Endometrial osseous metaplasia and infertility: a case report

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Summary

Endometrial osseous metaplasia is a rare clinical entity. It causes infertility and occurs in more than 80% of cases after an abortion. Various theories have been proposed and the most accepted theory is metaplasia of the stromal cells into osteoblastic cells that produce bone. This disease may be misdiagnosed. However once diagnosed, the complete removal of bone spicules by hysteroscopy allows, in most cases, fertility to be restored. We present the case of a 36-year-old patient nulliparous with a history of abortion for eight years who consulted May 5, 2008 to become pregnant. Detailed examination showed chronic endometritis with bone metaplasia as a possible cause of her infertility. Seven months after complete removal of bone fragments by hysteroscopy, the patient had a spontaneous pregnancy with normal development. She gave birth to a male infant weighing 3,000 g with an Apgar score of 9 at 1 and 5 min. Delivery and postpartum were normal.

Key words: Bone metaplasia; Endometrium; Infertility; Hysteroscopy.

Introduction

Endometrial osseous metaplasia, a rare but not exceptional disease, is characterized by the presence of bone tissue in the endometrium. It is often diagnosed in women with secondary infertility [1, 2] and more than 80% of reported cases occur after an abortion [2-4]. However, there is controversy as to the etiology and pathogenesis of this disease [3] despite the many reports in the literature. We report the first documented case in the Ivory Coast.

Case Report

The patient, 36-year-old, consulted on 05/05/2008 with secondary infertility and the desire to become pregnant. Her gynecological history revealed menarche at age 13 year, a regular cycle 25-28 days, primary dysmenorrhea, and a period of menstruation of five days. An abortion in 2000 at 13 weeks of gestation occurred with a normal evolution. Physical examination and laboratory tests were unremarkable. Analysis of the husband's semen was normal. Transvaginal ultrasonography revealed a linear hyperechogenic area in the uterine cavity measuring 13 mm (Figure 1). This image persisted over several ultrasound (US) images. Hysterosalpingography displayed an incomplete cervicoisthmic picture due to uterine synechia with bilateral tubal patency maintained. The patient was subjected to diagnostic hysteroscopy. Hysteroscopy was done and revealed an irregular structure at the uterine isthmus with a few spikes that looked whitish and hard after ablation. Histological analysis of parts removed from the uterus showed some fragments of endometrial and osteoid tissue with a small inflammatory lymphoplasmocytic infiltrate due to chronic endometritis with bone metaplasia (Figure 2). A month later, control US and hysteroscopy were normal. Six months later after this control, the patient became pregnant with a normal evolution and delivery by natural means resulting in the birth of a male infant weighing 3000 g with an Apgar score of 9 at 1 and 5 min. The postpartum period was normal.

Discussion

Frequency

Ossification of the endometrium is a rare clinical entity. Although its impact is not fully known, it has been estimated that it represents 0.15% of the cases referred for diagnostic hysteroscopy [3]. The incidence is much lower according to Makris *et al*. [5]. Despite the many reports in the literature by about 80 medical teams [6, 7], the etiopathogenesis of this disease remains controversial [3].

Etiopathogenesis

In patients with a history of endometrial ossification, over 80% of cases occur after an abortion (our observation), spontaneous or therapeutic [1-3, 6, 7], *suggesting the responsibility of embryonic or fetal fragments in osteogenesis*. This may be pure fetal skeletal retention [7] which is possible when the abortion is incomplete and the age of the pregnancy is greater than three months of gestation [2, 7, 8]. Nevertheless, a study in the literature shows that most documented cases involve pregnancy less than three months (also our observation). Therefore it appears unlikely that endometrial ossification is of fetal origin, especially as the histological study of biopsies never revealed fetal tissue (our observation, Figure 2) [6]. Some authors described individualized bone structures in the embryo at six weeks of gestation, but those bones did not show the usual appearance of endometrial ossification which is almost always laminar [7]. Others think that fetal

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Fig. 1

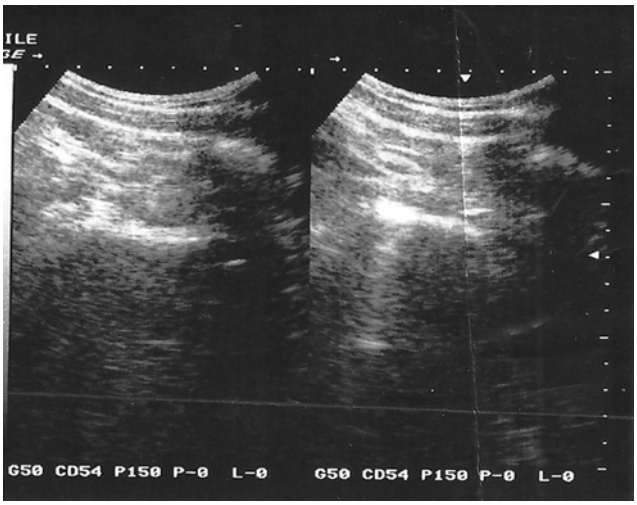

Fig. 2

Figure 1. — Ultrasound: linear hyperechogenic area in the uterine cavity measuring 13 mm.
Figure 2. — Histological analysis: Endometrial fragments and osteoid tissue with a small inflammatory lymphoplasmocytic infiltrate due to chronic endometritis with bone metaplasia.

bone fragments could be reabsorbed and secondarily induce alternative osteogenesis [9]. Finally for some, embryonic cells to osteoblastic potential could be due to curettage in the deep layer unregulated by the endometrium [10, 11]. However these embryo-fetal theories do not allow the explanation of endometrial bone formation in the absence of curettage after spontaneous miscarriage among nulligravida women, or in the postpartum period [7].

Some metabolic disorders have been associated with bone metaplasia, such as hypercalcemia, hypervitaminosis D, hyperphosphatemia and hyperthyroidism [12] without any clear correlation. In the same sense, prolonged estrogenic stimulation of the endometrium has also been questioned [13]. In the largest series [3, 7], none of these factors were associated with bone metaplasia of the uterus, suggesting that the contributions of these pathogenic mechanisms are not effective [14].

Chronic endometritis, chronic endocervicitis, and traumatic injuries have been implicated in the proliferation of mesenchymal cells which are kown have metaplastic power [10, 15]. It has been suggested that chronic postabortion endometritis may promote superoxide radicals and tumor necrosis factors from the inflammatory cells. The long-term exposure of superoxide radicals and tumor necrosis factor on multipotent stromal cells would lead to the differentiation of endometrium and could change endometrial stromal cell metaplasia into osteoblastic cells [4, 16].

Already in 2009, the study of Cayuela *et al*. [17] proved the maternal origin of endometrial ossification after a comparative analysis of DNA from the bone and endometrium of the mother. Also another study analyzing the DNA of endometrial bones showed 14 samples (although all patients had a history of abortion): eight cases in which maternal origin of endometrial ossification was proven (95% confidence interval 63-100%, level of evidence III) and six cases in which the origin remained unclear [3]. Thus the maternal origin of endometrial ossification appeared highly likely or almost certain from these two studies.

Diagnosis

The only pathognomonic sign of endometrial ossification is the spontaneous expulsion of small bone fragments, which is in fact an exceptional event [7]. Other signs mentioned in the literature are nonspecific and may be associated with other alterations of the endometrium (endometritis and synechiae): bleeding or hypoamenorrhea, pelvic pain, menstrual irregularities, and dyspareunia, vaginal discharge [7, 14, 18]. The most common complaint was menorrhagia (50%), followed by infertility (43%), in the series of Parente *et al*. [3]. In general, the time between abortion and discovery of the disease varies between eight weeks and 14 years [4], and up to 40 years [3] (eight years in our observation). In practice, the clinical expression of endometrial ossification is generally poor; the desire for pregnancy is the main reason for consultation, as in our case [1-20]. Indeed, in addition to endometrial abnormalities that lead to bone fragments, endometrial ossification acts as a real intrauterine contraceptive device with inflammation preventing any nesting [4, 7, 19], which is why infertility occurs more frequently.

US examination plays a primary role in the diagnosis. Endometrial ossification appears at US as a hyperechogenic image which is often linear (Figure 1) mimicking an intrauterine device or calcifications which constitute the

main differential diagnosis. Hysterosalpingography can view the bone fragments as subtraction images and synechiae (as in our case) or intracavitary fibroids can be suspected. Diagnostic hysteroscopy visualizes bone fragments, takes stock of intracavitary lesions and allows for biopsies. Pathological examination of biopsies will show fragments of endometrial tissue and osseous metaplasia in the stroma (Figure 2) [2].

Treatment

Conventional curettage has been abandoned because of its blind and traumatic character to the uterine mucosa. The removal of bone fragments in the clamp under hysteroscopic control seems much better. Recent studies recommend hysteroscopic removal of the bone under US guidance which helps proper visualization and complete removal of the bony spicules that may be embedded in the myometrium [4, 17, 20]. Antibiotic treatment and anti-inflammatories are required. Sequential estrogen-progestin treatment is often recommended for the following cycle after curettage. The complete removal of bone spicules of the uterine cavity can restore, in the majority of cases, fertility and spontaneous conception as in our observation [1, 4, 6, 18].

Conclusion

Endometrial ossification is a rare disease whose etiopathogenesis remains unclear, but the maternal origin of the ossification is currently the most accepted. It may be the cause of infertility, but once diagnosed, the complete elimination of bone fragments of the uterine cavity by hysteroscopy allows fertility to be restored in the majority of cases.

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