Osseous metaplasia of the endometrium

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Osseous metaplasia should be kept in mind as a rare cause of failure to conceive, even in patients with primary infertility. We report a case of osseous metaplasia of the endometrium as a cause of primary infertility and present a literature review. The condition may be more common than expected or generally accepted, and should be kept in mind even in patients with primary infertility. Hysteroscopy is an effective diagnostic as well as treatment modality. The human endometrium contains populations of epithelial progenitor cells and mesenchymal stem cells. These cells are multipotent but rare, and are the most likely origin of the endometrial ossification. The cells can also differentiate into adipogenic and chondrogenic lineages.

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Endometrial osseous metaplasia is an uncommon clinical condition in which mature or immature bone is present in the endometrium. Patients often have a history of abortion or delivery. The causation and pathogenesis are controversial. Endochondral ossification of retained fetal bones is the most widely accepted aetiological hypothesis. The condition may also be caused by transformation of mesenchymal tissue into bone in response to inflammation and the reparative process induced by abortion.[1-3] A few cases of endometrial ossification without a previous history of pregnancy have been reported and may be due to true heterotopia with metaplasia of mature endometrial stromal cells.

We present a case of endometrial ossification and primary infertility.

Case report

A 29-year-old nulligravida had been trying to fall pregnant for 8 months. Because of a history of pelvic inflammatory disease, her general practitioner sent her for a consultation. Her husband had a 12-year-old child from a previous relationship.

The patient had normal menstrual periods, with 5 - 6 days of menstruation and a cycle length of 28 - 30 days. She had been treated for an episode of pelvic inflammatory disease, but otherwise nothing of note emerged from her medical history. Her surgical history revealed that she had only had an ear operation. Findings on clinical examination were normal. Pelvic examination revealed a normal-sized, anteverted uterus and normal adnexa, a transvaginal ultrasound scan showed an 11 mm thick echo-dense endometrium, and blood test results, including a hormone profile, were normal. The husband had no medical or surgical history of note, and a spermiogram was normal.

The patient underwent hysteroscopic and laparoscopic examination under general anaesthesia. During hysteroscopy a Hamou hysteromat and a Bettocchi 3.7 mm diameter hysteroscope (Karl Stortz GmbH & Co KG, Tuttlingen, Germany) were used with saline as distension medium. Several hard, bony spicules (Fig. 1) were found to be embedded in the endometrium. They were removed through a hysteroscope using a forceps, and the specimens were sent for histopathological examination. Definite bleeding occurred from the centre of the spicules wherever they broke at removal.

At laparoscopy, several adhesions to both tubes and ovaries, as well as in the pouch of Douglas, were freed. After the operation, both tubes were free and spilling with functional fimbria.

Histological examination of the spicules revealed bone surrounded by occasional osteoclastic giant cells, and mixed inflammatory cells including neutrophils, macrophages and an occasional eosinophil. No viable osteocytes were noted in the lacunae.

Two months after laparoscopy and hysteroscopy, a spontaneous intra-uterine pregnancy was confirmed by means of an ultrasound scan. At term the patient was delivered of a normal baby by caesarean section for obstetric reasons. At the time of writing, she was pregnant with her second baby.

Endometrial osseous metaplasia may be more common than is generally accepted. Hysteroscopy is an effective diagnostic as well as treatment modality.

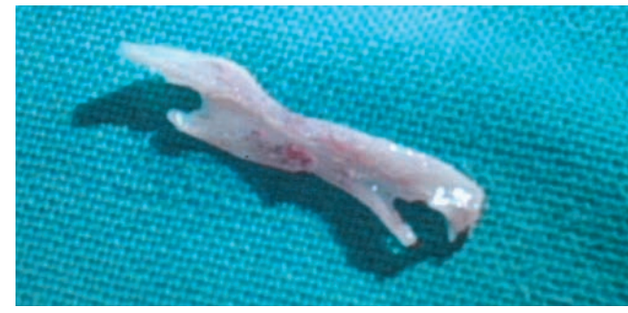

Fig. 1. Spicule of bony material from the uterine cavity.

Discussion

Osseous metaplasia is a rare disorder of the endometrium that occurs in approximately 0.3/1 000 women.

The most commonly reported symptom is secondary infertility. Other common clinical presentations are menstrual irregularities, pelvic pain, dyspareunia and vaginal discharge, with bony particles in menstrual or vaginal discharge in some cases.[4] Primary infertility was our patient's only complaint.

Single or multiple hyper-echogenic bands with acoustic shadowing situated in the uterine cavity can be seen on an ultrasound scan.[4] Our patient's uterine cavity had the appearance of an 11 mm echo-dense endometrium.

There is controversy regarding the cause and pathogenesis of osseous metaplasia and bone fragment retention. The majority of patients have a history of abortion or delivery. The condition is often attributed to fetal remnants.[4,5] Other authors view the cause as a true metaplasia.[6]

Parente *et al*.[7] analysed solitary bone fragments from the uterine cavity of 8 patients through DNA genotyping. In all 8 cases it was found that bone formation was caused by osseous metaplasia, because the DNA in the bone fragment and in the patient's blood was identical. There was no contribution from the paternal allele. This result was completely unexpected and very different from what the literature suggested. The finding was confirmed by other workers.[8]

Endometrial stem/progenitor cells were only identified in 2004, when Gargett *et al*.[9] investigated key stem cell properties of individual clonogenic epithelial and stromal cells obtained from human endometrium. They found rare single human endometrial EpCAM+ epithelial cells and EpCAM- stromal cells that demonstrated self-renewal by serial cloning more than three times and underwent more than 30 population doublings over 4 months in culture. Clonally derived epithelial cells differentiated into cytokeratin+ gland-like structures in three-dimensional cultures. Single stromal cells were multipotent as their progeny differentiated into smooth-muscle cells, adipocytes, chondrocytes and osteoblasts.[9,10] This suggests that the human endometrium contains populations of epithelial progenitor cells and mesenchymal stem cells. These cells are multipotent but rare, and therefore the most likely origin of the endometrial ossification.

The patient reported here was a nulligravida, and had a history of previous pelvic inflammatory disease of which evidence was found at laparoscopy. These factors as well as the facts mentioned above suggest that the endometrial ossification must have been from the patient's own tissue. The question that arises is whether the pelvic inflammatory disease stimulated the endometrial stromal cells to differentiate into osteoblasts.[8]

Infertility in these patients is caused by the bone fragments that are embedded in the endometrium, which act as an intrauterine contraceptive device that prevents implantation of the blastocyst.[11,12]

Hysteroscopic removal of the bone fragments from the endometrium can restore fertility, with spontaneous conception and birth.[12] In our case hysteroscopic removal of the bony spicules and laparoscopy with adhesiolysis were successfully performed. Two spontaneous pregnancies followed the procedures.

The condition may be more common than is generally accepted. Ultrasound and hysteroscopy are effective diagnostic as well as treatment modalities. The condition should be kept in mind during work-up for infertility in all patients, even if they have not previously had a miscarriage.

1. Ceccacci L, Clancy G. Endometrial ossification: Report of an additional case. Am J Obstet Gynecol 1981;141(1):103-104.
2. Acharya U, Pinion SB, Parkin DE, Hamilton MPR. Osseous metaplasia of the endometrium treated by hystroscopic resection. BJOG 1993;100(4):391-392. [http://dx.doi.org/10.1111/j.1471-0528.1993.tb12988.x]
3. Rodriguez BD, Adamson GD. Hysteroscopic treatment of ectopic intrauterine bone: A case report. J Reprod Med 1993;38(7):515-520.
4. Onderoglu LS, Yaraldi H, Gulteken M, Katlan D. Endometrial osseous metaplasia: An evolving cause of secondary infertility. Fertil Steril 2008;90(5):2013.e9-2013.e11. [http://dx.doi.org/10.1016/j.fertnstert.2008.01.001]
5. De Brux J, Palmer R, Ayoub-Despois H. Osssifications of the endometrium [in French]. Gynecol Obstet (Paris) 1956;55:494-504.
6. Van den Bosch T, van Schounbroeck D, Timmerman D, Deprest J. Uterine intramural bone after mid-trimester termination of pregnancy may not effect fertility: A case report. Ultrasound Obstet Gynecol 2003;22(4):407-408. [http://dx.doi.org/10.1002/uog.220]
7. Parente RC, Patriarca MT, de Moura Neto RS, et al. Genetic analysis of the cause of endometrial osseous metaplasia. Obstet Gynecol 2009;114(5):1103-1108. [http://dx.doi.org/10.1097/AOG.0b013e3181bd198c]
8. Gargett CE, Masuda H. Adult stem cells in the endometrium. Mol Hum Reprod 2010;16(11):818-834. [http://dx.doi.org/10.1093/molehr/gaq061]
9. Gargett CE, Schwab KE, Zillwood RM, Nguyeen HPT, Wu D. Isolation and culture of epithelial progenitors and mesenchymal stem cells from human endometrium. Biol Reprod 2009;80(6):1136-1145. [http://dx.doi.org/10.1095/biolreprod.108.075226]
10. Cayela 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.e1-1293.e4. [http://dx.doi.org/10.1016/j.fertnstert.2008.12.026]
11. Polat I, Sahin O, Yildirim G, Karaman E, Erim A, Tekirdag AI. Osseous metaplasia of the cervix and endometrium: A case of secondary infertility. Fertil Steril 2011;95(7):2434.e1-2434.e4. [http://dx.doi.org/10.1016/j.fertnstert.2011.02.001]
12. Kramer HM, Rhemrev JP. Secondary infertility caused by the retention of fetal bones after an abortion: A case report. J Med Case Rep 2008;2(1):208. [http://dx.doi.org/10.1186/1752-1947-2-208]