

# Is fibromyoma always safe for conservative management?

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In the era of evidence based medicine, gynaecologists have to face a great clinical challenge in having to assess a leiomyoma (LM) planned for conservative treatment, regarding its present nature and possibility of turning malignant in near future. At the same time, the clinician cannot afford to go for hysterectomy in every case as a radical treatment to avoid the risk of missing a malignant condition. Presently many effective medical treatments have been made available as an alternative for surgery for selected cases. Minimally invasive surgery, conventional surgery like myomectomy, uterine artery embolization, magnetic resonance guided focused ultrasonography, radiofrequency fibrolysis and endometrial ablation are also available for a large group of patients as a treatment option while sparing the uterus. Ofcourse barring myomectomy, in all the non-invasive and minimally invasive procedures, the fibroid tissue is not available for histopathological examination which is essential to diagnose a malignant condition. Though leiomyoma is the commonest benign tumour of the uterus with an incidence of 70-80% ( at the age of 50), transformation to a malignant condition like leiomyosarcoma (LMS) is rare with an incidence of 0.05-0.1%. Though extremely rare, the prognosis of the disease is very poor. It has been observed that out of all the leiomyosarcomas only 10% are derived from Leiomyoma, others are arising de novo. Incidence of 3 to 7 per 100000 women has been observed in the United States. Women with darker skin suffered twice more often<sup>1</sup>. A review of literature suggests however, that only a limited number of case reports have demonstrated a histologic transition of a benign leiomyoma (LM) into a leiomyosarcoma (LMS)<sup>2</sup>.

Malignant transformation of leiomyoma to leiomyosarcoma can happen in certain patients, with large myomas, post menopausal women, rapidly growing myomas and in certain subset of leiomyomas<sup>3</sup>.

According to Leibsohn and coworkers, histological diagnosis of leiomyosarcoma was made in 7 out of 1429 hysterectomies ( 0.49%) performed on presumed benign leiomyomata. There was no evident malignancy in the endometrial sampling of any of these 7 patients and the diagnosis was suspected on 3 intraoperatively. In a woman between 41 and 50 years of age with presumed symptomatic leiomyomata, there is 1 in 112 chance of leiomyosarcoma being present. One out of 371 woman operated on for rapidly growing myomas was found to have a leiomyosarcoma<sup>4</sup>. A sarcoma is likely to occur in a rather large leiomyoma and toward the center of the tumor, where the blood supply is poorest. The tissue is typically soft and homogeneous and is described as resembling raw pork. Later as necrosis of the malignant tissue occurs, it becomes more friable and haemorrhagic<sup>5</sup>.

## **Genetic relation to leiomyosarcoma**

Cytogenetic study supports that leiomyosarcoma arises de novo in most cases. Recent microarray data identified a rare subset of myomas with deletion of chromosome 1 that have transcriptional profiles that cluster with those of LMS suggesting that some rare LMS arise from a specific subset of leiomyoma<sup>6</sup>. P - 53 and P - 16 gene deficit is involved in low-grade leiomyosarcoma. On the other hand high cellularity with 1p deletion was associated with aggressive variety of LMS.

## **Diagnostic dilemma**

In some of leiomyoma with high cellularity there is diagnostic dilemma among the pathologists. Tumours with

mitotic figures more than 5, but less than 10 per high power fields are termed cellular leiomyoma or smooth muscle tumour of uncertain malignant potential (STUMP). Other histologic indicator of malignancy, are to be looked after in such cases. These are as follows-

- Severe atypia
- Coagulation tumour cell necrosis
- Vascular invasion

#### **Diagnosis of leiomyosarcoma (LMS)**

Diagnosis of leiomyosarcoma by clinical features are usually in late cases, while histological diagnosis is more likely to be early and specific. Usually perimenopausal and menopausal women are affected. A big size myoma which is increasing in size rapidly is more likely to be a LMS. Rapid growth of myoma is arbitrarily defined as 6 weeks or more gestational size increase within a year or less. Otherwise, 89% increase in size in 18 weeks, or increase of 2cm myoma, to 4 cm size within 4-5 weeks. Growth is faster in smaller size tumour than the bigger one.

Pre operative diagnosis, of leiomyosarcoma is possible by the following investigations:

1. Increase of total serum LDH ( Lactic dehydrogenase)
2. Increase LDH isoenzyme 3
3. Dynamic MRI and DWI (Diffusion weighted imaging)
4. Transcervical needle biopsy ( in selected cases)

Intra operative diagnosis is achieved by the following findings:

1. High vascularity
2. Soft or cystic consistency
3. Local infiltration
4. On cut section - soft, friable - 'raw pork'- appearance, sometimes necrotic or haemorrhagic
5. Lymphadenopathy

Most confirmatory diagnosis is by histopathological examination with following features:

- Mitotic figure more than 10 in 10 high power field
- Evidence of cytological atypia
- Necrosis

Using LDH measurement and Gd- DTPA ( Gadolinium enhanced diethylenetriamine pentaacetic acid) a study of 87 women with uterine LM and 10 women with LMS and 130 women with degenerating fibroids reported 100% specificity 100% positive predictive value and 100% negative predictive value and 100% diagnostic accuracy for LMS<sup>7</sup>.

#### **Prognosis of leiomyosarcoma**

Overall prognosis is poor. More so when diagnosed intraoperatively or clinically, better prognosis for those who are diagnosed histologically. Worse prognosis when vascular spaces are affected. Depending on spread, 5 years survival rate are as follows -

- 1) 63% when localized to uterus.
- 2) 36% when extended to outside uterus in pelvis.
- 3) 14% when there is distant metastasis ( heart, lung).

Poor prognosis is observed in tumour with following features –

- 1) 10cm or more in diameter.
- 2) Mitotic index more than 20 per high power field.
- 3) Positive for K; 67 and -ve for Bel-2 immunostaining.

Good prognosis is expected in tumors with following features -

1. Less than 10 cm diameter.
2. Mitotic index less than 20 mitosis per 10 HPF
3. Negative for K; 67

#### **Prevention of leiomyosarcoma (LMS)**

A high degree of clinical suspicion and meticulous workout while managing a leiomyoma, especially in the perimenopausal or menopausal age group is of paramount importance for prevention of LMS. A rapidly growing fibromyoma of significant size, a myoma not regressing after menopause or following medical treatment should be reviewed carefully. Sudden deterioration of general health of the patient or appearance of clinical feature are also suspicious. A sub mucous myoma should always be addressed properly which is vulnerable for turning LMS. A hystoscopic assessment with endometrial biopsy is always helpful. Estimation of LDH, LDH isoenzyme-3 and dynamic MRI will definitely help in diagnosing and differentiating the condition. A color doppler study of the fibroids may also indicate towards diagnosis. In suspicious cases, non invasive and minimally invasive methods should preferably be avoided, lest one may miss the diagnosis in want of tissue for histological examination. In case of laparoscopic myomectomy, endobag is to be used for collecting and delivering the fibroids. Use of power morcellator is controversial in their conditions. Of course now a days use of morcellator in endobag through vagina recommended by some authority.

### **Conclusion**

After review of available literature it has been observed that while adopting for conservative management of leiomyoma specially in a perimenopausal or menopausal lady, one should extremely be cautious and rule out the possibility of a leiomyosarcoma. In such a case proper counselling and follow up is essential. In case of doubtful histological finding repeated study of further tissue and expert opinion is necessary to rule out possible malignancy. At the advent of the modern technology advancement, dynamic MRI and DWI (Diffusion weighted imaging) has added a great deal of perfection in diagnosis of leiomyosarcoma in the present day. Further research in molecular biology and immunology would probably show a clear vista in early diagnosis and prediction of leiomyosarcoma in near future..

**Conflict of interest:** None. **Disclaimer:** Nil.

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