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Case Series

Hysteroscopic management of osseous endometrial metaplasia causing secondary infertility

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ABSTRACT

Osseous endometrial metaplasia is a rare pathological condition frequently associated with infertility. Despite multiple theories about its development, the exact mechanism, the source of the osseous tissue and the possible treatment outcomes are not clearly defined. Moreover, it is yet not clear whether surgical removal of the osseous tissue can restore fertility in the patients. We present three patients who presented to us with secondary infertility and were diagnosed to have osseous endometrial metaplasia. They were then treated with hysteroscopic removal of the osseous fragments. All three patients had spontaneous conception after the procedure. Hysteroscopic removal of bony spicules can provide reasonable chances of spontaneous conception in such patients provided the metaplasia does not extend deep into the myometrium.

Keywords: Endometrial metaplasia, Hysteroscopic excision, Osseous metaplasia, Secondary infertility

INTRODUCTION

Osseous metaplasia of endometrium is an uncommon disorder of the endometrium commonly associated with secondary infertility. It is characterized by metaplasia of endometrial cells into osteoblastic cells and leads to presence of mature or immature bone in the endometrium. It is important to note that this tissue is not related to embryonic or fetal origin and is a true metaplasia of endometrial cells. There is paucity of cases described previously in literature nearing about 80 cases.[1] Hence, the estimated incidence is also low about 3/10,000 cases.[2] There are broadly two types of theories for the origin of this kind of tissue. Most commonly accepted is metaplasia of pluripotent endometrium stromal cells into those of osteoblastic lineage which in turn synthesize bone.[3,4] The other theory represents ossification of retained fetal bones following abortion. This may lead to secondary infertility and remains a rare cause amongst the various diagnoses of secondary infertility. Here we present a series of three cases diagnosed to have osseous endometrial hyperplasia with varied clinical presentations. All three patients gave appropriate informed consent for publication.

CASE SERIES

Case 1

A 32-year-old patient from a rural part of India was referred to our gynecology outpatient service with history of secondary infertility and irregular menstrual bleeding since 1 year. She had a history of one living child and a

missed miscarriage in first trimester 18 months ago followed by dilatation and curettage. Post the curettage she had persistent complaints of inter-menstrual bleeding for she underwent a repeat procedure at a tertiary hospital 6 months after the abortion. On a 3-D Trans-vaginal sonography done post menstrual at our setup, the endometrial cavity appeared hyperechogenic suggestive of calcification with irregular endometrium (Figure 1).

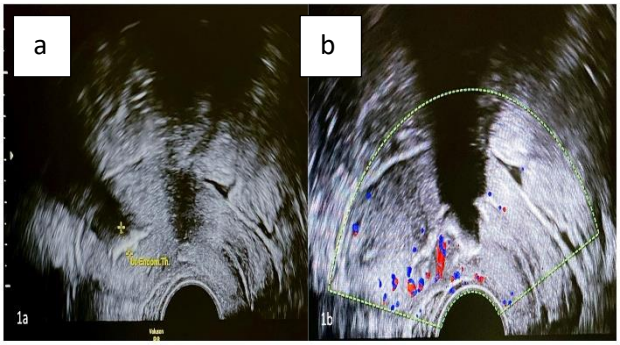

Figure 1: a) Demonstrating ultrasonographic picture of hyper echoic endometrium suggestive of calcification with posterior acoustic shadowing, b) corresponding doppler image for the same patient demonstrating no vascularity.

Her routine blood investigations including her endocrine profile and serum calcium were normal. She was counselled for hysteroscopy after her next menstrual cycle. On the 7th day post-menses, she underwent hysteroscopy under spinal anesthesia with Bettocchi 4 scope that is a 1.9 mm and 30 degree forward oblique scope with continuous flow suction & irrigation with Normal saline and EASI endomat with intrauterine pressure 45 mmHg. With vaginoscopic technique the external uterine orifice (EUO) was negotiated and in the cervical canal osseous trabecular material was seen, it was gradually removed with 5 Fr crocodile grasper.

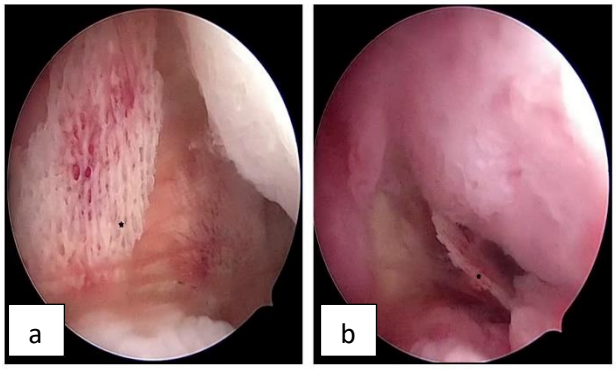

Figure 2: a) Hysteroscopic intra-procedure photograph depicting a 'Coral reef' appearance of bony spicules (star) in the first patient, b) Hysteroscopic intra-procedure photograph depicting osseous tissue embedded in endometrium and the uterine cavity (star).

The internal uterine orifice (IUO) was occupied by bony fragments which were removed and then the uterine cavity was visualized studded with multiple trabecular osseous material with spicules mimicking a 'coral reef' which were gradually removed only with a grasper (Figure 2). Few spicules were embedded in the myometrium where the combination of cold 5 Fr scissors and grasper was needed to create the right plane and separate the bony spicules. Once the cavity was empty both the ostia could be visualized. No adhesions or other pathologies seen. Time taken to complete the procedure was 45 minutes. All the material was sent for histopathological examination. The histopathological exam confirmed the presence of well-formed mature bony trabeculae without any inflammation suggestive of endometrial metaplasia (Figure 3). Endometrial sample was also sent for Gene xpert for tuberculosis testing, but that was negative. Patient was started on doxycycline 100mg twice daily for 5 days. She was called for follow up after 7 days which was uneventful. Subsequent TVS was done after next menstrual cycle which confirmed endometrium was thin with no persistent hyperechogenicity. She had spontaneous conception about 12 weeks after the procedure. A supplementary video (video S1) demonstrating the important hysteroscopy procedure findings of this patient is availabe.

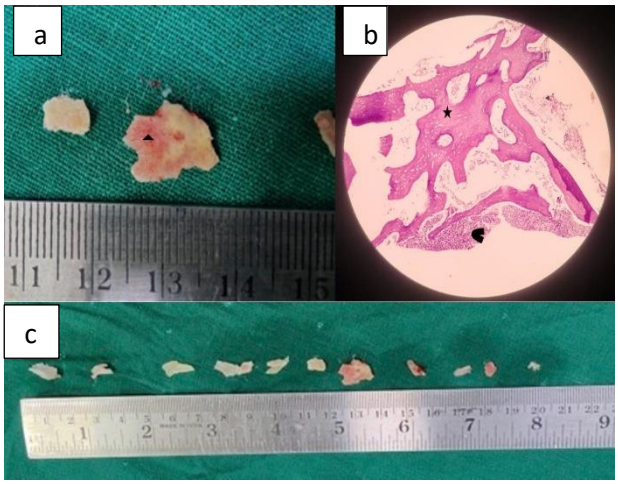

Figure 3: a) The specimen retrieved after the hysteroscopic removal showing trabecular bony pattern (triangle), b) Histopathological examination of the same showing osseous metaplasia without inflammation (star) and the adjacent endometrial glandular tissue (arrow head), c) Picture depicting the cumulative bony tissue retrieved during hysteroscopic removal in the third patient.

Case 2

A 30 yrs old patient with previous history of medical termination of pregnancy and two living issues, presented to gynecology OPD with chronic pelvic pain with vaginal discharge for last 6 months and failure to conceive. She had undergone a second trimester 16 wks termination of

pregnancy 2 yrs back. Ultrasonography showed a similar picture of endometrial hyperechogencity suggestive of calcification. Swabs of the vaginal discharge showed chlamydial infection which was treated with oral doxycycline preoperatively and then the patient was managed by hysteroscopic removal of bony spicules. This case was handled as an office procedure without any anesthesia and the patient experienced minimal pain (VAS score-2) during the procedure. Duration of the procedure was 25 minutes. Patient missed her next period and had spontaneous conception.

Case 3

A 27-year-old presented with inability to conceive since two years (secondary infertility) with history of two first trimester spontaneous abortions, D & E done in both. No history of any menstrual complaints or vaginal discharge or dysmenorrhoea. Clinical examination and blood tests unremarkable. Ultrasound was suggestive of a mass in endocervical canal that exhibits a densely calcified margin circumferentially and with few linear calcified shadows seen randomly within the central part of the mass with no vascularity on doppler. She was managed with hysteroscopic resection of the osseous material (Figure 3). She was able to conceive spontaneously after the procedure.

DISCUSSION

The earliest reports of bone formation inside the endometrium is attributed to Virchow who has described this as early as 1884.[5] He postulated differentiation of fibroblasts into osteoblasts as the mechanism for this finding. This finding was also later reported by Thaler et al and De Brux et al.[6,7] The WHO classification divides endometrial metaplasia into epithelial and non-epithelial types.[8] Among the non-epithelial types, common ones are: smooth muscle, osseous, cartilaginous and fatty tissue. This condition is typically reported during the reproductive years of the patient although there have been reports in menopausal women as well. Majority of patients report history of abortion in the first trimester like in our case scenario 1 and 3. The difference between abortion and endometrial ossification has been described from 8 weeks to 14 years.[9] The most important recognized risk factor is the presence of recurrent abortions. Multiple theories have been postulated for the development of osseous metaplasia in the endometrium. One theory is related to spontaneous metaplasia of endometrial stromal cells (fibroblasts) into osteoblasts.[10,11] This may occur in conditions pertaining to long standing endometrial inflammation, or metabolic disorders related to hypercalcemia and hypervitaminosis D. Presence of mycoplasma and chlamydia infection is also reported. The second important theory relates to persistence of fetal parts after an incomplete abortion. This could be explained by the fact that persistent fetal tissues may promote endometrial osteogenesis where fetal bones serve a supply for calcium.[12] However, there have been reports of endometrial ossification in patients with abortion in very early weeks of gestation where no fetal bones were developed. In that case it is presumed that embryonic parts must have induced osseous metaplasia.[13] The origin of this bony tissue (maternal/foetal) has also been questioned and analyzed by DNA analysis of the osseous tissue. Tulandi et al have reported this tissue to be genetically related to the fetus and Cayuela et al have reported the DNA analysis to match the patient rather than the fetus.[14,15] In India, genital tuberculosis is an important cause of secondary infertility and it is also associated with dystrophic calcification of retained necrotic tissue with chronic endometritis. The patients commonly present with secondary infertility, abnormal uterine bleeding, dysmenorrhoea, chronic pelvic pain and dyspareunia. All three of our cases primarily presented with secondary infertility post abortions. Ultrasound remains an important modality to diagnose osseous metaplasia.[16] There is a typical hyperechogenic pattern suggestive of the diagnosis. It frequently appears as linear hyperechogenicity with posterior acoustic shadowing in the uterine corpus (Figure 1). Calcific endometritis may be indistinguishable from osseous metaplasia on USG and final diagnosis is confirmed with histopathological examination only by presence of chronic inflammation along with calcific foci. The USG appearance may also mimic that of a intrauterine device but history will prove beneficial to rule this out. Hysterosalpingogram has been used for diagnosis in some cases but hysteroscopy remains the gold standard for diagnosis.[9-15] The osseous tissue can be easily visualized and removed piece meal also giving a histological diagnosis. Hysteroscopy and removal of the bony tissue completely may provide a good endometrial bed for future pregnancy as seen in our cases. However, it may be difficult to remove the entire tissue if it extends to the myometrium. USG guided hysteroscopic resection may also be utilized for removal.[16,17] In cases where satisfactory removal is not anticipated, laparoscopic guided hysteroscopy may be utilized as well to reduce the chances of uterine perforation.[18] Hysterectomy has also been utilized for cases where extensive osseous metaplasia is suspected and there is no demand for future pregnancy. This metaplasia may sometimes extend to endocervix as well as reported by Hoshiko et al.[3] They postulated that it could be secondary to long standing inflammation and tissue damage associated with repeated abortions. The high prevalence of genital tuberculosis in India should always warrant a culture and antibiotic sensitivity testing for TB in cases where endometritis is also present alongside osseous changes in the endometrium.

CONCLUSION

As endometrial osseous metaplasia is rare but a significant contributor to infertility and menstrual complaints, each of us should be well versed with the entity to facilitate early detection and offer early treatment. Hysteroscopic resection is the gold standard treatment of osseous metaplasia of endometrium offering a solution to the infertility and menstrual complaints caused by it.

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