International Journal of Innovative Studies in Medical Sciences (IJISMS)
ISSN 2457-063X (Online) www.ijisms.com Volume: 2 Issue: 1 | 2018

Ovarian Fibromas : A Clinicopathological Study of 18 Cases

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Abstract: *Ovarian fibromas are uncommon tumours of pure stromal cell origin accounting for 4% of all ovarian neoplasms. The aim of the present study was to provide an updated overview on ovarian fibromas. We retrospectively reviewed eighteen cases of ovarian fibromas that were diagnosed at the pathology department of Mongi Slim hospital over a thirteen-year period (2002- 2014). The patients of our series ranged in age between 18 and 75 years (mean = 42 years). The presenting clinical symptoms were dominated by pelvic pain (n=11) and mass (n=4), followed by metrorrhagia (n=3), perimenopausal bleeding (n=1) and menorrhagia (n=1). All tumours were unilateral and the mean size was 8,77 cm. Twelve patients underwent unilateral salpingo-oophorectomy, whereas total hysterectomy and bilateral salpingo-oophorectomy was performed in five cases. Only one patient underwent tumorectomy. Histopathological examination of the surgical specimen confirmed the diagnosis of ovarian fibroma in all cases. All patients remained tumour free with no evidence of recurrence during a mean follow-up period of 17 months. Clinical, ultasonographic and tumour marker data remain the best preoperative approach currently available for ovarian tumours. However, the diagnosis remains histological. Tumorectomy, if possible, is well indicated for young patients with ovarian fibromas; however, radical treatment is indicated for perimenopausal and menopausal patients.*

Keywords: *ovary; sex cord stromal tumour; fibroma.*

1. INTRODUCTION

Fibromas are rare benign tumours of gonadal-stromal cell origin, growing from connective tissue of ovarian cortex. They account for 1-4,7 % of ovarian tumours [1-3]. Ovarian fibromas are often difficult to diagnose preoperatively and are usually misdiagnosed as uterine myoma, because of the solid nature of the mass on clinical examination and the ultrasound similarities between the two lesions. In this paper, the authors report 18 cases of ovarian fibromas that were diagnosed at our institution over the past 13 year period.

2. PATIENTS AND METHODS

We undertook a retrospective study of 18 patients who were operated on for ovarian fibromas at the gynaecology department of Mongi Slim hospital of Tunis between March 2002 and September 2014. The cases were retrieved from the files of the registry of gynaecology of the same hospital. Medical records were scrutinized for epidemiologic characteristics, initial manifestations of the disease, methods of diagnosis, laboratory findings and surgical treatment. Diagnosis of the ovarian neoplasms was based upon clinical, imaging and histopathologic findings. All patients underwent imaging evaluation during the preoperative period. All specimens were surgically obtained. Tissues were fixed in 10% phosphate buffered formaldehyde, embedded in paraffin and sections were prepared for routine light microscopy after staining with haematoxylin and eosin. Patient confidentiality was maintained.

3. RESULTS

The clinicopathological features of our patients are summarized in table I.

Table 1: *Clinicopathological characteristics of ovarian fibromas in our series.*

Case Nº	Age	size (cm) / Location	Symptoms	Treatment	Evolution
1	59	11 / left ovary	Perception of a pelvic mass	Total hysterectomy and bilateral salpingo-oophorectomy	Favourable no recurrence Follow-up = 3 months
2	61	4,5 / left ovary	Pelvic pain	Total hysterectomy and bilateral salpingo-oophorectomy	Favourable no recurrence Follow-up = 4 months
3	35	3 / left ovary	Pelvic pain	Left salpingo-oophorectomy	Favourable no recurrence Follow-up = 3 months

4	44	2 / right ovary	Metrorrhagia	Right salpingo-oophorectomy	Favourable no recurrence Follow-up = 12 months
5	50	2 / right ovary	Metrorrhagia	Right salpingo-oophorectomy	Favourable no recurrence Follow-up = 29 months
6	25	6 / left ovary	Pelvic pain	Tumorectomy	Lost to follow-up
7	52	6 / left ovary	Perimenopausal bleeding	Left salpingo-oophorectomy	Favourable no recurrence Follow-up = 24 months
8	49	8 / left ovary	Pelvic pain	Left salpingo-oophorectomy	Favourable no recurrence Follow-up = 3 years
9	71	9 / left ovary	Pelvic pain	Total hysterectomy and bilateral salpingo-oophorectomy	Lost to follow-up
10	43	10 / right ovary	Perception of a pelvic mass	Right salpingo-oophorectomy	Favourable no recurrence Follow-up = 16 months
11	33	10 / left ovary	Pelvic pain Metrorrhagia	Left salpingo-oophorectomy	Lost to follow-up
12	18	8 / left ovary	Pelvic pain	Left salpingo-oophorectomy	Favourable no recurrence Follow-up = 10 months
13	44	15 / right ovary	Pelvic pain	Right salpingo-oophorectomy	Favourable no recurrence Follow-up = 24 months
14	75	23 / right ovary	Perception of a pelvic mass Pelvic pain	Total hysterectomy and bilateral salpingo-oophorectomy.	Favourable no recurrence Follow-up = 7 months
15	38	13,5 / right ovary	Perception of a pelvic mass	Right salpingo-oophorectomy	Favourable no recurrence Follow-up = 24 months
16	20	8 / right ovary	Menorrhagia Pelvic pain	Right salpingo-oophorectomy	Favourable no recurrence Follow-up = 12 months
17	47	8 / right ovary	Pelvic pain	Right salpingo-oophorectomy	Favourable no recurrence Follow-up = 48 months
18	70	11 / right ovary	Pelvic pain	Total hysterectomy and bilateral salpingo-oophorectomy	Favourable no recurrence Follow-up = 36 months

4. CLINICAL FINDINGS

Our study group included 18 female patients between 18 and 75 years of age (mean = 42,44 years). Six patients were postmenopausal. During the same period of the study, 320 patients underwent surgery for ovarian neoplasms. The frequency of ovarian fibromas was 5,6%. Two patients presented with co-morbidities namely hypertension (n=1) and diabetes (n=1). The presenting clinical symptoms were dominated by pelvic pain (n=11) and mass (n=4), followed by metrorrhagia (n=3). Perimenopausal bleeding was noted in one case and menorrhagia in one case. In seven cases, the adnexal mass could be identified as a firm-solid mass on bimanual examination.

5. BIOLOGY

Laboratory examination of the serum cancer antigen-125 (CA-125) tumour marker was performed in 8 cases and was within normal range (less than 35 IU/ml) in all cases.

6. RADIOLOGICAL FINDINGS AND LOCALIZATION OF OVARIAN FIBROMAS

Diagnostic imaging techniques included ultrasonography in all cases. Ultrasonographic findings were ovarian echogenic tumour in ten cases, hypoechogenic tumour in four cases, mixed tumour showing heterogeneous content in four cases (Figure 1).

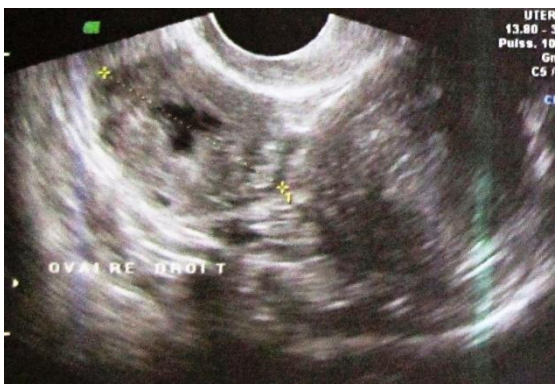

Figure 1: *Abdominal ultrasonography showing a heterogeneous predominantly solid mass of the right ovary with cystic foci.*

7. TREATMENT

Frozen section was performed in five cases. After frozen section confirmation of benign tumour, the five patients underwent unilateral salpingo-oophorectomy.

The rest of the patients underwent unilateral salpingo-oophorectomy (n=7), total hysterectomy and bilateral salpingo-oophorectomy (n=5) and tumorectomy (n=1).

8. PATHOLOGIC FINDINGS

In all cases the diagnosis was established by histological examination. Grossly, fibromas ranged in size from 2 to 23 cm (mean = 8,77 cm). On cut section, all tumours were firm, gray-white to tan, chalky or yellowish (Figures 1a, 1b, 1c & 1d). Areas of oedema and cystic degeneration were noted in four cases (Figure 1b & 1d). Calcifications were present in two cases. Histopathological examination of the surgical specimen revealed that fibromas were composed of cells with spindled to ovoid nuclei and scant cytoplasm (Figure 2a & 2b). The cells were arranged in intersecting bundles, sometimes with a storiform pattern. Collagen bands or hyalinized plaques were often present (Figure 2c). Mitoses were absent in 16 cases. In two cases the mitotic index was 2 mitoses / 10 high power fields. Immunohistochemical study was performed in five cases and showed negative immunostaining of neoplastic cells for inhibin (Figure 2d). All cases of our series were positive for smooth muscle actin.

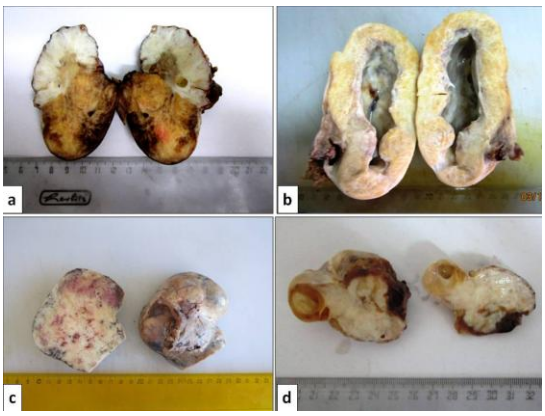

Figure 2: *Macroscopic findings of fibromas and fibrothecomas.*

Figure 2a: *The cut surface showed a well-circumscribed solid yellow and white tumour.*

Figure 2b: *The sectioned surface was tan to yellow with cystic degeneration.*

Figure 2c: *The cut surface showed a well-circumscribed solid whitish tumour with focal hemorrhage.*

Figure 2d: *The cut surface showed a well-circumscribed solid white tumour with peripheral cystic degeneration.*

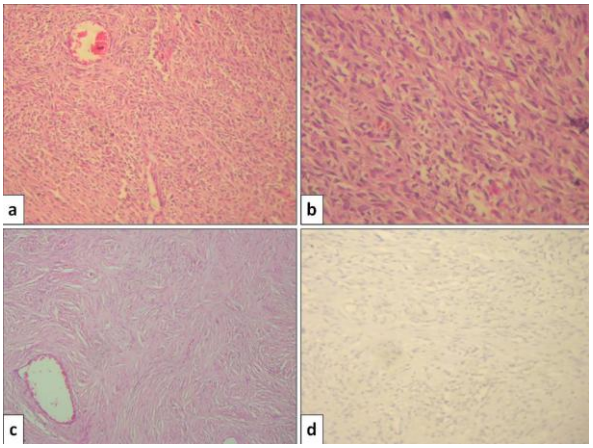

Figure 3: *Histopathological findings of fibromas.*

Figure 3a: *Spindled cells arranged in intersecting bundles admixed with collagen. (Hematoxylin and eosin, magnification × 400).*

Figure 3b: *Spindled cells with bland nuclei and scant cytoplasm (Hematoxylin and eosin, magnification × 400). Mitoses and nuclear atypia were absent.*

Figure 3c: *Fibroma with hyalinized plaques, (Hematoxylin and eosin, magnification × 100).*

Figure 3d: *Neoplastic cells showed negative immunostaining with inhibin, (Immunohistochemistry, magnification × 400).*

Operative morbidity and postoperative complications :

Postoperative course was uneventful in all cases.

9. FOLLOW-UP AND EVOLUTION

All patients remained tumour free with no evidence of recurrence during a mean follow-up period of 17 months. Three patients were lost to follow-up. The other patients are still being followed-up.

10. DISCUSSION

Fibrothecomas are benign neoplasms which belong to the estrogenic group of sex cord tumours with differentiation in fibroblastic or theca cells. Fibroma is purely composed of mature fibroblastic cells producing abundant collagen and thecoma contains many cells resembling theca cells and/or lutein cells as well as a number of fibroblastic cells. However, in some instances, differentiation between fibroma and thecoma is often difficult, justifying use of the term 'fibrothecoma' [4]. The different series of ovarian fibromas and fibrothecomas reported in literature are summarized in table II [5-10]. Ovarian fibromas occur most frequently in middle age women (mean, 48 years), but they can be seen in any age group [3]. In our

series, the patients were aged between 18 and 75 years (mean = 42,44 years). Six were postmenopausal and only one patient was aged less than 20 years (case Nº12). Most patients present with an incidental or symptomatic ovarian or pelvic mass. Rarely, they may be associated with steroid hormone production. Approximately 15% of patients with fibromas measuring >10 cm present with ascites [11] and a minority of them also have Meigs' syndrome (ascites and pleural effusion) [12, 13], which usually resolve after tumour removal. Rarely, fibromas may also be associated with the nevoid basal cell carcinoma syndrome (Gorlin syndrome) and these tend to occur in younger patients. In our series, none of our patients had ascites, Meigs'

syndrome or nevoid basal cell carcinoma syndrome. CA125 serum levels are usually normal. Rarely, high serum levels are noted and they become normal after tumour removal. In our series, CA125 serum levels were within normal range in 8 cases [14]. Trisomy and / or tetrasomy 12 are often found in tumours in the fibroma-thecoma group, although not specific for these tumour types. Loss of heterozygosity at 9q22.3 (PTCH) and 19p13.3 (STK11) have been reported to be frequent in cellular fibromas [15]. The investigation of ovarian fibromas is based, like all ovarian tumours, on ultrasonography. A broad spectrum of ultrasonographic features are reported and include especially echogenic and mixed echogenicity masses. Hypoechoic masses are also reported. In our series, ultrasonographic findings were ovarian echogenic tumour in ten cases, hypoechogenic tumour in four cases, mixed tumour showing heterogeneous content in four cases. The standard of treatment for ovarian fibroma is surgical removal of tumour followed by intraoperative frozen section. In all post-menopausal women and those who have completed their family, total abdominal hysterectomy is the treatment of choice; however, owing to benign nature of the disease, a fertility-preserving surgery with unilateral salpingo-oophorectomy in young premenopausal women can be contemplated [10]. In our series, 12 patients underwent unilateral salpingo - oophorectomy, whereas total hysterectomy and bilateral salpingo-oophorectomy was performed in five cases. Only one patient underwent tumorectomy. Grossly, The vast majority of fibromas are unilateral but they may be bilateral (8%), especially in patients with Gorlin syndrome [15]. They have a mean diameter of 6 cm [15]. In our series, all ovarian fibromas were unilateral with a mean diameter of 8,77 cm (range : 2 - 23 cm).

Table 2 : *Series of fibromas and fibrothecomas reported in literature.*

Authors	Year	Number of cases	Histological subtypes
Chechia A et al., [5]	2001	12	Fibromas : n = 7 Fibrothecomas : n = 5
Leung SW et al., [3]	2006	23	Fibromas : n = 23
Farah-Klibi F et al., [6]	2008	20	15 Fibrothecomas 3 Fibromas 2 thecomas
Numanoglu C et al., [7]	2013	43	Fibromas : n = 13 Fibrothecomas : n = 29 Fibrosarcoma : n = 1
Zhang Z et al., [8]	2015	26	Fibromas : n = 4 Fibrothecomas : n = 6 Thecomas : n = 16
Chung BM et al., [9]	2015	28	Fibromas : n = 19 Fibrothecomas : n = 7 Thecomas : n = 2
Parwate NS et al., [10]	2016	23	Fibromas : n = 23
Our series	2016	18	Fibromas : n = 18

Fibromas have a smooth or lobulated surface [15]. Most neoplasms are solid, with a firm to rubbery, white to pale yellow cut surface. Areas of oedema and cystic degeneration may be present, especially when the tumour is large. Haemorrhage or necrosis can be present, secondary to torsion [15]. Histologically, fibromas are composed of cells with spindled to ovoid nuclei and scant cytoplasm. The nuclear features are bland. The cells are arranged in intersecting bundles, sometimes with a storiform pattern. Collagen bands or hyalinized plaques are often present [15]. Mitoses are uncommon in most cases. Approximately 10% of fibromas are densely cellular with scant collagen. In the presence of only mild nuclear atypia, these are referred to as cellular fibromas [15]. Cellular fibromas may have mitotic activity of > 4 per 10 HPF (mitotically active cellular fibroma). Haemorrhage and necrosis may occur, sometimes secondary to torsion. Focal or diffuse calcification is present in some cases [15]. Fibromas stain diffusely for vimentin and can also show immunoreactivity for WT-1, CD56, smooth muscle actin, desmin, and CD34 [15]. Focal weak staining for inhibin and calretinin has also been reported but they are typically negative for CD10 and CD99 [15]. Stromal hyperplasia, fibromatosis, and thecoma should be considered in the differential diagnosis of conventional fibroma while fibrosarcoma, metastatic endometrial and primary endometrioid stromal sarcomas, smooth

muscle tumours, as well as gastrointestinal stromal tumour should be included in the differential diagnosis of cellular/mitotically active fibroma. Most of ovarian fibromas are benign. A small proportion especially cellular fibromas is associated with ovarian surface adhesions, rupture or extra-ovarian involvement at the time of presentation. Those with adhesion or rupture are at risk of local recurrence often after a long interval [15]. An accurate preoperative diagnosis of ovarian fibromas is often difficult because of its uncommon occurrence and more importantly its solid nature makes it frequently misdiagnosed as uterine myomas. Clinical, ultasonographic, and tumour marker data remain the best preoperative approach currently available for ovarian tumours. However, the diagnosis remains histological.

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