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Case Report

Pathology Section

Osseous Metaplasia in Uterine Leiomyoma: A Case Report

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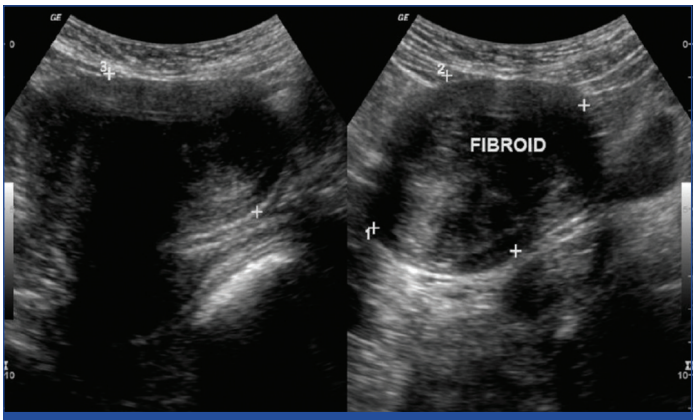
ABSTRACT

The leiomyoma uteri is one of the most common tumours of the female genital tract. It is more common in women above 50 years and is known to shrink in size after menopause. The symptoms it produces depend upon its location, whether it is submucosal, intramural, or subserosal. It is known for its histological variations in the form of hyaline degeneration, myxoid degeneration, calcification, and cyst formation. Heterologous tissue differentiation is an uncommon phenomenon, and osseous metaplasia is even rarer. Here, we report a rare case of leiomyoma with osseous metaplasia in a nulliparous woman. A 30-year-old nulliparous female presented with a history of abnormal uterine bleeding and abdominal pain, with an obstetric history of two spontaneous abortions at eight weeks and 10 weeks of gestation, respectively. Her biochemical and haematological investigations were within normal range. Ultrasound examination revealed multiple submucosal fibroids, with the largest one measuring 6×4×4 cm, for which the patient underwent myomectomy. The histopathological examination revealed leiomyoma with osseous metaplasia and hyaline degeneration with areas of calcification. There was no atypia, mitosis, or necrosis. Patient was discharged, and her two sequential follow-ups were uneventful. The novelty of this case report lies in the fact that osseous metaplasia in leiomyoma is quite a rare entity, with very few cases reported in the literature. Its recognition lies in its diagnostic significance to rule out sarcoma with heterologous differentiation. It highlights the importance of adequate sampling of gross specimens and careful histopathological examination to rule out this benign entity.

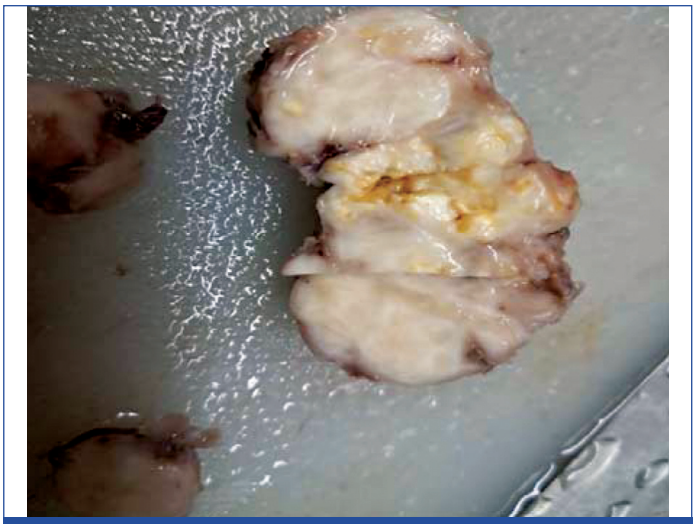
Keywords: Calcification, Leiomyoma, Nulliparous, Uterus

CASE REPORT

A 30-year-old nulliparous female presented with a history of abnormal uterine bleeding and abdominal pain for the past six months. Obstetric history revealed a history of two spontaneous abortions at eight weeks and 10 weeks of gestation, one year and two years back, respectively. Her urine pregnancy test was negative. Her biochemical and haematological investigations were within normal range. Ultrasound examination revealed multiple well-defined mixed echogenic lesions in the uterus, with the largest measuring 6×4×4 cm, suggestive of a submucosal fibroid [Table/Fig-1]. A clinical diagnosis suggestive of degenerated submucosal leiomyoma of the uterus was made. She underwent myomectomy. The removed multiple masses were well circumscribed and varied from 2×2×2 cm to 6×4×4 cm. The cut surface of the mass showed grey-white areas with a whorled appearance, along with yellowish hard areas that were difficult to cut [Table/Fig-2]. No necrotic or haemorrhagic areas were identified. Microscopic examination using haematoxylin and eosin-stained sections showed a well-circumscribed lesion disposed of in fascicles composed of spindle cells with cigar-shaped nuclei having blunt ends with indistinct cell boundaries. Areas of hyalinisation were present. Close to areas of hyaline degeneration were areas of bony trabeculae [Table/Fig-3] along with foci of calcification [Table/Fig-4]. There was no evidence of nuclear atypia, mitosis, or necrosis. A histopathological diagnosis of leiomyoma uterus with osseous metaplasia and hyaline degeneration with areas of calcification was given. The patient's serum calcium and phosphate were within normal range. The patient was discharged on the third postoperative day and was free of any kind of morbidity on the subsequent two follow-up visits.



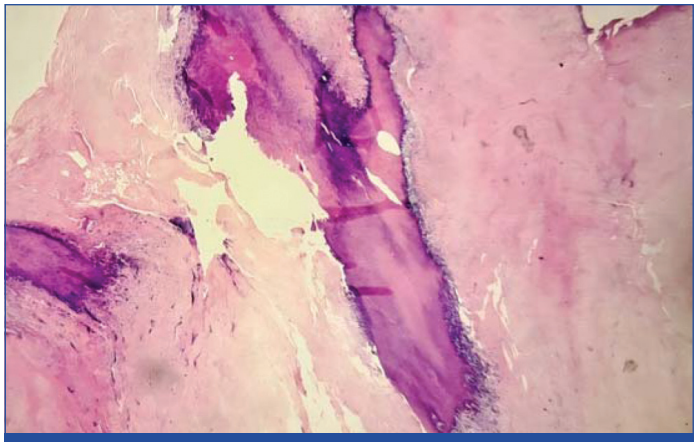
[Table/Fig-1]: Transabdominal ultrasound done by a curvilinear probe shows multiple submucosal fibroids in the anterior wall of the uterus and the largest measuring 6×4×4 cm.



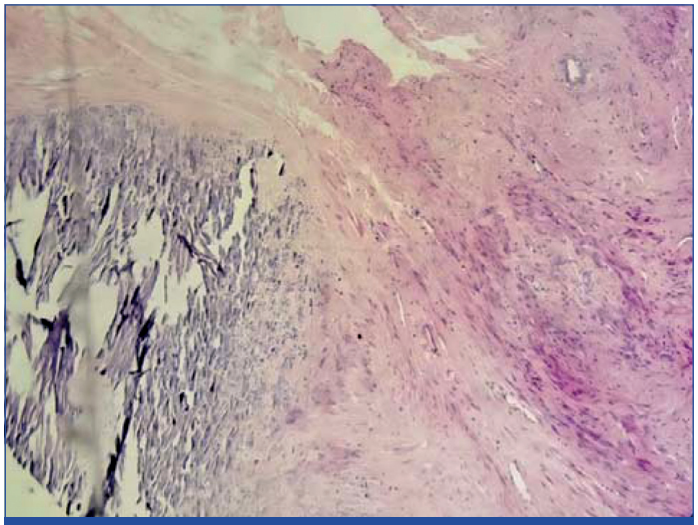
[Table/Fig-2]: Gross specimen: Cut surface showing grey-white areas with a whorled appearance, along with yellowish areas.

DISCUSSION

Leiomyomas are the most prevalent uterine tumours in women. The most common clinical presentations are abnormal uterine bleeding, anaemia, pelvic pain, dyspareunia, urgency or incontinence in the urine, and constipation. It is well known for a variety of histological



[Table/Fig-3]: Haematoxylin and eosin-stained sections Showing bony trabeculae close to areas of hyaline degeneration of leiomyoma (4x).



[Table/Fig-4]: Haematoxylin and eosin-stained sections showing areas of calcification (4x).

variations in the form of cellular leiomyoma, mitotically active leiomyoma, atypical leiomyoma, and epithelioid leiomyoma that require careful histopathological examination to label them as benign or malignant. Lipomatous change is seen in 0.03% to 0.2% of cases [1] and calcification in 8% of cases [2], but osseous metaplasia of leiomyoma is a highly rare condition, and very few cases till now have been reported in the literature. Osseous metaplasia in uterine fibroid means the transformation of cells of leiomyoma into immature or mature bone. Osteoid matter could be an after-effect of an old missed abortion, evolving upon dystrophic calcification, or it could be a result of a metaplastic event [3]. Ossification in leiomyoma is usually present with other degenerative changes like calcification and hyalinisation. Calcification and persistent inflammation are a part of the pathophysiology [2]; nevertheless, the exact root cause of osseous metaplasia in uterine leiomyoma has largely remained unknown. Metaplasia due to reprogramming of stem cells or undifferentiated mesenchymal cells is among the various theories proposed in the pathophysiology of ossification [4]. Signals produced by cytokines, growth factors, and elements of the extracellular matrix in the cell's environment cause this differentiation [5]. Other theories include hyperphosphataemia, hypercalcaemia, inflammation like pyometra and chronic endometritis, persistent oestrogen stimulation, retained foetal bones, and dystrophic calcification of necrotic tissue [3].

Patel M et al., and Kaur P et al., described ossification in leiomyoma in postmenopausal women with a history of uterine prolapse [3, 6]. None of their study mentions a history of abortion, and one of them also had areas of hyalinisation and calcification. Suranagi VV et al., reported leiomyoma with ossification and extensive hyalinisation along with calcification in an autopsy of a 65-year-old hypertensive female with a history of consumption of organophosphorus compounds [7]. Mohan H et al., in their study of 900 cases of leiomyoma found in hysterectomy specimens, diagnosed five cases of ossification as a secondary change, out of which four were postmenopausal and one was premenopausal [8]. Only one of them was nulliparous. Hyalinisation was seen in three cases, while calcification was seen in two cases on microscopic histopathological examination. Shekhar S et al., described a submucosal leiomyoma with areas of hyalinisation and osseous metaplasia in a 49-year-old perimenopausal woman with a history of three spontaneous deliveries at term [2]. In contrast, there is a study documenting leiomyoma with osseous and cartilaginous metaplasia, hyaline, and myxoid degeneration in women in the reproductive age group [9]. Similar cases of osseous metaplasia have also been reported in the broad ligament and detached remnant leiomyoma [4,10]. Clinicopathological features of recently reported cases of osseous metaplasia in uterine/broad ligament leiomyoma are tabulated in [Table/Fig-5] [4,6,9-11].

S. No	Study	Age	Chief complaints	Microscopy
1	Kaur P et al., 2020 [6]	60 years postmenopausal	Pain in the abdomen, difficulty in passing urine, and complaints of prolapse	Hyalinisation, calcification, ossification
2	Bolde SA et al., 2022 [11]	Age of the patients ranged from 20 to 72 years with peak incidence in the fourth decade	The majority of the patients were presented with menorrhagia as the predominant presenting complaint, which constituted 34 cases (48.58%), followed by abdominal pain in 22 cases (31.43%)	Osseous metaplasia, 38 cases (79.17%) had hyaline degenerative changes
3	Al Jumaily M and Mikhail E, 2022 [10]	37 years	Infertility for the past year	Osseous metaplasia in detached remnant leiomyoma
4	Saxena R et al., 2022 [4]	45 years	Abnormal uterine bleeding	Osseous metaplasia with areas of calcification in hyalinised degenerated leiomyomas
5	Mishra S and Patkar RR, 2024 [9]	39 years	Abnormal uterine bleeding and abdominal discomfort	Osseous and cartilaginous metaplasia, hyaline and myxoid degeneration.

[Table/Fig-5]: Clinicopathological features of recently reported cases/studies of osseous metaplasia in uterine/broad ligament leiomyoma [4, 6, 9-11].

Among the reproductive age group with osseous metaplasia in leiomyoma, the majority of documented cases had a history of abortion. The period between the preceding abortion and the revelation of ossification ranged between eight weeks to 14 years [4]. Our case is similar in the respect that our patient had a history of two previous spontaneous abortions. Her serum calcium and phosphate levels were within normal range, and any metabolic reason for ossification was ruled out.

CONCLUSION(S)

Histopathological variation is common in leiomyoma, but very few cases in the literature have reported osseous metaplasia in uterine leiomyoma. Present case is one of the extremely rare cases of osseous metaplasia in uterine leiomyoma in a nulliparous woman. It also highlights the importance of adequate sampling of the gross specimen and careful histopathological examination to confirm its benign nature and to rule out sarcomas with heterologous elements.

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