Ossification in uterine leiomyomas in a postmenopausal woman: a rare case report

Manthan Patel1,*, Sudhamani. S2, Rajiv Rao3, Prakash Roplekar2

1Resident at Department of Pathology - Dypatil school of medicine, Navi Mumbai
2Professor at Department of Pathology - Dypatil school of medicine, Navi Mumbai
3Associate professor at Department of Pathology - Dypatil school of medicine, Navi Mumbai

ABSTRACT

Ossification in uterine leiomyoma represents heterotopic bone formation, usually seen in long standing leiomyoma. It is often associated with other degenerative changes like calcification and hyalinization. It is exceedingly rare and important to recognize, as these cases can mimic malignant tumors of uterus like malignant mixed mullerian tumor, which shows heterotopic cartilage or bony metaplasia, especially in postmenopausal women.

We present one such unusual finding in a case of 81 year old postmenopausal female who underwent vaginal hysterectomy for uterine prolapse. Gross and microscopy showed mature bone formation in multiple intramural leiomyomas. There was no evidence of malignancy in the uterus. Therefore it is important to recognize this entity.

Keywords: ossification in leiomyomas, bone in uterus, degeneration.

INTRODUCTION

It is common for leiomyoma to undergo various secondary changes like hyaline degeneration, cystic change, myxoid degeneration, infection, necrosis, calcification, red degeneration and very rarely ossification. They are said to result from inadequate blood supply resulting in replacement of muscle fibres by hyaline material, collagen, calcium, mucopolysaccharides or a combination of these. There is scarcity of literature regarding ossification of leiomyomas.1 Only 8 cases of ossified leiomyoma have been reported.2 The occurrence being 0.55% it has to be distinguished from endometrial osseous metaplasia, seen in young females which may lead to secondary infertility. It is important to recognize this entity as non-neoplastic as it can masquerade malignant mixed mullerian tumor, especially in older women.

We present this case because of its rarity.

CASE REPORT

82 years old female came with history of something coming out of vagina since 6 months. She also complains of dysuria and burning micturition. Per vaginal examination revealed features of procendentia which was reducible manually. On ultrasonography atrophied uterus and ovary noted. Hysterectomy performed and specimen was sent for histopathological examination. We received specimen consisting of atrophied uterus with cervix measuring 11x4x3cm. Multiple fibroids of intramural, subserosal and submucosal types were seen; with whorled grey white appearance. (Fig-1)

**Figure 1:** Measuring 11x4x3cm. Multiple fibroids of intramural, subserosal and submucosal types were seen; with whorled grey white appearance

Leiomyomas were gritty and bony hard to cut, and were kept for decalcification. Extensive sampling was done.

**Figure 2:** Multiple leiomyomas with large areas showing ossification with formation of mature bony lamellae and hyaline degeneration
On microscopy endometrium showed cystic atrophy. Decalcified bits of myometrium revealed multiple leiomyomas with large areas showing ossification with formation of mature bony lamellae and hyaline degeneration. There was no evidence of atypia or malignancy. Cervix revealed features of procidentia. (Fig-2)

**DISCUSSION**

As early as 1884, Virchow attributed the formation of bone in the endometrium to spontaneous differentiation of fibroblasts into osteoblasts. Pathogenic mechanisms related to the histogenesis of heterotopic bone into the endometrium include: osseous metaplasia from multipotential stromal cells, usually fibroblasts, which become osteoblasts; continuous and strong endometrial estrogenic stimulation; retention of fetal bones that secondarily promote osteogenesis in the surrounding endometrium; implantation of embryonic parts without pre-existing bone after abortions at an early stage; dystrophic calcification of retained and necrotic tissues, usually after an abortion; chronic endometrial inflammation such as endometritis or pyometra; and metabolic disorders such as hypercalcemia, hypervitaminosis D or hyperphosphatemia. The actual contribution of these pathogenic mechanisms is unknown.

The history of osseous metaplasia in uterus goes back a century ago, when in 1901 a German pathologist, Mayer, first reported the presence of bony tissue in the uterus. In 1923, Thaler linked the presence of this bony tissue in uterus to previous abortion. De Brux et al. gave, in 1956, the first description of osteogenesis within the genital tract.

Ossification in uterus was seen as ectopic intrauterine bone, heterotopic intrauterine bone and endometrial ossification. Endometrial ossification usually presents in young women with dyspareunia, menstrual irregularities, pelvic pain, vaginal discharge, secondary or primary infertility.

Ossification is said to be due to either increased prostaglandin production as proposed by Marcus et al (8), or its action as an intrauterine contraceptive device. The aetiopathogenesis of endometrial ossification has been described by theories; such as hypercalcaemia, hypervitaminosis D or hyperphosphatæmia and chronic endometrial inflammation; persistent stimulation of the endometrium by oestrogen or osteogenesis in the surrounding endometrium promoted by retained foetal bones and the dystrophic calcification of retained and necrotic tissue. However, the most accepted theory is the metaplasia of the endometrial stromal cells, usually fibroblasts, which change to osteoblasts and thus produce bone in the endometrium. A previous history of abortion may lead to osseous changes in the endometrium.

It is important to be aware of osseous metaplasia in the differential diagnosis of patients with uncertain history, who present with a sonographic image resembling an intrauterine contraceptive device or malignant tumor. Endometrial tuberculosis which is common cause of infertility in Indian females and can sometimes show calcification and subsequent ossification in the endometrium. Retained foetal tissue can also mimic osseous metaplasia. The absence of surrounding tissue reaction and endochondral ossification may differentiate osseous metaplasia from the retained fetal tissue.

Leiomyomas are commonly seen in premenopausal, multiparous women. The proposed theories for the development of leiomyoma of uterus includes estrogen influence, growth hormone and progesterone. Leiomyomas are said to undergo regression after menopause. These are grossly circumscribed, solid, white with whorled appearance. A variety of degenerative changes that can take place in leiomyomas are attributable to inadequate blood supply. The degree and rapidity of vascular insufficiency is said to decide the type of degenerative change. The various types of degenerations include hyaline, myxoid, mucinous, cystic, hemorrhagic, calcification and rarely ossification.

Ossification in uterine leiomyoma is said to be an example of heterotopic bone formation which is of membranous type. Frank osteoid material may be found as a sequele to an old missed abortion in reproductive age group due to dystrophic calcification or as metaplasia. Secondary change of ossification is usually associated with other degenerative changes like hyalinization and calcification. It is said that calcification is a process of deposition of calcium in the tissue in the form of carbonate and phosphate while ossification is a process of differentiation of connective tissue alongwith presence of collagen fibres blended with
mucopolysaccarides and enclosing living cells. The calcium salt is not enough in inducing ossification but presence of proliferating mesenchymal cells capable of metaplasia are equally essential.

In one study out of 900 leiomyomas studied only 5 cases (0.55%) showed changes of ossification which were associated with other hyalinization and calcification indicating a gradual transformation of degeneration from one stage to another. This secondary change of ossification in postmenopausal females could be due to ignorance and late reporting to the gynaecologist which is common in India.  

In our case also, ossification of leiomyoma was an incidental finding in postmenopausal woman, operated for uterine prolapse.

Intrauterine contraceptive device, malignant mixed mulleriantumour, endometrial tuberculosis and retained foetal tissue are the common differential diagnoses for the bone in the uterus. Before classifying the heterologous tissue as benign, the pathologist should exclude the possibility that the tissue in question is not a deceptively bland, appearing component of a malignant mixed mulleriantumour or an adenosarcoma.  

Therefore it is important to recognise this unique entity.

CONCLUSION

Even though many degenerative changes are commonly encountered in uterine leiomyoma, it is extremely rare to find ossification as a secondary change. Therefore it is important to differentiate this entity from mature bone seen in malignant mixed mullerian tumor.

REFERENCES