Short Communication

Endometrial Osseous Metaplasia: An Hysteroscopic Incidental Finding – An Overview

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Abstract

Endometrial osseous metaplasia (EOM) is an uncommon clinical entity with the presence of bone in the endometrium which requires clinical and therapeutic framework. It is also described by various other names such as endometrial ossification, ectopic intrauterine bone, and heterotopic intrauterine bone. Ossification could have various locations as the cervix the ovary, and the vagina. This overview highlights the attention on the actual pivotal points of EOM.

Keywords: Ectopic bone, metaplasia, miscarriage

Introduction

Endometrial osseous metaplasia (EOM) is a rare cytomorphological transformation of uterine epithelial cells from the usual endometrial phenotype to bone-type mesenchymal elements. It is characterized by the presence of mature or immature ectopic bone tissue within the endometrium and it must be distinguished from the persistence of embryonic or fetal bones, with consequent calcification or ossification.[1] About 100 cases have been described in the literature, with an estimated incidence of about 0.3/1,000. EOM is most often found in women of reproductive age, although it has also been described in the perimenopausal period.[2] Due to the lack of literature on a clear picture of this condition, this study highlights the attention on the pivotal points of EOM. This study was exempted from institutional review boards performed at Policlinico of Bari because the data for this analysis belong to the public source.

Etiopathology

In most of the reported cases, patients present a history of previous pregnancy or abortion, whether spontaneous or therapeutic. It has been speculated a relationship between this type of transformation and the inflammatory and reparative process induced by abortion. The time interval between the antecedent abortion and discovery of endometrial ossification varies from 8 weeks to 14 years in the reproductive age group.[3] Indeed, it appears that EOM is the result of persistent inflammation caused by necrotized nonbony embryonic tissue retained in the uterine cavity. Chronic inflammation is a frequent condition underlying EOM and the transformation process could also be favored by local inflammatory changes, curettage trauma, and other sources of chronic inflammation such as genital tuberculosis, unspecific chronic endometritis, or pyometra.[2] According to this theory, the transformation process could be considered an adaptive change of endometrial cells in response to changes in the environment.[4] Multipotential mesenchymal elements, especially those cells derived from Mullerian

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ducts or fibroblasts,[3] have the ability to transform into chondroblasts or osteoblasts. It was hypothesized that at the endometrial level chronic inflammation promotes the release of oxygen free radicals (in particular superoxide) or tumor necrosis factor by mononuclear phagocytes, inducing the metaplastic transformation of endometrial multipotential stromal cells (usually fibroblasts) in osteoblasts, when the endometrium is deficient in the protective activity of superoxide dismutase. To explain metaplasia's origin, other pathogenetic theories have also been described in addition to the transformation of multipotential stromal cells: Continuous and constant endometrial estrogenic stimulation; retention of fetal bones that secondarily promote osteogenesis in the surrounding endometrium; dystrophic calcification of retained and necrotic tissues following one or more abortions; metabolic disorders such as hypercalcemia, hypervitaminosis D or hyperphosphataemia;[5] Mullerian origin, arising in the myoendometrial transitional zone. Between infective agents that can be responsible for this condition's pathogenesis, *Streptococcus agalactiae* has been long investigated. *S. agalactiae* of group B could resist phagocytosis and like any intracellular microorganism can survive inside epithelial cells, endothelial cells, and macrophages. This bacterium-killing mechanism consists of inducing apoptosis and necrosis in all these kinds of cells. Apoptosis is characterized by a number of biochemical events, including protein kinase C activity, caspase activation, and increase in cytoplasmic calcium content that can trigger the further deposition of calcium and formation of macroscopic bone structures.

Ossification has also been reported in the cervix, ovary, vagina and mesosalpinx. Like has been said, persistent heterologous tissue, such as retained fetal bone, has been suggested as the etiology of osseous metaplasia of the endometrium. However, it is unlikely that the endometrial bone is of fetal origin because there was no fetal tissue found in the biopsy material studied after the first-trimester abortion, and the biopsy also showed minimal or no tissue reaction. Leiomyoma with osseous differentiation and mature teratoma can mimic osseous metaplasia nodules.

Clinical Presentation

Clinically, EOM is associated with a history of recurrent miscarriages, pelvic pain, dyspareunia, and menstrual irregularities, such as hypermenorrhea, and dysmenorrhea but may also present with endometritis, oligomenorrhea, dyspareunia, pelvic pain, and vaginal discharge.[3,4,6] This condition can also be recognized as an incidental find at ultrasound examination made for infertility assessment.

Indeed, some patients may present with primary or secondary infertility, as the bone fragments act as a foreign body and increase endometrial prostaglandins preventing blastocyst correct implantation.[5]

Ultrasound Features

Transvaginal ultrasound plays a primary role in the diagnosis of this condition. On 2D ultrasound, the picture is characterized by a linear or irregular hyperechoic pattern with rear acoustic shadowing, strongly indicative of retained bone tissue inside the uterine cavity. Usually, the hyperechoic region is located at the center of the fundus, but it can also be found in the isthmic part of the uterus, or in multiple areas. Given its low incidence, EOM is often a source of misdiagnosis, being mistaken for intrauterine devices (IUD), Asherman's syndrome, calcified submucosal fibrosis, and Mullerian tumor. Useful in this regard is the 3D ultrasound which provides the coronal plane of the uterus showing the irregular shape of the bone fragments, making it easy to differentiate an IUD (with clearly regular borders) from an EOM.[4] Ultrasound examination should be confirmed by hysteroscopy, the gold standard for management. Finally, a histological examination should be performed to confirm the diagnosis.

Management

Nowadays, hysteroscopy allows minimally invasive diagnosis and, in some cases, even treatment of benign and malignant endometrial pathology and is taking a great consideration in office setting, with new future prospective and incoming approaches of this procedure.[5-9] Hysteroscopy is a key tool for endometrial metaplasia management. In the past, when EOM diagnosis was made, bone tissue removal was performed by dilatation and curettage. This procedure, which is still considered the gold standard in many contexts, unfortunately, presents several possible complications such as uterine perforation or bowel damage, even reaching the point, in some cases, of requiring emergent hysterectomy or bowel resection. It seems clear that these complications can be catastrophic for fertile or infertile women who still have pregnancy desires. Nowadays, the safest and most effective therapeutic approach is the hysteroscopic removal of ectopic intrauterine bone, being able to ensure complete removal under direct visualization.[10] If the bone fragment to remove is a very large one, a morcellation can be tried in an office setting always remembering that removing the whole metaplastic fragment can be a challenging task.

In our center experience, we have performed these procedures in an office setting, being the patient under general anesthesia, and we have chosen Karl Storz 26 Fr Resectoscope with a 30° optic and a continuous flow. Endometrial metaplastic fragments appear such as multiple small and hard bony spicules. Fragments

can be easily removed like a foreign body with slicing loop and, for the most adherent pieces, electrified loop can be used, while some authors prefer a hysteroscopic grasper.[10-12] After osseous fragments removal by hysteroscopy or dilatation and curettage, 55.6% of the infertile patients achieved a pregnancy, spontaneous pregnancy should be expected for at least 1 year following the "complete" restoration of the endometrial cavity. Hysteroscopy has abundantly proved successful in the treatment of EOM cases associated with infertility. In patients with extensive plaques of EOM and bone fragments embedded in the myometrium, where satisfactory hysteroscopic removal is difficult, the usefulness of laparoscopic control during the procedure has been highlighted, which allows for greater accuracy and minimization of risks and complications such as uterine perforation.[10-15] At hysteroscopy, osseous metaplasia appears as osseous lamellae, white in color, fan or disc-shaped, and embedded in the mucosa, or as an intracavitary structure. On reviewing the literature, this kind of complication was not discovered until hysterectomy in some patients and was misdiagnosed in several cases. It is reasonable that antibiotic prophylaxis must be tailored for each case, taking into account patient's history, furthermore in patients with a history of pelvic inflammatory disease and in a prolonged hysteroscopic procedure treatment.

Conclusions

A better understanding of factors that trigger the metaplastic transformation is required to prevent EOM. Hysteroscopy and 2d–3d ultrasound are the key tools for endometrial metaplasia management. Chronic endometritis evokes metaplastic changes in the pluripotent endometrial stromal into osteoblastic cells that lay down bone. Pathologists should be aware of EOM to avoid misdiagnosis of malignant mixed Müllerian tumor.

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Conflicts of interest

There are no conflicts of interest.

References

1. Umashankar T, Patted S, Handigund R. Endometrial osseous metaplasia: Clinicopathological study of a case and literature review. J Hum Reprod Sci 2010;3:102-4.
2. Cayuela E, Perez-Medina T, Vilanova J, Alejo M, Cañadas P. True osseous metaplasia of the endometrium: The bone is not from a fetus. Fertil Steril 2009;91:1293.e1-4.
3. Bahçeci M, Demirel LC. Osseous metaplasia of the endometrium: A rare cause of infertility and its hysteroscopic management. Hum Reprod 1996;11:2537-9.
4. Grigore M, Pristavu A, Gafitanu D. Ultrasound features of osseous metaplasia of the endometrium-case series and review of the literature. Clin Imaging 2018;52:260-3.
5. Damiani GR, Tartagni M, Crescini C, Persiani P, Loverro G, Von Wunster S. Intussusception and incarceration of a fallopian tube: Report of 2 atypical cases, with differential considerations, clinical evaluation, and current management strategies. J Minim Invasive Gynecol 2011;18:246-9.
6. Trojano G, Damiani GR, Casavola VC, Loiacono R, Malvasi A, Pellegrino A, *et al.* The role of hysteroscopy in evaluating postmenopausal asymptomatic women with thickened Endometrium. Gynecol Minim Invasive Ther 2018;7:6-9.
7. Trojano G, Olivieri C, Tinelli R, Damiani GR, Pellegrino A, Cicinelli E. Conservative treatment in early stage endometrial cancer: A review. Acta Biomed 2019;90:405-10.
8. Caponio MA, Addati T, Popescu O, Petroni S, Rubini V, Centrone M, *et al.* P16(INK4a) protein expression in endocervical, endometrial and metastatic adenocarcinomas of extra-uterine origin: Diagnostic and clinical considerations. Cancer Biomark 2014;14:169-75.
9. Damiani RG, Muzzupapa G, Trojano G, Cicinelli R, Cicinelli E. Remodelling of anterior arches of post-caesarean niche (ROAN) with intrauterine morcellator: It is possible? Arch Gynecol Obstet 2022;306:1845-6.
10. Damiani GR, Seghezzi U, Gaetani M, Riva D, Tartagni M, Loverro G. Intrauterine bone fragments and endometrial plaque of osseous metaplasia. Acta Obstet Gynecol Scand 2012;91:1001.
11. Kadirogullari P, Seckin KD, Selcuki NFT. Osseous Metaplasia of the Endometrium and Successful Hysteroscopic Resection: A Video Case and Review of the Literature. Gynecol Minim Invasive Ther 2022;11:244-6. doi: 10.4103/gmit.gmit_121_21.
12. Wang PH. A Powerful Value of Hysteroscopy. Gynecol Minim Invasive Ther 2018;7:143-4.
13. Yen CF, Chou HH, Wu HM, Lee CL, Chang TC. Effectiveness and appropriateness in the application of office hysteroscopy. J Formos Med Assoc 2019;118:1480-7. doi: 10.1016/j.jfma.2018.12.012.
14. Roy KK, Gajapathy SR, Rai R, Zangmo R, Das A, Singhal S. Assessment of Tubal Patency with Selective Chromopertubation at Office Hysteroscopy versus Modified Minilaparoscopy in Infertile Women. Gynecol Minim Invasive Ther 2021;10:159-65.
15. Harzif AK, Anggraeni TD, Syaharutsa DM, Hellyanti T. Hysteroscopy role for female genital tuberculosis. Gynecol Minim Invasive Ther 2021;10:243-6.