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Histomorphological spectrum of uterine leiomyoma and its secondary changes: A retrospective study

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Abstract---Aim and Background: Leiomyoma is one of the most common causes for abnormal uterine bleeding in females. Furthermore, sometimes leiomyoma is clinically, radiologically, and histologically believed to be malignancy. Thus, there is a need for more studies to know the different variants and secondary changes occurring in leiomyoma. Methods: This study was carried out at the Department of Pathology, Dr. Vasantao Pawar Medical College, Hospital, and Research Centre. Over a period from January 2019 to June 2023, 355 cases were received and included in this study. The specimen was examined grossly, processed, stained, and studied microscopically. Results: In the current study, cellular leiomyoma was the most common variant and the hyaline degeneration was the most common secondary change identified. Conclusion: The current study gives insights into the clinicopathologic spectrum of uterine leiomyoma along with their clinical presentation, variants and

associated secondary changes, in comparison with the findings from similar studies of different areas.

Keywords---Leiomyoma variants, Hyaline degeneration, Secondary changes, Hysterectomy.

1. Introduction

One of the most important female reproductive organs which is responsive to several hormones is Uterus (Begum and Khan 2004). Endometrium which is the mucosal lining of the uterus is made up of several blood vessels, stroma and glands. Uniform endometrial lining appears from the fundus and uterus with only slight variation from each other depending on the position of tissue with respect to the endomyometrial junction and surface epithelium (Khan et al 2016). The myometrium is the thick, smooth muscle coat of uterus underneath the endometrium and is covered by peritoneum derived serosa (Whitaker and Critchley 2016). Among the diverse benign lesions observed in myometrium, leiomyoma is the most common visceral neoplasm affecting the females in the reproductive age group (Melmed et al 2016). The chief causes for hysterectomy all over the globe are leiomyoma, adenomyosis, leiomyosarcoma, endometrial stromal tumors, secondary tumours and vascular lesions etc (Rosai 1989). Leiomyoma (Fibroid) is the most common benign smooth muscle tumor of female genital tract (Geethamala et al 2016). Clinically it results into abnormal bleeding during menstruation, abdominal pain, infertility, anemia and fatigue thus affecting patient socially and economically (Kurman et al 2014, Dayal et al 2014). Regardless of its benign nature, the leiomyoma can cause major problems from menorrhagia, dysmenorrhea, infertility, repeated miscarriages (Crum et al 2004). Several secondary changes and histological variants of leiomyomas have been reported, making it difficult to differentiate from malignant neoplasms like leiomyosarcoma (LMS). Thus, knowledge of the commonly occurring variants, secondary changes and growth patterns is warranted (Mutter et al 2008). Within the female genital tract, the myometrium is the commonest site for leiomyoma but in rare occasions it may occur in vulva, vagina, broad ligament and other unusual sites like ovary and urinary bladder (Christopher 2009). More than twenty variants of leiomyoma have been identified, while a variety of secondary changes which include hyaline change, myxoid change, cystic change, calcification and fatty metamorphosis have been reported (Baral and Shrestha 2021). The variants include red degeneration, apoplectic cellular, symplastic, mitotically active, leiomyoliopma, palisaded, epithelioid and leiomyoma with lymphocytic infiltration.^[13] Some leiomyomas are recognized on the basis of growth patterns such as cotyledonoid, dissecting, parasitic, diffuse and intravenous (Khan et al 2020, Reis et al 2016). Leiomyomas are fibroid, fibromyoma and myoma. Both estrogen and progesterone affect the growth of leiomyoma. While the development and proliferation of leiomyoma is being influenced the action of progesterone, the estradiol is known to increase the availability of progesterone receptors thereby increasing the tissue sensitivity to progesterone (Reis et al 2016).

Leiomyomas show great variability as regards to clinical presentation, site, number, and presence of degenerative changes. A hysterectomy is the most

common surgical intervention. Accurate knowledge of the different variants and secondary changes that occur in leiomyoma is essential, as some of these may mimic malignancy clinically, radiologically, and histologically. Comprehensive knowledge of all the variants is mandatory to avoid misdiagnosis. Therefore, the objective of the current study was to analyze various histopathological changes within the uterine leiomyoma in both hysterectomy and myomectomy specimens. Further, we also observed the site, size, number, degenerative and secondary changes, and their clinical manifestations.

2. Methodology

2.1. Settings

The study was carried out at the Department of Pathology, Dr. Vasanttrao Pawar Medical College, Hospital and Research Centre, Nashik, India, after approval by the Institutional Ethical Committee (Dr. VPMCH&RC/IEC/83/2023-2024). Data was collected for the period of January 2019 to December 2023. Patients diagnosed with leiomyoma on histopathological examination of a hysterectomy specimen (n = 365) were included in the study. The socio-demographic information and detailed clinical history were recorded from the histopathological requisition forms.

2.2. Histopathology of the sections

The surgical specimens were allowed to fix in 10% formalin for 24-48 hours. The gross examination of leiomyoma included location, number, size, and secondary changes. Tissue bits from representative areas were taken for histopathological examination, and paraffin blocks were prepared. Five-micron thick sections were cut and stained with routine hematoxylin and eosin stain. A Microscopic examination was done by a consultant histopathologist, and it was diagnosed as leiomyoma. The histologic features were studied and recorded.

2.3. Statistical analysis

Microsoft Excel was used to analyze the data. The data is represented as the number of cases (percentage of cases).

3. Results

In this study, a total of 365 cases of uterine leiomyoma were obtained from hysterectomies (Total/Subtotal/Pan) abdominal, vaginal, or laparoscopic, and myomectomies specimens. Fig. 1 shows leiomyoma having elongated cells with blunt end nuclei arranged in an interlacing pattern. Hysterectomy specimens were 296 (81.09%), followed by myomectomies at 69 (18.90 %). In the current study, out of 365, 224 (61.36%) were cases of single leiomyoma and multiple in 141 (38.63%).

All the females were in the age group ranging from 21-70 years with 203 women (55.61%) falling in the age group of 41-50 years (Table 1). With respect to location, intramural leiomyomas were commonest in 214 cases (58.63%), followed by subserosal in 88 cases (24.10%) and submucosal in 59 cases (16.16%) in this

study. 4 women had leiomyomas at location other than intramural, subserosal, and submucosal. Out of 365 leiomyoma cases, 289 (79.17%) were solitary, and 76 (20.82%) showed leiomyomata. The commonest clinical manifestation was menorrhagia in 128 cases (35.06%), followed by dysmenorrhea in 93 cases (25.47%) (Table 2).

Various histopathological patterns of endometrium in uterine leiomyoma were seen in our study, with the most common being the proliferative phase in 235 cases (64.38%), followed by the secretory phase in 93 cases (25.47%). 31 cases (8.49%) had a disordered proliferative phase, while 6 cases (1.64%) had endometrial hyperplasia. The most common uterine pathology along with leiomyoma, was found to be chronic cervicitis, with 191(52.32%), followed by adenomyosis, with 115 (34.05%) (Table 3).

Out of 365 cases of leiomyoma, 253 (69.31%) showed secondary changes. The most common secondary change was hyaline degeneration (Fig. 2) in 198 (78.26%) cases, followed by cystic changes in 31 (12.25%) cases and calcification in 19 (07.50%) cases. 4 cases (1.58%) had myxoid degeneration change, while only 1 case (0.39%) had red degeneration. Different variants were identified in 14 (03.83%) leiomyoma cases, with the most common being cellular, with 9 (64.28%) variants (Fig. 3) followed by palisaded in 4 (28.57%) variants.

3. Discussion

Uterine leiomyoma is the most common benign smooth muscle tumor in the pelvic area in females. Leiomyomas show diverse clinical, radiological, and morphological patterns and are responsive to several hormones. On the basis of morphology, leiomyomas have been separately classified as variants and as secondary changes. The diagnosis of these variants and changes plays an important role in the management of the patient. It has been reported that leiomyoma is one of the most common indications for hysterectomy followed by Adenomyosis (Rani and Thomas 2013).

In the present study, single leiomyoma was more common than multiple leiomyoma. Similar results have been reported by Lahori et al. with single (56.96%) and multiple (43.04%) cases (Lahori et al 2016). A study done by Sarfarz showed a predominance of multiple leiomyomas with 60.87% (Sarfaraz et al 2010). In our study, the age group ranged from 21 to 80 years old, and the majority of cases were 41-50 years of age. These results are comparable with studies done by Khan et al. (59.16%) (Khan et al 2020), Lahori et al. (46.82%) (Lahori et al 2016), Gupta et al. (51.40%) (Gupta et al 2009) and Bhatta et al. (54.76%) (Bhatta et al 2018).

In the present study, menorrhagia was the most common clinical presenting feature, with 128 (35.06%), followed by dysmenorrhea in 93 (25.47%). Similar findings were reported by Rather et al. (35.43%) (Rather et al 2013), Gowri et al. (49.03%) (Gowri et al 2013) and Manjula K. (35.4%) (Manjula et al 2011).

Intramural leiomyomas were the most common site for leiomyoma, with 214 (58.63%) cases out of 365, followed by subserosal with 88 (24.10%). A study by

Jung et al. showed similar findings (55.70% intramural and 16.3% subserosal) (Reis et al 2016). A study by Gowri et al. reported intramural leiomyomas as the most common site (48%) (Gowri et al 2013).

The Proliferative phase is the most common histopathological pattern of endometrium, with 64.38%. Similar results were reported by Khan et al. and S Lakshmi (Khan et al 2020, Lkshmi et al 2022). The degenerative changes in leiomyomas occur due to inadequate blood supply, which may result in hyalinization, most commonly followed by cystic, hemorrhagic, hydropic, or calcification, and occasionally followed by malignant degeneration, or LMS. The type of secondary change depends on the rapidity and degree of vascular insufficiency (Geethamala et al 2016).

In our study, out of 365 cases of leiomyoma, 253 (69.31%) showed secondary changes. The most common secondary change was hyaline change, with 78.26%, which occurs due to ischemia following rapid growth of the tumor. It is characterized by the accumulation of mucopolysaccharide around the muscle fibres (Simms-Stewart et al 2012). It is necessary to differentiate it from coagulative necrosis since necrosis is seen as more likely with leiomyosarcoma (Simms-Stewart et al 2012). Cystic changes were observed in 12.25% of cases, followed by calcification in 7.50% of cases. Similar findings were reported by Simms-Stewart D (Reis et al 2016). Cystic change is considered to be the end result of severe oedema (Rani et al 2016) while calcification is often seen in postmenopausal females (Kaushik et al 2008). Similar results were reported by Lakshmi S. (Lakshmi et al 2022) and Kaur M. (Kaur et al 2018).

In the present study, 14 (3.83%) different variants were seen. Similar results were noted by a study done by Manjula K (Manjula et al 2011) which included cellular being the most common, followed by palisaded and symplastic. Similar findings were observed by a study done by Lahori M (Lahori et al 2016).

4. Conclusion

Leiomyoma is the most common uterine benign smooth muscle tumor seen, with menorrhagia as the most common clinical presentation. The most common affected age group is 41 to 50 years. Intramural locations were the most common site. The most common pattern of endometrium observed is proliferative. Hyaline degeneration was commonest secondary change observed. Therefore, conscientious histopathological examination should be mandatory and of paramount importance for confirmed diagnosis, optimal management, and surveillance of the concerned patients.

Limitation of study

The current study is descriptive in nature and has included only uterine fibroids. More in-depth analysis of the results is warranted.

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Figure Legends:

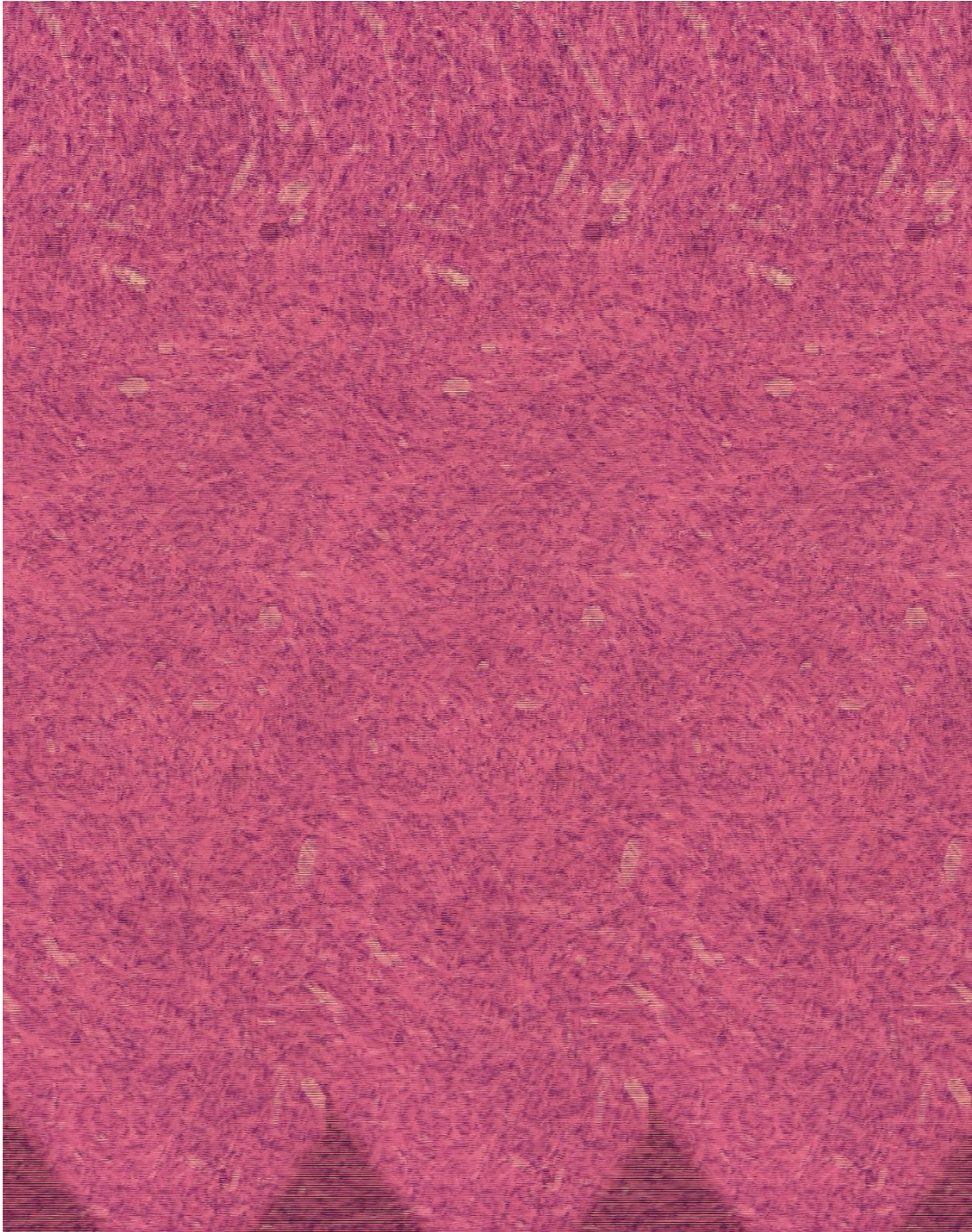


Figure 1. Leiomyoma having elongated cells with blunt end nuclei arranged in inter lacing pattern

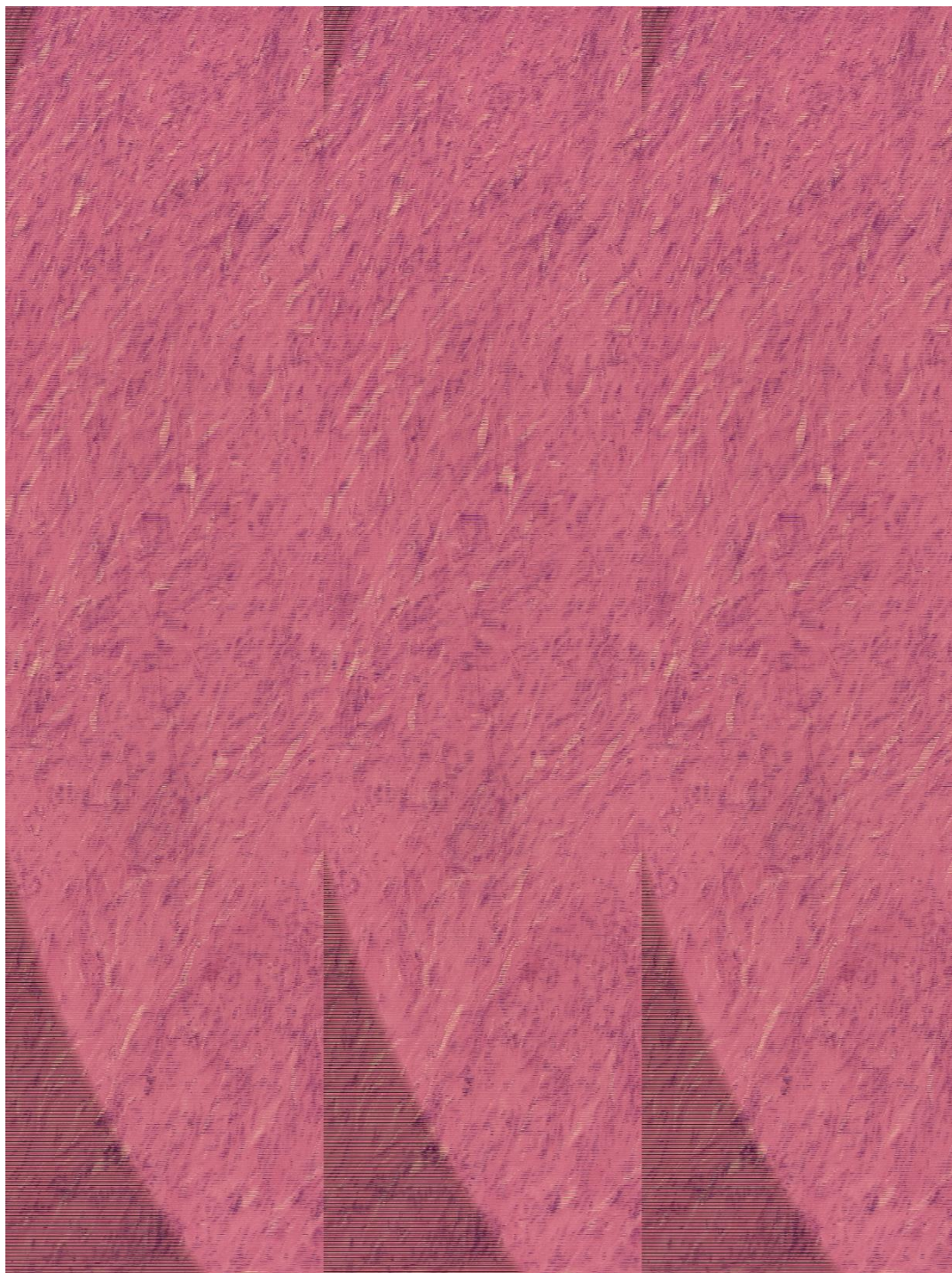


Figure 2. Leiomyoma showing secondary change hyaline degeneration

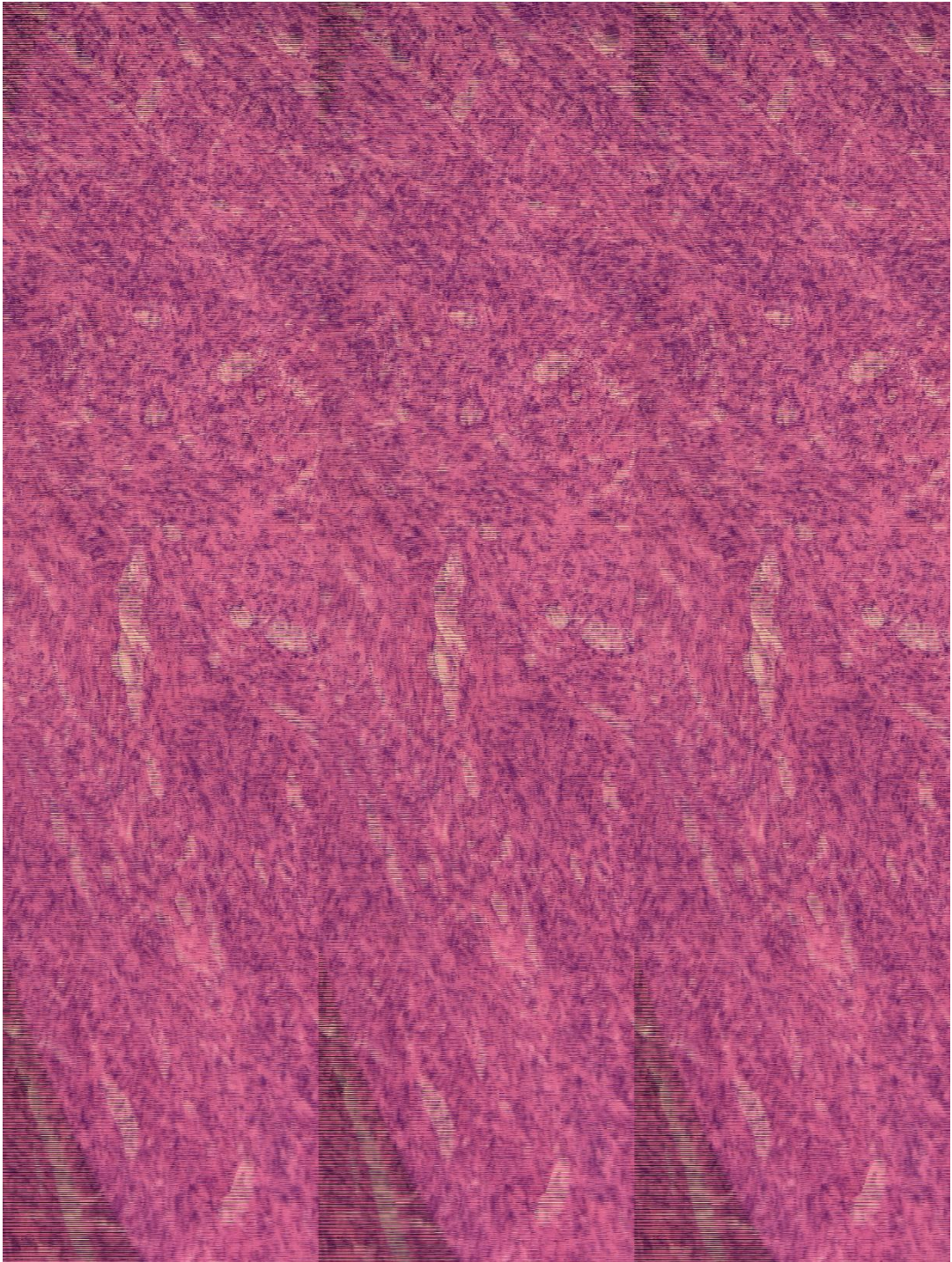


Figure 3. Leiomyoma showing cellular variant

Table Legends:

Table 1: Age wise distribution of cases included in the study

AGE GROUP	Number of cases	Percentage (%)
21-30	08	02.19
31-40	92	25.20
41-50	203	55.61
51-60	43	11.78
61-70	14	03.82
>70	05	01.30
Total	365	

Table 2: Clinical Manifestation and distribution of cases

Clinical Manifestation	Number of cases	Percentage (%)
Menorrhagia	128	35.06
Dysmenorrhea	93	25.47
Pain in abdomen	68	18.63
Polymenorrhea	37	10.13
Post-Menopausal bleeding	35	9.58
Infertility	4	1.09
Total	365	

Table 3: Uterine Pathology wise distribution of cases

Uterine Pathology	Number of cases	Percentage (%)
Chronic Cervicitis	191	52.32
Adenomyosis	115	34.05
Ovarian Cystadenoma	22	06.02
Endometrial Polyp	17	04.65
Ovarian Cystadenocarcinoma	06	01.64
Endometrial Carcinoma	01	0.27
No pathology	13	03.56
Total	365	