

Endometrial Osseus Metaplasia during Infertility Evaluation: A Case Series

J. O. Imaralu^{1*}, A. A. Akadri¹, T. O. Solaja², O. I. Odelola³ and C. C. Nwankpa¹

¹Department of Obstetrics and Gynaecology, Babcock University Teaching Hospital, Ilisan-Remo, Nigeria.

²Department of Morbid Anatomy and Histopathology, Babcock University Teaching Hospital, Ilisan-Remo, Nigeria.

³Department of Obstetrics and Gynaecology, Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/ARRB/2021/v36i930428

Editor(s):

(1) Dr. Md. Torequul Islam, Federal University of Piaui, Brazil.

Reviewers:

(1) Sirisha Psnrs, Sri Ramachandra Institute of Higher Education and Research, India.

(2) Atmajit Singh Dhillon, Deemed University, India.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/74337>

Case Report

Received 13 July 2021
Accepted 23 September 2021
Published 28 September 2021

ABSTRACT

Aims: To highlight the pathogenesis of endometrial osseus metaplasia, its importance as a rare cause of infertility and the benefit of hysteroscopic evaluation of infertile women with risk factors for osseus metaplasia.

Presentation of Case: A diagnosis of endometrial osseus metaplasia was confirmed histologically in three women undergoing diagnostic hysteroscopy as part of infertility evaluation. They all had chronic vaginal discharge and a preceding history of induced second trimester abortion. Two of the patients were referred for evaluation before in-vitro-fertilization (IVF). Hysteroscopy was done with a 30° telescope, initially using a 2-channel diagnostic sheath, which was later replaced with a 4-channel operating sheath for tissue retrieval.

Discussion: Endometrial osseus metaplasia is a rare condition characterized by the presence of mature or immature bone in the endometrial cavity. Endometrial retention of embryonic tissue following an abortion is the commonest theory of etio-pathogenesis. It is an important cause of infertility and while other causes of infertility can be easily by-passed in an IVF cycle, endometrial

*Corresponding author: E-mail: imaraluj@babcock.edu.ng;

factors may not be addressed by IVF alone, as a defective endometrium is a risk for failure. Although there is no consensus on routine hysteroscopy for women undergoing IVF, it is the mainstay of evaluation and treatment of women with endometrial osseus metaplasia.

Conclusion: Only complete removal of metaplastic tissue would restore fertility, in patients with osseus metaplasia. Hysteroscopy done in infertile women with risk factors for endometrial osseus metaplasia may enhance early treatment and ultimately increase successful spontaneous and IVF pregnancy rates.

Keywords: Abortion; assisted conception; bone; endometrium; hysteroscopy; infertility; osseus metaplasia.

1. INTRODUCTION

Endometrial osseus metaplasia is a rare condition characterized by the presence of mature or immature bone in the endometrial cavity [1]. Several pathophysiologic mechanisms have been proposed to explain this intriguing condition. The most common theories are: retention of foetal bone after an abortion, transformation of endometrial mesenchymal tissue into bone and dystrophic calcification [1,2]. Endometrial osseus metaplasia may follow spontaneous, induced or missed abortion and is commonly associated with infertility [1,3,4]. Endometrial, ovarian and tubal factors are important causes of infertility [2]; while other factors can be easily by-passed in an in-vitro-fertilization (IVF) cycle, endometrial factor, may be more difficult to manage through IVF and sometimes IVF in this instance may require a surrogate. Hysteroscopic evaluation before IVF is becoming popular, although, there is no consensus on routine hysteroscopy for women undergoing IVF. We present here three cases of patients with endometrial osseus metaplasia following induced second trimester abortion, which were diagnosed during evaluation for secondary infertility.

2. PRESENTATION OF CASES

2.1 Case Series

A diagnosis of endometrial osseus metaplasia was confirmed histo-pathologically in three patients who were found during hysteroscopic evaluation for secondary infertility to have foreign bodies within the endometrium. All of the three patients were being evaluated for infertility; they also had preceding history of induced second trimester abortion. Hysteroscopy was done during the proliferative phase of the menstrual cycle in all the patients with a 30° telescope, within an initial 2-channel diagnostic sheath, which was later replaced with a 4-channel

operating sheath, to aid tissue manipulation and retrieval, which were done with hysteroscopic scissors and graspers. The distension medium used was normal saline and the Karl Storz Hamou –Endomat® 26331020, was used to generate pressure in all cases. The retrieved tissues from all of the three patients were negative for tuberculosis on Gene Xpert testing.

2.2 Case 1

A thirty three year old woman, who was P₀+1 who had secondary infertility of five years duration and was undergoing evaluation for possible IVF. She had terminated a twenty-week pregnancy, by dilatation and evacuation, thirteen years earlier. A few weeks after the procedure, she developed foul smelling vaginal discharge and occasional abdominal pain which had been recurrent until presentation. She had been evaluated several times and treated for chronic vaginal discharge. However, a recent 3-dimensional trans-vaginal pelvic ultrasound scanning revealed an intrauterine echogenic calcified structure, which was partly embedded in the posterior myometrium and jutting out into the endometrial cavity (Fig.1).

Hysteroscopy revealed four pieces of preserved bone-like structures embedded within the endometrial wall with parts jutting into the cavity (Fig. 2). The endometrial volume was grossly normal and the unaffected aspects of the endometrium grossly proliferative. The indent V-shaped central portion of the anterior lip of the cervical external cervical os, was suggestive of forceful avulsion. The cervical canal and internal os however appeared grossly normal. The tissue fragments were then removed one after the other and sent in a formalin solution for histology.

The findings at histology, included macroscopically, four pieces of hard greyish white tissue fragments, the largest measuring 0.6cm X 0.4cm X 0.2cm and the smallest,

measuring 0.3cm X 0.2cm X 0.2cm. Microscopic section revealed mature bony trabeculae with non-hematopoietic bone marrow within a bland fibro-collagenous stroma and some surrounding areas of chronic inflammatory cells (Fig.3). The vaginal discharge stopped immediately after the procedure. Repeat hysteroscopy done 8 weeks later confirmed complete removal of all osseous tissue and grossly normal endometrium.

2.3 Case 2

A forty seven year old woman, who was P₀⁺¹ and who was referred from another hospital for hysteroscopic retrieval of a foreign body within the uterus that was recently noticed on trans-vaginal ultrasound scanning. She had been married for 18 years but unable to conceive. She had persistent vaginal discharge for about 23 years which changes in consistency from serous to purulent and in volume from light to heavy depending on antibiotic usage. This complaint started a few weeks after having dilatation and curettage done on her 23 years earlier, for an unwanted 16-week pregnancy, which she had before marriage.

Hysteroscopy showed a grossly normal capacious proliferative endometrial cavity, with a

spicule of hard bony tissue in the posterior uterine endometrium stuck into the endomyometrium in a downwards and backwards direction, with the free end facing the anterior endometrial wall and pointing cephalad (Fig. 4). The cervical external os, internal os and canal all looked grossly normal. A hysteroscopic grasper was first used to dislodge it in an upwards and backwards direction, to release it from the tract where it was lodged, before successful removal. The tissue specimen was then sent for histology, which revealed macroscopically, a hard cord-like greyish white cylindrical tissue, measuring 1.5cm X 0.2cm X 0.2cm. Microscopic section showed mature bony trabeculae with non-hematopoietic bone marrow within a bland fibro-collagenous stroma. Occasional chronic inflammatory cells were also seen (Fig.3). The pathologic diagnosis was endometrial content with features in keeping with endometrial calcification. She presented for follow up and after three visits, there was no longer any complaint of vaginal discharge. A repeat hysteroscopy confirmed complete excision of the metaplastic tissue and revealed grossly healthy endometrium. She was then referred back for assisted conception for which she was planned.

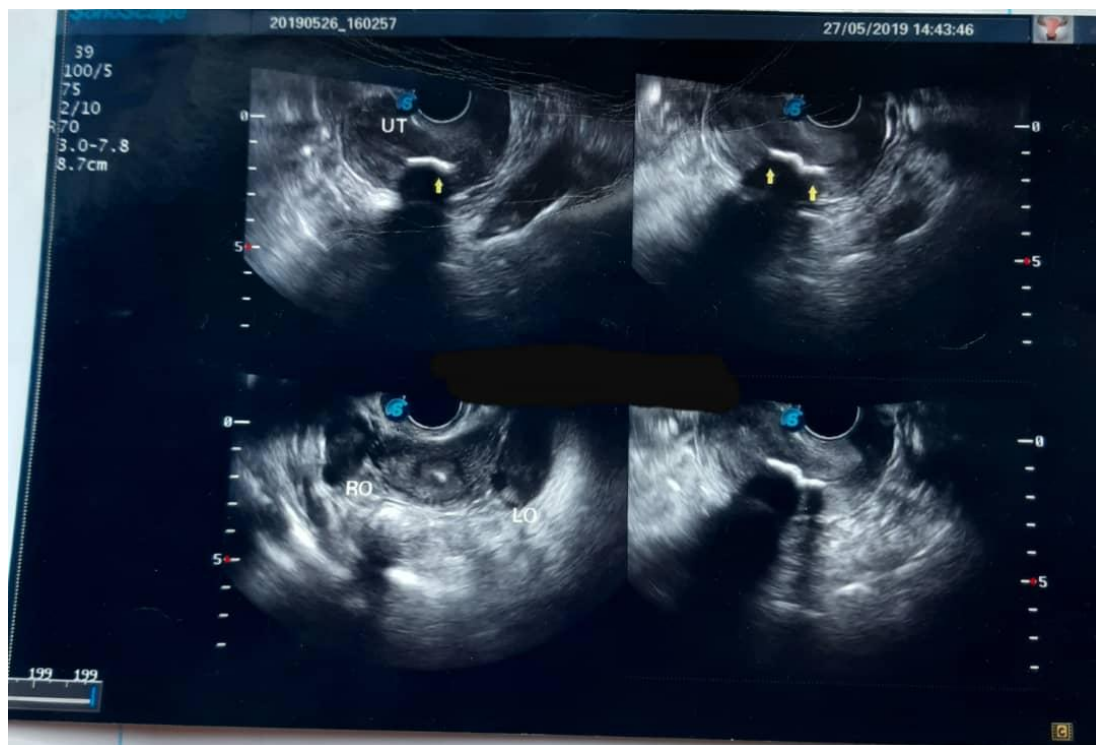


Fig. 1. Trans-vaginal ultrasound scanning image, showing an echogenic calcified structure (yellow arrows), within the endometrial cavity which was partly embedded in the posterior myometrium and jutting out into the endometrial cavity

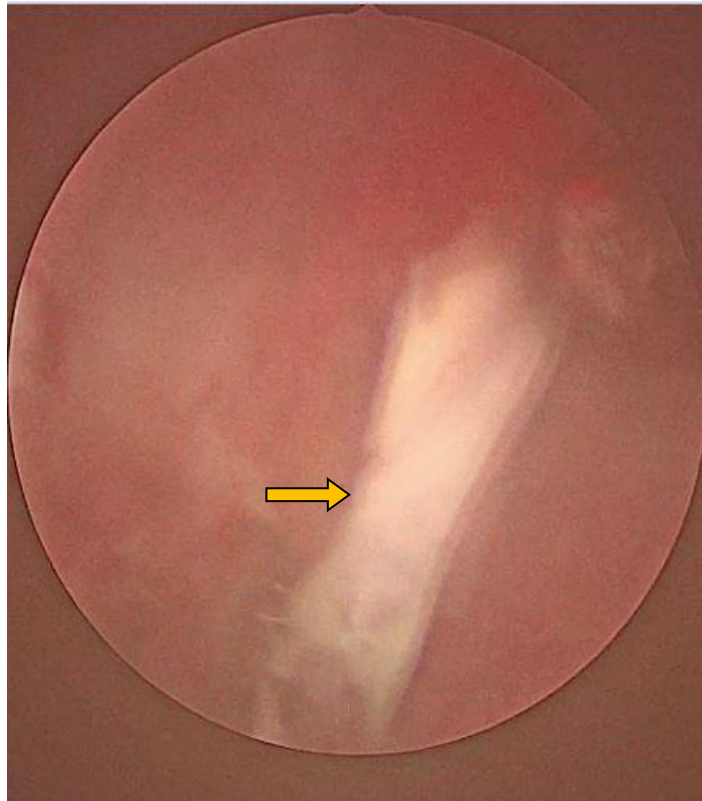


Fig. 2. Hysteroscopic image of bone tissue fragment (yellow arrow) within the endometrial cavity of case 1

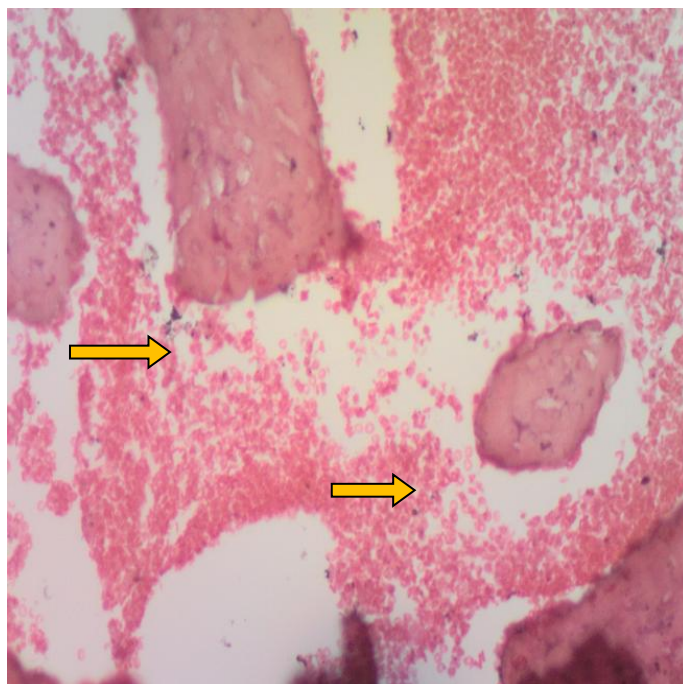


Fig. 3. Photomicrograph showing proliferating mature bony trabeculae with non-hematopoietic bone marrow within a bland fibro-collagenous stroma and some areas surrounded by chronic inflammatory cells (arrow) consistent with dystrophic calcification (Haematoxylin and Eosin, Original magnification, X40)

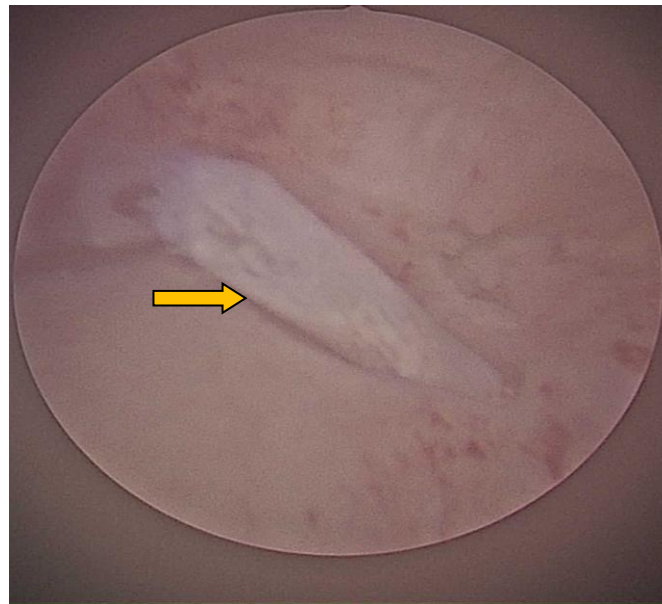


Fig. 4. Hysteroscopic findings of a Spicule of bone tissue (yellow arrow) within the endometrium sticking through into the myometrium of case 2

2.4 Case 3

A 27 year old P₀+1 presented for evaluation of infertility of three years duration. She had been treated several times for recurrent foul smelling vaginal discharge of five years. Seven years prior to presentation, she had an induced abortion, for a 13 week pregnancy, initially done by manual vacuum aspiration, then repeated by dilatation and curettage, when bleeding persisted and ultrasound scanning confirmed retained products of conception. Ultrasound scanning investigations were reportedly normal. She however presented for infertility evaluation, during which hysteroscopy revealed sheets of tissue in a membrane-like fashion lying over the posterior endometrium wall, with the superior edge of the lowermost one floating in the normal saline distension medium (Fig. 5). The anterior endometrial wall and the unaffected portions of the posterior endometrium appeared grossly proliferative. The grossly capacious endometrium, internal cervical os and cervical canal, were devoid of adhesions or deposits. These sheets were gently teased off with hysteroscopic scissors and the fragments retrieved with graspers and sent for histopathological examination in a formalin medium. A size 10Fr Foley catheter was inserted into the uterine cavity and balloon inflated with 3ml of sterile water, to prevent post-operative adhesions. Histo-pathological examination revealed macroscopically three tiny pieces of greyish-white tissue altogether measuring 0.5 X

0.2cm (AE X 1). Microscopic section showed fragments of mature bony trabeculae within a bland fibro-collagenous stroma with mild infiltration by mixed population of inflammatory cells. The histopathology report was; endometrial biopsy specimen with features consistent with dystrophic calcification. There was no longer any complaint or evidence of abnormal vaginal discharge as of the time of this report, 3 months after the removal of the osseous material. Repeat hysteroscopic confirmation of complete removal and endometrial assessment had not been done for financial reasons.

3. DISCUSSION

Endometrial osseous metaplasia has remained an intriguing finding and a rare cause of persistent vaginal discharge and infertility. Although there is no consensus on a single definite etiopathogenesis for this occurrence, transformation of mesenchymal tissue as a result of inflammatory changes following an abortion process is the most popularly held hypothesis [1,5]. Most reports of endometrial osteogenesis have a preceding history of an abortion whether spontaneous or induced and reported intervals from an abortion to detection have ranged from 8 weeks to 14 years [4,6]. All of the cases presented here followed abortions and the intervals to detection of osseous metaplasia were 13, 23 and 7 years, respectively. A similar 20 year interval was reported from Eastern Nigeria [7]. A much longer interval to detection of 37

years had however been reported in a Japanese patient [8].

Continued proliferation of retained fetal bone tissue following uterine curettage, for an abortion, has been postulated as a reason for endometrial ossification. In addition, chronic non-specific inflammation with calcification apart from continuous proliferation is another cause of ossification of retained embryonic tissue after endometrial curettage [9].

The pluripotential property of endometrial stem cells have been hypothesized as reason for de-novo osteoblastic transformation following an abortion, especially when enhanced by chronic inflammation and endometritis [10,11]. The chronic inflammation that follows the retention of products of conception may lead to the release of free superoxide radicals and tumor necrosis factor from macrophages. This may persist in the absence of free radical scavengers like superoxide dismutase, thus resulting in osteoblastic metaplasia [1,6]. Endometrial ossification in a patient without a history of pregnancy, abortion, or endometrial instrumentation has however been reported [12].

Other theories of endometrial osteogenesis include; tissue destruction from instrumentation during repeated abortions, repeated endometrial chronic inflammation of various infective or inflammatory origin, such as endometrial tuberculosis [4]. Heterotopic calcification in individuals with some inherited metabolic disorders, high calcium intake and long term

hypervitaminosis D are also recognized risk factors for ossification within the endometrium [1].

The bone tissue present within the endometrium excites an inflammatory response which may be acute or chronic with repeated cycles of acute inflammation resulting in an increase of endometrial inflammatory cells, white blood cells and tissue debris which often presents clinically as persistent or repeated vaginal discharge. All three cases in this series had this history of recurrent vaginal discharge and treatment with antibiotics and antifungal agents. Similar histories have been observed in many earlier reports [3,4,7]. Although vaginal discharge is the commonest reported symptom, evaluation leading to definitive diagnosis has been done mostly for patients with infertility as found in earlier reports [3,4,7,11–13]. All the cases in our series were diagnosed during evaluation for infertility.

It appears as though the inflammation within the endometrial cavity is responsible for infertility as most case reports have histologic evidence of inflammation within the endometrium [3,4,11,12]. It has also been postulated earlier that the inflammation and influx of inflammatory cells into the endometrium may result in death of spermatozoa and embryo, from direct toxic injury, prevention of implantation and obliteration of the endometrial cavity [12]. Reports of successful pregnancies after removal of the osseous metaplastic tissues support the contraceptive effects of this condition [3,11,12].



Fig. 5. Hysteroscopic image of sheets of bony tissue plastered on the endometrium of case 3

Other symptoms of endometrial osseous metaplasia include; menorrhagia, dysmenorrhea and chronic pelvic pain. Spontaneous vaginal expulsion of bony fragments during menstruation have also been reported [3,4,13].

Although endometrial ossification, first described over five decades ago, is still considered a rare occurrence, increasing hysteroscopic evaluation for infertility may increase the rate of diagnosis of endometrial osseous metaplasia to much greater than the 0.15% of hysteroscopies observed for abnormal uterine bleeding by Makris et al, since the commonest complaint leading to detection is infertility [3,4,7,11,12,14]. Ultrasound scanning, magnetic resonance imaging and computerized tomography are useful ancillary investigations for evaluation and to guide treatment but hysteroscopic evaluation clearly has greater potential to clinch the diagnosis and ensure adequate removal of ossified tissue. Ultrasound guided hysteroscopic removal of bone ensures complete removal of metaplastic tissue, which may be implanted deeper in adjacent myometrium.[1–4,11,12].

Although cost is a major deterrent to routine hysteroscopic evaluation of women with infertility, as also observed in one of our patients who defaulted from repeat hysteroscopy for financial reasons; a case can however be made for this procedure in women undergoing in-vitro fertilization because of the already high cost of the IVF. Another reason why hysteroscopy may be advocated is the fact that apart from more accurate diagnosis, adequate and appropriate treatment can only be given when tissues are removed hysteroscopically. Excision or resection by hysteroscopy is the mainstay of treatment of endometrial ossification [3,11,12,14]. Although the role of routine diagnostic hysteroscopy for all patients planned for IVF remains controversial, hysteroscopy was however shown in a recent meta-analysis and systematic review to improve implantation and clinical pregnancy rates in women with recurrent implantation failure undergoing IVF [15,16]. Hysteroscopy may be indicated in patients with previous pregnancy losses, induced abortion, and previous failed IVF, to help detect and remove endometrial factors that may adversely affect IVF success.

4. CONCLUSION

Endometrial osseous metaplasia is an important cause of infertility, most cases follow a pregnancy loss and hysteroscopy is the mainstay

of evaluation and treatment. Only complete removal of metaplastic tissue would restore fertility. Hysteroscopy done in infertile women with risk factors for endometrial osseous metaplasia, may enhance early treatment and ultimately increase successful spontaneous and IVF pregnancy rates.

CONSENT

A written informed consent for publication was obtained from each patient permitting the use of their medical history and images for publication purposes. Confidentiality was ensured by removing any identifying features like names and facial appearance.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Umushankar T, Patted S, Handigund R. Endometrial osseous metaplasia: Clinicopathological study of a case and literature review. *J Hum Reprod Sci* 2010; 3:102–4. 2010;3:102-4.
2. Patil S, Narchal S, Paricharak D, More S. Endometrial osseous metaplasia: Case Report with Literature Review. *Ann Med Health Sci Res*. 2013;3(Suppl):S10–2.
3. Bouzid A, Ayachi A, Mourali M. Osteoid Metaplasia of the Endometrium: A Case Report and Literature Review. *Gynecol Obstet (Sunnyvale)*. 2016;6:361.
4. Rosa-e-Silva J, Barcelos I, Navarro P, Rosa-e-Silva A, Nogueira A, Ferriani RA. Osseous metaplasia of the endometrium associated with infertility: a case report and review of literature. *J Med Case Reports*. 2009;3:7427.
5. Cayuela E, Perez-Medina T, Vilanova J, Alejo M, Canadas P. True osseous metaplasia of the endometrium: the bone is not from a fetus. *Fertil Steril*. 2009; 91(4):1293 e1291-1294.
6. Bahneci M, Demirel L. Osseous metaplasia of the endometrium: a rare cause of infertility and its hysteroscopic management. *Hum Reprod*. 1996;11: 2537–639.
7. Okafor C, Okafor C, Ukah C, Obionwu I, Oguaka V. Prolonged Retention of Foetal Bones Following Induced Abortion as a Possible Cause of Secondary Infertility: A

- Case Report. Ann Med Health Sci Res. 2017;7:432–4.
8. Shimizu M, Nakayama M. Endometrial ossification in a postmenopausal woman. J Clin Pathol. 1997;50:171–2.
 9. Singh Y. Training and credentialing in laparoscopic surgery-the need of the day. . Med J Armed Forces India. 2005;61:7–8.
 10. Park K. Epidemiology of communicable diseases. In: Park JE, Eds. Park's Textbook of Preventive and Social medicine. In India: Barnasidas Bhanot Publishers; 2014;154–5.
 11. Horoa G, Akaa K, Toureb A, Koffia A, Senia K, Konea M. Endoscopy Management of Endometrial Ossification Associated With Secondary Infertility: A Case Report and Review of Literature. J Clin Gynecol Obstet. 2016;5(1):45–9.
 12. Kapur A, Khan S, Sharma S. Osseous Metaplasia of Endometrium: The Bony Womb and Its Hysteroscopic Management. Journal of Gynecologic Surgery. 2021; 37(1):40–3.
 13. Makkar M, Pandey P, Gupta C, Kapur K. Endometrial Ossification: An Unusual Cause of Infertility. J Clin Diagnostic Research. 2011;5(3):613–5.
 14. Makris N, Stefanidis K, Antaklis A. The incidence of retained fetal bones revealed in 2000 diagnostic hysteroscopies. JSLS. 2008;10:76–7.
 15. Surrey E. Should diagnostic hysteroscopy be performed before in vitro fertilization-embryo transfer? J Minim Invasive Gynecol. 2012;19:643–6.
 16. Mao X, Wu L, Chen Q, Quang Y, Zhang S. Effect of hysteroscopy before starting in-vitro fertilisation for women with recurrent implantation failure. A meta-analysis and systematic review. Medicine. 2019;98(7): 1–9.

© 2021 Imaralu et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<https://www.sdiarticle4.com/review-history/74337>