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Case Series

Endometrial hyperplasia and tubal ectopic: a correlation

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ABSTRACT

Anovulation due to polycystic ovarian syndrome (PCOS) is one of the causes of endometrial hyperplasia in infertile women. Tubal ectopic apart from tubal factors can also be the result of hampered endometrial receptivity in these women which could be due to disturbed hormonal mileu, endometrial hyperplasia at cornua thereby interfering with transport of embryo from fallopian tube to uterus, or could be because of mechanical damage caused while taking endometrial biopsy. We are presenting case series of eight women of PCOS who presented to infertility clinic within two years with history of ectopic pregnancy or had subsequent ectopic pregnancy (after taking endometrial biopsy) with histopathology report of endometrial hyperplasia with or without atypia were enrolled. Out of 1200 PCOS women presenting to infertility clinic, eight women had coexistence of both endometrial hyperplasias and ectopic pregnancy. It is rare to find endometrial hyperplasias causing ectopic pregnancy. The causative factor in these cases could be the faulty endometrium by not being receptive thereby causing the embryo to implant in the fallopian tube or the tubes due to subtle infection secondary to repeated endometrial evaluation.

Keywords: Endometrial Hyperplasia, PCOS

INTRODUCTION

An ectopic pregnancy refers to the implantation of an embryo outside of the uterus. The fallopian tube, predominantly the ampullary region of the fallopian tube is the most common site of ectopic pregnancy.[1]

The overall rate of ectopic pregnancy is 1–2% in the general population and little higher (2–5%) among patients undergoing assisted reproductive technology (ART). It is the delicate balance between the controlled environment of fallopian tube facilitating oocyte transport, fertilization, and migration of the early embryo to the receptive endometrium of uterus for implantation.

It is an established fact that tubal ectopic pregnancy results from abnormal embryo transport and an alteration in the tubal environment, which enables abnormal implantation to occur. It may be further hypothesized that in some cases the impaired endometrial receptivity and cyclical changes in fallopian tube which may be responsible for making favourable environment inside fallopian tube than endometrium thereby allowing implantation to occur in the tube itself.

We are hereby presenting a case series of eight such PCOS patients who presented to us with tubal ectopic having endometrial hyperplasia.

CASE SERIES

We are presenting case series of eight women of PCOS who presented to us in the department of obstetrics and gynaecology, Postgraduate Institute of Medical Education and Research, Chandigarh over two years and had history of ectopic pregnancy or who had subsequent ectopic pregnancy with diagnosis of endometrial hyperplasia with or without atypia.

Table 1 demonstrates age, presenting complaint, obstetric history, histopathology and mode of conception in patients. Out of 1200 PCOS women, 8 had history of ectopic pregnancy and endometrial hyperplasia. In patients (1, 2, 3, and 4) endometrial biopsy was routinely done as per our institutional protocol to rule out genital tuberculosis in all infertile women when a sample is tested for presence of mycobacterium and also for histopathology. These patients already had a history of ectopic pregnancy. In patients (5, 6, 7, and 8) who presented to us with primary infertility and diagnosed to have endometrial hyperplasia without atypia and subsequently had spontaneous ectopic pregnancy. In all patients tubal factor was ruled out by doing hysterosalpingography as a work up for primary infertility.

Table 1: Age, presenting complaint, obstetric history, histopathology, mode of conception.

S. no.	Age (in years)	Presenting complaint	Obstetric history	Histopathology	Conception (ectopic pregnancy)
1	32	Secondary infertility	Previous one abortion and one ectopic	Endometrial hyperplasia without atypia	Spontaneous
2	25	Secondary infertility	Previous tubal ectopic	Endometrial hyperplasia without atypia	Letrozole (with timed intercourse)
3	32	Secondary infertility	Previous tubal ectopic	Endometrial hyperplasia with atypia	Following IVF cycle
4	34	Secondary infertility	Previous one abortion and now tubal ectopic pregnancy	Endometrial hyperplasia with atypia	Letrozole plus gonadotropins f/b IUI
5	26	Primary infertility	Ectopic pregnancy	Endometrial hyperplasia with atypia	Spontaneous
6	27	Primary infertility	Ectopic pregnancy	Endometrial hyperplasia with atypia	Spontaneous
7	28	Primary infertility	Ectopic pregnancy	Endometrial hyperplasia with atypia	Spontaneous
8	32	Primary infertility	Ectopic pregnancy	Endometrial hyperplasia with atypia	Spontaneous

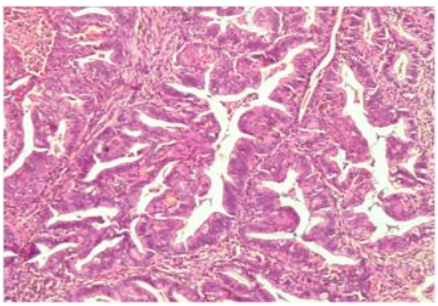

Figure 1: Photomicrograph showing back-to-back arrangement of endometrial glands (complex hyperplasia) H and E of 20X.

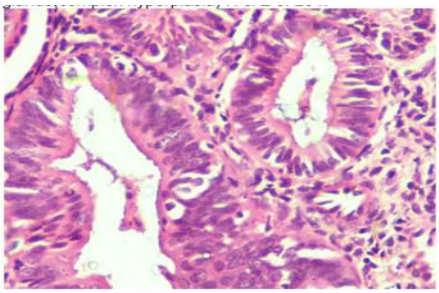

Figure 2: Higher magnification of the same shows closely spaced glands with minimal nuclear atypia of the epithelium. H and E of 40X.

DISCUSSION

Various etiologies are responsible for tubal ectopic. Previous ectopic pregnancy, prior pelvic inflammatory disease, previous tubal surgery, cigarette smoking, increased maternal age are some of the risk factors for ectopic pregnancy.[2] At the molecular level various changes can be seen in fallopian tube such as reduced levels of estrogen and progesterone receptors, increased levels of uteroglobulin (low molecular weight peptide), IL-8 especially in chlamydial infections, leukemia inhibitory factor (LIF), VEGF, increased expression of homeobox protein A 10, and decreased levels of MUC 1.[3-9]

Similarly in endometrium factors that are responsible for promoting adhesiveness between embryo and endometrium such asintegrins, a1b1, a4b1 and avb3 which (largely accepted as markers of receptivity) are reduced.[10] PCOS is one of the main causes for endometrial hyperplasia in infertile patients due to unopposed action of estrogen in them.[11] All of our eight patients had history of PCOS and had endometrial hyperplasia. In our third and fourth case endometrial hyperplasia could be because of PCOS or IVF treatment (received from outside) or could be because of both. Infertility treatments by ovulation induction or controlled ovarian stimulation cause a hyperestrogenic milieu by the supraphysiological gonadotropin levels that could provide the maintenance

and progression of endometrial hyperplasias.[12] There have been only two case reports in literature on coexistence of endometrial cancers and tubal ectopic though there are many cases of pregnancy associated endometrial carcinoma in the first trimester in the literature.[13,14] Endometrial hyperplasias hamper the receptivity of endometrium thereby causing implantation defect locally. Successful implantation requires cross talk between the developing embryo and receptive endometrium in a time period of window of implantation. Regulation of progesterone hormone receptors plays a critical role in implantation of the embryo and decidualization of the endometrium which may not be the case in endometrial hyperplasia where it may be unhealthy.[15,16] The endometrial environment may also be affected by the history of curettage or biopsy in these women. There is a possible delay in transit of the fertilized embryo due to intake of progesterone leading to ectopic pregnancy or cornual obstruction due to hyperplasia. The possible cause of the failure of implantation of the embryo to the endometrium in our cases could be impaired receptivity of endometrium due to hyperplasias and favourable cyclic changes in the tubal epithelium allowing the attachment of the embryo to the fallopian tube.

CONCLUSION

It is rare to find endometrial hyperplasia causing ectopic pregnancy. We need more robust data to finally prove that it is not only the tubes which can be the causative factor but it can be the endometrium also by not being receptive thereby causing the embryo to implant in the fallopian tube.

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