2	0.90

Hemorrhage and edema, whether luminal and mucosal or extramuscular and /or serosal were ubiquitously present in all the cases of ectopic tubal gestation. The next most frequent and consistent observation was the presence of an inflammatory infiltrate in the tubal wall seen in 203 out of 220 cases. The chronic inflammation comprising of lymphomononuclear cells was seen in an overwhelming 140 (63.64%) cases. A significant number of eosinophils were observed in 12% of the cases. A mixed inflammatory infiltrate comprising of both lymphocytes and neutrophils was seen in 34 (15.45%) cases whereas a predominantly neutrophilic infiltrate was present in 28 (12.73%) cases (Table1). Depending on the type of inflammatory infiltrate i.e. lymphomononuclear, mixed or neutrophilic, the tubal pathology was labelled as chronic salpingitis (Fig:3), acute on chronic salpingitis and acute salpingitis respectively (Table 2).

The condition labelled as follicular salpingitis was diagnosed in 11(5%) cases (Table 2) when in addition to a chronic inflammatory infiltrate, the mucosal rugae had lost their normal structure and were represented by thickened mucosal folds adherent to one another, forming partitioned cavities of variable size. A single case of granulomatous salpingitis was encountered (0.45%) showing presence of epitheloid granulomas with langhans giant cells.

Necrosis was another widely prevalent morphological feature seen in 142 (64.55%) out of 220 cases. Though focal mucosal or intramural patches of necrosis were frequently encountered, a transmural necrosis of the entire tubal wall was invariably evident in ruptured tubes.

Fibrosis of the tubal wall with replacement of tubal smooth muscle by fibroblasts and collagen was seen in 78 (35.45%) cases. In majority of these cases the accompanying chronic inflammation pointed to the underlying salpingitis. In 22 cases (10%) well developed fibrosis was seen with cystically dilated gland-like formations surrounded by hypertrophic muscle. All these cases were labelled as salpingitis isthmica nodosa (SIN) (Table2, Fig 4). A chronic inflammatory infiltrate was well appreciable in 12 out of the 22 cases of SIN.

In 3 cases a well-formed embryo was identified grossly and microscopically.

The invasion of the tubal wall by the chorionic villi/ trophoblasts was transmural, extending upto the serosa in 143 (65%) cases and upto the smooth muscle in 77 (35%) cases.

The tubal luminal contents were cellular comprising of trophoblastic tissue or inflammatory cells in 85(38.64%) cases whereas in majority of the cases the luminal contents were necrotic and hemorrhagic.

A well decidualised stroma comprising of large polygonal cells with vesicular nuclei and abundant eosinophilic cytoplasm was evident in 110(50%) cases.

We observed 15 cases (6.81%) showing presence of walthard cell nests as incidental findings and out of these, 10 cases had concomitant chronic salpingitis. 2 cases (0.90%) also showed incidental presence of inclusion cysts.

Thus, based on the morphological features studied above the pathological conditions associated with the ectopic tubal gestation were classified as depicted in Table 2.

Table 2: Pathological conditions associated with ectopic tubal gestation.

Pathological conditions	No. of cases	Percentage (%)
Chronic salpingitis	117	53.18
Acute on chronic salpingitis	34	15.45
Acute salpingitis	28	12.73
Follicular salpingitis	11	5.00
Granulomatous salpingitis	1	0.45
Salpingitis isthmica nodosa (SIN)	22	10.00
Walthard cell nests	15*	6.81
Inclusion cysts	2	0.90

*10 out of 15 cases showing walthard cell nests also showed a chronic

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inflammatory infiltrate and hence were included in chronic salpingitis.

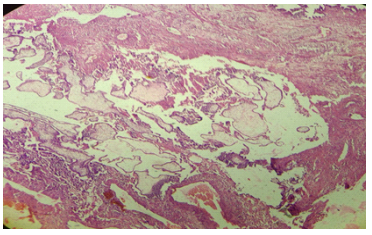

Fig 3:Photomicrograph showing ectopic tubal gestation with chronic salpingitis (H&E) 40X

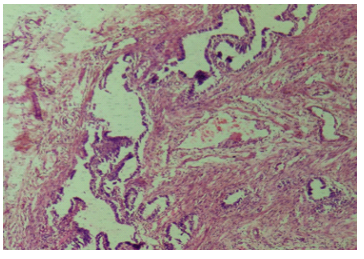

Fig 4: Photomicrograph showing salpingitis isthmica nodosa with trapped dilated glands within the hypertrophied smooth muscle (H&E stain) 100X.

DISCUSSION

Ectopic tubal pregnancy continues to be a significant cause of morbidity and mortality in women of reproductive age group throughout the world, with rupture tube and consequent maternal death being its most dreaded complications.5 A history of infertility is associated with an increased risk of tubal pregnancy.10 In view of the high rate of tubal pregnancy and highly variable incidence of pathological changes in the tube, this study was conducted to study the histological patterns of tubal pathology in confirmed ectopic tubal pregnancies. 220 cases of ectopic tubal pregnancy were studied in detail for histomorphological alterations in fallopian tubes harbouring an ectopic gestation.

Majority (appx 80%) of the females in this study were in the age group of 18-32yrs. Multigravidae outnumbered primigravidae (15.45%) and most women presented at less than two months of gestation. 65% of the cases had ruptured tubes. Right fallopian tube was more commonly involved than the left (59.55% vs 40.45%) and within the tube, the ampulla (73.64%) was the preferred site for implantation of the gestational sac.

Ectopic tubal pregnancy is a disease of females in the reproductive age group and most observers have reported highest incidence (appx 70%) in the third decade of life.11,12,13 Gravida 2 or 3 females are more likely to have tubal pregnancy in comparison to the primigravidae.13,14 The classic presentation of ectopic pregnancy includes amenorrhea with subsequent vaginal bleeding and/or abdominal pain. Tubal rupture is associated with intra-abdominal hemorrhage.15,16,17 Most studies have documented higher incidence of ruptured ectopics (54% to 78%) against unruptured ones.11,13,14,18 Diagnosis of ectopic tubal pregnancy is clinical. In tubal pregnancy the gestational sac is completely made of thin walled tubal tissue. With a significant number of cases in various studies presenting initially with rupture, the early recognition and management of this potentially life threatening condition becomes imperative. The frequency of left- versus right-sided ectopic tubal pregnancies is similar, but they are slightly more common on the right and rare cases are bilateral.12,13,14,15,16,17,18,19 This predilection of ectopics for right fallopian tubes has been attributed to spread of infection from appendicitis, the resulting salpingitis, in turn, predisposing to ectopic gestation.20 The ampullary portion of the fallopian tube has been documented to be the preferred site for embryo implantation by many authors.11,14,18,19 Previous history of LSCS, abortion, an ectopic pregnancy or any abdominal surgery may increase the risk of ectopic tubal gestation in subsequent pregnancies.14,18,21 A history of infertility also predisposes to an increased risk of tubal pregnancy.[10]

The pathology most frequently associated with ectopic tubal pregnancy, as observed in the present study, was inflammation of the fallopian tube or salpingitis. Chronic salpingitis was observed in 53.18% cases followed by acute on chronic salpingitis in 15.45% cases and acute salpingitis in 12.73% cases. 5% of the cases were labelled as follicular salpingitis and there was a single case (0.45%) of granulomatous salpingitis due to tuberculosis. 12% cases of salpingitis showed prominence of eosinophils.

The reported incidence of salpingitis in ectopic tubal pregnancy is variable (22% to 84%).11,12,13,22 Chronic salpingitis due to chronic pelvic inflammatory disease (PID) has been documented as one of the most important risk factors in the development of ectopic pregnancy. A history of previous PID is the most important etiologic factor in 35–45% patients.16 The risk of ectopic is known to increase 7-fold after an episode of acute salpingitis. Studies have shown that a reduction in PID is associated with a decline in the incidence of ectopic pregnancy.23,24 Inflammation within the fallopian tube, resulting from infection or smoking, may affect embryo-tubal transport by disrupting smooth muscle contractility and ciliary beat activity. This inflammatory environment also provides many of the pro-implantation signals recognized by the arrested embryo, such as increased IL-8 expression and decreased MUC1 expression.[25]

A prominence of eosinophils in the inflammatory infiltrate may indicate a parasitic pathology. Parasitic infestation of the fallopian tube as a part of PID secondary to infiltration of parasite such as Enterobius vermicularis has been documented.26,27 A possible role of eosinophilic granulocytes in the fibrotic process of pelvic adhesion disease has also been postulated. Thus eosinophilic inflammation may simply be an indicator of an ongoing fibrotic process in the tube.[28]

One of the other causes for chronic salpingitis, especially in India, is genital tuberculosis. In India, the incidence of genital TB in patients undergoing surgery for acute ectopic pregnancy was as high as 35.29–40%.29 The present study had one case of tuberculous salpingitis.

Salpingitis isthmica nodosa (SIN), which is often bilateral, post inflammatory distortion of the fallopian tube with diverticula of tubal epithelium into the muscular layer, was encountered in 10% of the cases in the present study. The reported incidence of SIN in ectopic tubal pregnancies varies from 10-43%.11,12,21,30

Since ectopic pregnancy is a serious and a potentially life threatening complication of PID, the recognition and early treatment of the condition is essential to prevent the morbidity and mortality associated with the disease. Moreover, underlying tubal disease (chronic salpingitis, follicular salpingitis, or salpingitis isthmica nodosa) is the major factor identified that is associated with, and probably the cause for, recurrent tubal gestation.31 So when the resected fallopian tube shows features of salpingitis, aggressive therapy must be instituted to prevent recurrent ectopic in the contralateral fallopian tube. Hence, thorough examination of the fallopian tube must be done in all resected ectopic specimens to identify the features of acute/chronic salpingitis.

CONCLUSION

Ectopic pregnancy is a common life threatening emergency in the first trimester of pregnancy. As is evident from the observations in this study and also on review of medical literature, inflammation of the fallopian tube i.e. salpingitis is the pathological condition most commonly associated with ectopic tubal pregnancy and may have a role in its etiology as well. Salpingitis, usually, is a component of a more generalized PID in most of the cases. These conditions not only lead to loss of pregnancy but also increase the chance of recurrent ectopic gestations and adversely affect a woman's future fertility. With evolving knowledge, advanced technologies and experience, early detection of genital infections followed by adequate antibiotic treatment in early phase of disease can reduce the incidence of ectopic tubal gestation. Moreover, histopathological examination of the resected fallopian tubes with ectopic gestation can throw light on to the underlying pathology and, in some cases, can also provide an insight into the treatment modality to prevent a recurrent ectopic gestation.

Conflicts of interest – nil.

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