

# Clinicopathological Spectrum of Leiomyomas at Unusual Locations: A Series of Eleven Cases

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## ABSTRACT

Benign smooth muscle tumours of the female genital tract are relatively common lesions, but they are not often encountered in other tissues. All the histopathological specimens received in the Department of Pathology at SCB Medical College, Cuttack, Odisha, India, were examined from March 2023 to March 2024. Cases histopathologically diagnosed as leiomyomas, excluding uterine leiomyomas, were included in the study and analysed. Complete history, clinical and radiological details, and preoperative investigation findings of all cases were collected and analysed. The mean age of the patients was 43.9 years, with male-to-female ratio of 7:4. A 70% of the cases involved skin. A few extrauterine cases were detected in breast, esophagus, colon, and ovary. Majority were solitary, non tender, with gradual course of presentation indicating benign nature, hence requiring no further treatment following surgical intervention. Accurate diagnosis and classification of smooth muscle tumours is important, as they can exhibit a varied range of clinical behaviour and may be associated with underlying syndromes.

**Keywords:** Histopathology, Immunohistochemistry, Leiomyosarcoma

## INTRODUCTION

Leiomyomas are the most common tumours of female reproductive tract. Uterine leiomyomas (also called fibroids) are benign growths that represent the most common neoplasms of the uterus, affecting 20% to 30% of women between the ages of 30 and 50 years [1]. They can occur in extrauterine locations such as the small bowel, skin, esophagus, ovary, broad ligament, fallopian tube, breast, urinary bladder, kidney, and abdominal wall [2-5]. Herein, authors present a series of ten cases of leiomyoma occurring in various extrauterine locations. Histopathology is the gold standard, and immunohistochemistry aided in final diagnosis.

## CASE SERIES

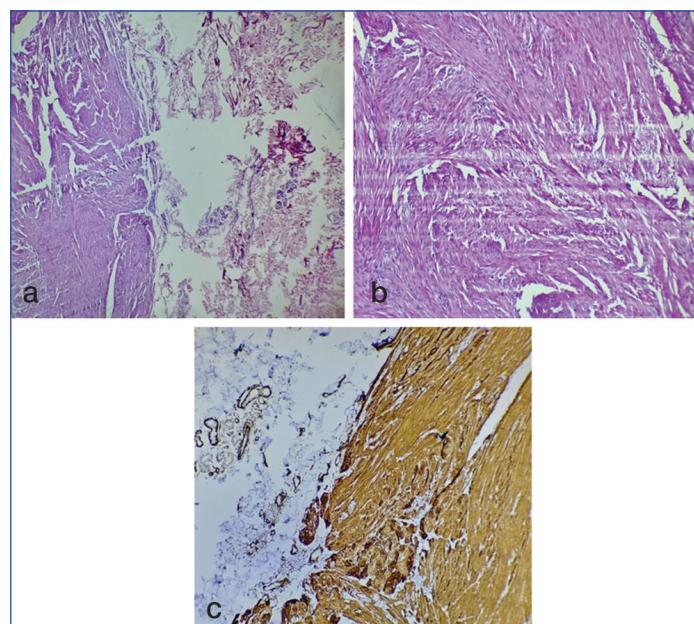
All the histopathological specimens received in the Department of Pathology at SCB Medical College, Cuttack, Odisha, India, were examined from March 2023 to March 2024. Those cases histopathologically diagnosed as leiomyoma in extrauterine sites were included in the study and analysed. Clinical details, past history, family history, and preoperative investigations were collected and analysed. After histopathological examination, the specimens were subjected to immunohistochemistry with Smooth Muscle Actin (SMA) and S100 for final confirmation.

Total 11 cases of leiomyomas at unusual locations were included in the study. The mean age of patients was 43.9 years, with ages varying from 23 to 65 years. Majority were males, with male-to-female ratio of 7:4. Majority of cases in our setting involved skin, followed by breast, while a few showed involvement of internal organs like oesophagus, colon, and ovary as well. The mean duration of presentation was 13.8 months, hence indicating a gradual course of presentation. Size of the tumours varied from 1 cm to 2.5 cm in diameter. The cutaneous lesions mostly presented as solitary, firm, non tender swellings on the body. Differential diagnoses of neurofibroma and fibroma were considered. All the cutaneous lesions were subjected to excisional biopsy, while the colonic and ovarian lesions were surgically operated on, and tissue samples were sent for histopathological examination.

Grossly, all the tumours were solid, greyish-white tissue without necrosis or haemorrhage. Histopathologically and histopathological examination (Haematoxylin and Eosin (H&E) shows all the tumours

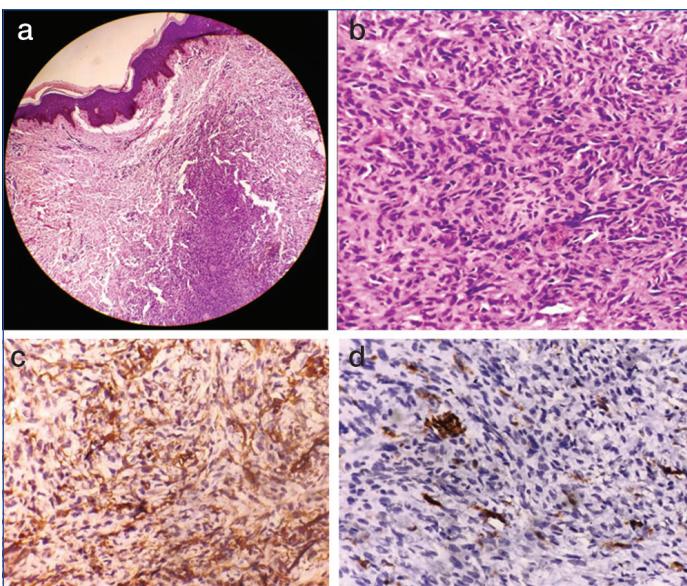
were well circumscribed, with interlacing bundles of smooth muscle cells. The cells were spindle-shaped, having a mild to moderate amount of eosinophilic cytoplasm, with elongated, cigar-shaped nuclei having blunt tapering ends and inconspicuous nucleoli.

An immunohistochemistry panel of Smooth Muscle Actin (SMA) and S100 were employed. There was strong diffuse cytoplasmic positivity for SMA in tumour cells in all cases, while S100 showed negative staining among tumour cells, indicating smooth muscle origin of the tumours. Detailed features of each tumour location can be seen in [Table/Fig-1-4].

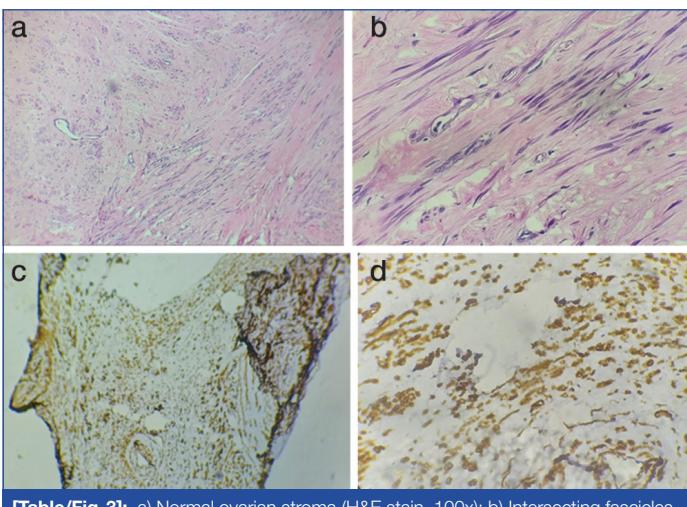


**[Table/FIG-1]:** a) Normal breast tissue along with tumour tissue (H&E stain, 40x); b) Typical spindle cell morphology with eosinophilic cytoplasm and elongated nuclei, characteristics for leiomyoma (H&E stain, 100x); c) Strong cytoplasmic positivity in tumour cells (IHC SMA, 100x).

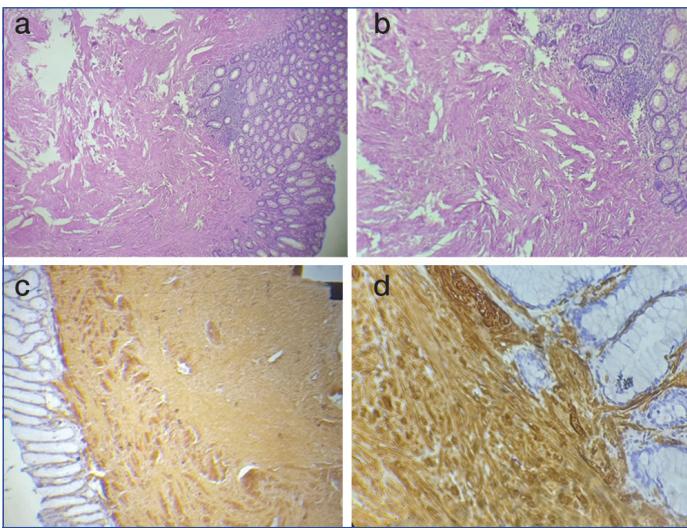
- Breast leiomyoma
- Cutaneous leiomyoma of back
- Ovarian leiomyoma
- Leiomyomatous colonic polyp



**[Table/Fig-2]:** a) Poorly circumscribed tumour in dermis (H&E stain, 100x); b) Spindle cells with eosinophilic cytoplasm and tapered nuclei (H&E stain, 400x); c) Strongly positive in cytoplasm of tumour cells (IHC SMA, 400x); d) Negative in tumour cells (IHC SMA, 400x).



**[Table/Fig-3]:** a) Normal ovarian stroma (H&E stain, 100x); b) Intersecting fascicles of spindle cells with eosinophilic cytoplasm and tapered nuclei (H&E stain, 400x); c) Strongly positive in cytoplasm of tumour cells (IHC SMA, 40x); d) Strongly positive in cytoplasm of tumour cells (IHC SMA, 100x).



**[Table/Fig-4]:** a) Normal colonic mucosa lined by glands with surrounding tumour cells (H&E stain, 40x); b) Intersecting fascicles of spindle cells with eosinophilic cytoplasm and tapered nuclei (H&E stain, 100x); c) Strongly positive in cytoplasm of tumour cells (IHC SMA, 100x); d) Strongly positive in cytoplasm of tumour cells (IHC SMA, 400x).

All the cases of leiomyomas diagnosed indicated a benign nature; hence, no further treatment was required except for regular follow-ups.

On follow-up, there was no case of recurrence among the 11 cases studied [Table/Fig-5].

## DISCUSSION

Leiomyomas are mesenchymal tumours composed of smooth muscle tissue and are benign in nature. Although uterine leiomyomas comprise the vast majority of all benign smooth muscle tumours when all anatomic sites are considered, among the remaining sites affected are of cutaneous origin [6]. They are considered as one of the most common mesenchymal neoplasms in the gastrointestinal tract and uterus. However, leiomyomas of skin, breast, and ovary are very rarely detected in present centre.

Fibroids of the uterus have been known to regress after menopause, which suggests that there is a hormonal aetiology. Thus, it has been suggested that leiomyomas of this site may be hormonal-dependent hyperplasias or benign neoplasms which regress on withdrawal of the stimulus. However, aetiology of leiomyomas at other sites still remains unknown.

A typical leiomyoma presents as a solitary, firm, nodular, well-circumscribed swelling, but may be multiple, as seen in present case case 4, which could be due to hereditary causes. Grossly, it presents as well-circumscribed, greyish-white lesions attached to skin in cutaneous and breast lesions, varying from 1 to 2 cm in diameter, without areas of haemorrhage or necrosis. The cut section reveals greyish-white homogeneous areas and shows the characteristic whorling. The histopathological properties of all leiomyomas are the same, irrespective of the organ involved. Microscopy reveals interlacing bundles of spindle-shaped smooth muscle cells. Individual cells are spindle-shaped, having moderate to abundant amount of eosinophilic, fibrillary cytoplasm with elongated, centrally placed, cigar-shaped nuclei with tapered ends, fine chromatin, and indistinct nucleoli. There is no necrosis, haemorrhage, mitotic activity, or any vascular invasion seen, indicating benign nature of tumour. Leiomyosarcoma is considered in differential diagnosis when extensive pleomorphism, increased mitosis, and necrosis are seen.

The origin of breast leiomyomas still remains uncertain. Various theories have been proposed, include smooth muscle cell proliferation surrounding the blood vessels, teratoid origins with significant overgrowth of myomatous elements, differentiation from multipotent mesenchymal cells in breast tissue, derivation from myoepithelial cells of breast ducts with clear differentiation to smooth muscle, or embryologically displaced smooth muscle cells from the nipple [7]. Diagnosing this condition is clinically important to differentiate it from other benign breast diseases and to provide adequate management in a timely manner.

Cutaneous leiomyomas can present as either solitary or multiple swellings. They often arise from erector pili muscle and present as painful swellings [8]. Angioleiomyoma, piloleiomyomas, and genital leiomyomas are various subtypes based on origin and clinicopathological features. They commonly present as painful swellings. Clinical differentials often considered include neurofibroma, eccrine spiradenoma, and glomus tumour. Sporadic leiomyomas have a non-specific origin; however, hereditary leiomyomas are associated with Reed's syndrome, which predisposes individuals to renal cell carcinoma.

Ovarian leiomyomas probably arise from smooth muscle cells in the ovarian hilar blood vessels, but other possible origins given are from the cells in the ovarian ligament, smooth muscle cells or multipotent cells in the ovarian stroma, undifferentiated germ cells, and cortical smooth muscle metaplasia [9,10].

Leiomyomas are most commonly seen in esophagus in the gastrointestinal tract. Esophageal leiomyomas present with non-specific symptoms like vague chest discomfort and dysphagia, and they are usually detected incidentally during routine investigations. Occasionally, these tumours become larger than 10 cm in diameter

S. No.	Age and gender	Location	Duration	Preoperative diagnosis	History and clinical examination	Histopathologic findings	Immunohistochemistry	Final diagnosis
1.	38 years and female	Breast	8 months	Right Breast lump: Leiomyoma Leiomyosarcoma	Right breast swelling in upper outer quadrant measuring 2x2x1 cm	Interlacing bundles of spindle shaped cells having moderate to abundant eosinophilic cytoplasm with elongated nuclei having rounded ends [Table/Fig-1a,b]	SMA showed diffuse cytoplasmic positive staining in >90% tumour cells [Table/Fig-1c]	Breast leiomyoma
2.	23 years and male	Back	1 year	Neurofibroma Molluscumcontagiosum Cutaneous leiomyoma	Single, tender, pink papule of 1 cm in diameter	Spindle cells in fascicles in dermis. Individual cells were spindle shaped having moderate eosinophilic cytoplasm with elongated nuclei having tapering ends [Table/Fig-2a,b]	SMA showed strong positive cytoplasmic staining in tumour cells [Table/Fig-2c] however S100 was negative in tumour cells [Table/Fig-2d]	Cutaneous leiomyoma of back
3.	42 years and male	Right thigh	7 months	Cutaneous leiomyoma	Solitary, firm, non-tender swelling of 2 cm in diameter	Dermis showing spindle cells in interlacing bundles with moderate eosinophilic cytoplasm, blunt nuclear ends and no areas of haemorrhage or necrosis	SMA showed strong cytoplasmic positivity, CD34 was negative in tumour cells	Cutaneous leiomyoma of right thigh
4.	59 years and male	Left arm	2 years	Cutaneous leiomyoma	Multiple firm tender papules, largest measuring 1.5 cm in diameter	Spindle shaped cells in fascicles in dermis having moderate eosinophilic cytoplasm, with tapered nuclear ends	-----	Cutaneous leiomyoma of left arm
5.	30 years and female	Right lumbar region	9 months	Spindle cell tumour	Single soft to firm non tender swelling measuring 2.5 cm in diameter	Spindle cells in interlacing fascicles in dermis having mild to moderate eosinophilic cytoplasm, with oblongated nuclei	-----	Cutaneous leiomyoma
6.	65 years and male	Rectum	2 years	Rectal polyp	Abdominal pain and distension	Spindle shaped cells in fascicles having moderate eosinophilic cytoplasm, with tapered nuclear ends [Table/Fig-4a,b]	SMA showed strong cytoplasmic staining in tumour cells [Table/Fig-4c,d]	Leiomyomatous colonic polyp
7.	50 years and female	Right anterior chest wall	3 years	Cutaneous leiomyoma	Single firm tender swelling measuring 1 cm in diameter gradually increasing in size	Bundles of spindled cells with eosinophilic, fibrillary cytoplasm. Nuclei are blunt ended and elongated with minimal atypia	SMA showed strong positive cytoplasmic staining in tumour cells however S100 was negative in tumour cells	Cutaneous leiomyoma
8.	60 years and female	Left ovary	6 months	Fibroids	Lower abdominal pain	Spindle cells in interlacing bundles having mild to moderate eosinophilic cytoplasm, with blunt nuclear ends interspersed with normal ovarian stroma [Table/Fig-3a,b]	SMA showed positive cytoplasmic staining [Table/Fig-3c,d]	Ovarian leiomyoma
9.	23 years and male	Left arm	8 months	Cutaneous leiomyoma Eccrineporoma Molluscumcontagiosum	Solitary, soft-firm, non-tender swelling of 2.5 cm in diameter	Spindle cells in interlacing fascicles having mild to moderate eosinophilic cytoplasm, with oblongated nuclei	SMA showed strong positive cytoplasmic staining in tumour cells However, S100 was negative in tumour cells	Cutaneous leiomyoma
10.	61 years and male	Right leg	1 year	Cutaneous leiomyoma	Single firm non tender swelling measuring 2x1.5x0.8 cm	Spindle shaped cells in fascicles having moderate eosinophilic cytoplasm, with tapered nuclear ends	SMA showed strong positive cytoplasmic staining in tumour cells however S100 was negative in tumour cells	Cutaneous leiomyoma of right leg
11.	32 years and male	Esophagus mass	6 months	Oesophageal submucosal mass	Epigastric discomfort and bouts of non bilious vomiting	Spindle shaped cells in short fascicles having moderate eosinophilic cytoplasm, with cigar shaped blunt nuclear ends	SMA showed strong positive cytoplasmic staining in tumour cells	Oesophageal leiomyomatous polyp

[Table/Fig-5]: Clinicopathological features of leiomyomas.

and present as mediastinal mass, known as giant esophageal leiomyomas.

Colonic leiomyomas are rare, usually asymptomatic, and diagnosed incidentally on colonoscopy as benign proliferations of non epithelial

tissue arising from underlying smooth muscle layer [11]. In majority of cases, colonic leiomyomas are small and sessile however, a few cases of intraluminal pedunculated cases have also been diagnosed. It is important to diagnose them clinically, as they are often misdiagnosed as adenomatous hyperplastic polyps during endoscopy.

Chin H et al., conducted a study on six patients and found various types of extrauterine fibroids in ovary and broad ligament. Preoperative counseling regarding the recurrence at extrauterine sites and possible dissemination of unexpected malignancy should be enquired [12]. Seidman MA et al., suggested the importance of diagnosing leiomyomas because of its chances of recurrences and malignant conversion [13].

When immunohistochemical analysis when done shows strong cytoplasmic positivity for SMA, desmin, irrespective of organs involved. H-caldesmon done helps to differentiate smooth muscle differentiation from myofibroblastic differentiation and also rules out endometrial stromal tumours in uterine leiomyomas.

If left untreated, leiomyomas continue to grow. Surgical excision, with or without skin grafts, is the treatment of choice [8]. Cryotherapy, electrodesiccation, and carbon dioxide laser treatment may be used for small lesions, but these techniques can lead to unwanted scarring. Medical management consists of pain management with drugs that cause smooth muscle contraction, like nitroglycerine, nifedipine, and phenoxybenzamine. Topical analgesics, like lidocaine or capsaicin, may also be used.

## CONCLUSION(S)

Benign smooth muscle tumours, though common in female genital tract, can be encountered in other tissues. The pathogenesis of benign smooth muscle tumours (excluding those of the female genital tract) is still uncertain. Leiomyomas of the breast and cutaneous leiomyomas are very rare, but they are a great mimicker

of other lesions of the mammary gland and skin, both clinically and radiologically. Benign and malignant lesions cannot be reliably distinguished using physical examination, imaging studies, or even by Fine Needle Aspiration Cytology (FNAC). Hence, simple excision followed by a meticulous histopathological evaluation, along with Immunohistochemistry (IHC), is required to arrive at a final diagnosis.

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