

Challenges in Management of Bartholin gland Leiomyoma: A Case Report

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Case report

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Abstract

Background: Leiomyomas are uncommon vulvar neoplasms often misdiagnosed as other Bartholin gland pathology. Due to their rarity and the absence of guidelines, their diagnosis and management remain challenging, largely based on expert opinion and evidence from case reports.

Case Presentation: This case report describes a 44-year-old woman presenting with accelerating growth of a vulvar mass. Based on clinical signs and symptoms, the initial diagnosis was Bartholin cyst. Surgical excision was provided for symptom control and aesthetic reasons. The histopathologic diagnosis was vulvar leiomyoma. The postoperative recovery was complicated by secondary haematoma and dehiscence of the surgical site. There was no recurrence at two years follow up. Therefore, we discuss the dilemma posed by physical examination of a vulvar mass, the challenges of the management, and report on secondary morbidity and long-term follow up, aspects of care for patients with vulvar pathology not commonly addressed in the literature.

Conclusions: Bartholin gland neoplasms are rare tumors, commonly misdiagnosed as Bartholin's cysts. Excision is the treatment of choice. Short time follow up allows prompt management of potential postoperative complications. Continuing long term follow up is recommended due to recurrence risk.

Background

Smooth muscle neoplasms are the most common tumors of the female genital tract. Most of these neoplasms develop in the uterus and there is abundant literature and numerous professional guidelines to facilitate their diagnosis and management. In contrast, smooth muscle neoplasms of the vulva are rather uncommon and represent a challenge for diagnosis and treatment. Three categories of vulvar smooth muscle tumors have been described: leiomyomas, atypical leiomyomas, and leiomyosarcomas (1, 2).

Leiomyomas of the vulva are rare, accounting for 0.03% of all gynecologic neoplasms and for 0.07% of all vulvar tumors (2). They most commonly arise from the labia majora, dartos muliebris muscle, and blood vessels walls, but also from the smooth muscle within the round ligament or female erectile tissue (2, 3). These tumors are usually clinically misdiagnosed as Bartholin cysts or abscesses (4). Vulvar leiomyomas occur typically in pre-menopausal women, in the 4th -5th decade of life. When present in postmenopausal women, the differential with a malignant tumor may cause a diagnostic dilemma. To date, in the literature there are less than 200 reported cases of vulvar leiomyomas, within which a wide range of management approaches have been described. There are no guidelines and their management is based on expert advice, cumulative evidence from case reports, and small size cohort studies (4). Surgical excision, with or without initial biopsy, provides symptoms control and is curative in most of cases. There is no consensus on the risk of recurrence and very little information is available on secondary morbidity and long-term outcomes.

To this end, we report a case of vulvar neoplasm and discuss the challenges of clinical diagnosis, the criteria for differentials, and the details of management, including our experience with postoperative morbidity and long-term follow up.

Case Presentation

Presentation

A 44-year-old woman, G3P1T1L1, was referred to gynaecology oncology services by her family physician (on the two-week wait pathway), for a suspected diagnosis of vulvar neoplasm. The woman presented at her local surgery with a large right labial mass that was causing persistent perineal discomfort. The mass measured approximately 30 × 40 mm in size and had been growing slowly over the past two years. When seen by the gynecology oncology team, a few weeks later, the woman denied local pain, itching, discharge or bleeding but she complained of increased discomfort with sitting and cycling. She reported no abdominal pain, urinary or bowel symptoms. She also had no symptoms of cachexia or infection.

The woman had a history of mild, seasonal, non-medicated asthma and depression, for which she was treated with Fluoxetine, 20 mg OD. She reported secondary amenorrhea, as a consequence of a Mirena IUS inserted 5 years previously for contraceptive purposes. Prior to the IUS insertion, she used oral contraceptives for almost 20 years. She was not sexually active at presentation. Her pregnancy and delivery were uneventful. Except for a Chlamydia infection in her early twenties, she had no other gynecologic history. Her Papanicolaou smear was normal, and her cervical screening was up to date. She did not smoke, drink alcohol, or used recreational drugs. She had no drug allergies. There was no history of gynecological cancer in her close family.

On examination, she was systemically well, and her vitals were stable. Her general physical examination was unremarkable. Local examination identified a 50 × 60 × 70 mm non-tender mass on the posterior aspect of the right labia majora. This was well delineated and has a moderately firm consistency. There were no signs of infection or inflammation or other suspicious features. There was no generalized lymphadenopathy or large inguinofemoral lymph nodes at bilateral palpation of the groins. The clinical impression was a large right Bartholin cyst, and the patient was counselled about management options, re-assured, and by mutual agreement was added to the surgical waiting list to be treated by the benign gynecology team.

While awaiting surgery, the patient noted enlargement and swelling of the vulvar mass that became painful. Referral and re-examination by the oncologic gynecologist four months later found an increased in size, now moderately tender labial mass of 80 × 80 × 70 mm. There was still no evidence of an inflammation or abscess. Except for accelerated growth, there were no other suspicious features of malignancy. Her surgery was planned in several weeks for excision of Bartholin gland cyst and replacement of Mirena coil.

Surgical procedure and findings

At the time of admission for surgery, the woman's routine blood tests were within normal range and urinalysis showed traces of blood and proteins. Her blood pressure was 143/91 to 144/85 mmHg, pulse 80/min, and SpO₂ 96% on room air. She had body mass index (BMI) of 27 kg/m². The patient underwent elective excision of the vulvar mass, removal of Mirena coil, and fitting a new Mirena device under general anesthesia. Examination under anesthesia found a right labia majora swelling of approximately 100 × 90 × 80 mm, the skin overlying the mass was very thin and there were with two areas of fine breaks in the skin, covered with a fine film of sanguinolent oozing. On vaginal examination, the mucosa of the vagina and the cervix was normal, the uterus was normal size and consistency, no adnexal masses or infiltration were identified. After the replacement of the Mirena IUS, 20 mL Marcaine 0.5% were injected around the lesion to create a dissection plan. Through a vertical linear incision on the medial aspect of the labia, the dissection plan of the tumor was identified, and the mass was methodically dissected and enucleated in one piece. The appearance and consistency of the specimen suggested this to be a solid tumor rather than a cystic one. The copious bleeding from the tumor attachment points was stopped with diathermy and haemostatic sutures. The excision of the tumor left behind a deep defect in the vulvar structures that required closure in two layers. At the end of the procedure, a Foley catheter confirmed integrity of the urethra and the bladder, while a rectal examination confirmed normal tone and integrity of the rectus and anal sphincters. The patient was discharged in good condition the same day.

Postoperative follow up

One week later the patient was seen in gynecology triage for perineal pain, bleeding, and unpleasant local odour for two days. She had no fever, urinary or bowel symptoms, and her vital signs were normal. Local examination showed a surgical site haematoma with the overlying skin erythematous and swollen. Upon haematoma drainage, the 2 cm wound gaping was left to heal by second intention under antibiotic protection. Cultures of the wound collection were negative. Two weeks after this episode, the patient was well, the vulvar haematoma and local inflammation were resolved, and the wound was healing well. Blood tests at follow up assessments were within normal range.

Histopathology

Macroscopic examination of the surgical specimen showed a circumscribed mass, 80 × 70 × 40 mm, weighting 117 gm. The external surface of the mass was ragged and tan coloured. The cut surface was solid with a white "whorled" appearance. Histological examination revealed a well circumscribed tumor (Fig. 1 **Panel A, B**), composed of intersecting fascicles of uniform spindle-shaped cells with elongated ovoid nuclei and fairly abundant eosinophilic cytoplasm (Fig. 1 **Panel C**). There was no cytological atypia or coagulative tumor necrosis, and the mitotic count was less than 1 mitotic figure per 10 high powered fields. Immunohistochemistry showed that the cells were diffusely positive for smooth muscle actin (SMA), desmin, and h-caldesmon (Fig. 2, **Panel A, B, and C, respectively**). The morphological and immunohistochemical features were those of a benign vulvar leiomyoma.

The patient was informed on the report of vulvar fibroid and re-assured regarding the benign character of the vulvar growth. Two years post surgery, the patient remains well, and is completely asymptomatic, with

no evidence of disease recurrence.

Discussion and Conclusions

Here we presented a case of vulvar smooth muscle neoplasm that mimicked a Bartholin gland cyst and was also suspected of possible malignant transformation. Although rare, vulvar leiomyomas may occur at the same location as Bartholin duct cysts or abscesses and, as illustrated by this case, the clinical diagnosis by physical examination is challenging. Most vulvar leiomyomas are initially clinically misdiagnosed as Bartholin cyst or abscess. In our case, the woman had no pain and inflammatory signs, which excluded the diagnosis of Bartholin's abscess. Absence of signs of infection combined with the latency in tumor growth prompted the initial patient referral to oncology specialist. The tumor characteristics on examination pointing rather to a cystic than a solid structure led to the specialist diagnosis of Bartholin cyst, a more common clinical encounter than that of a Bartholin fibroma.

Vulvar leiomyomas are uncommon benign mesenchymal tumors which are usually asymptomatic but can cause swelling and local discomfort. Leiomyomas are benign soft tissue tumors of mesenchymal origin. Vulvar leiomyomas are rare benign monoclonal tumors, that occur most commonly in the fourth and fifth decades of life (3). A recent review found 41 years the average age of occurrence, with a range from 15 to 73 years (2). As with our case, the personal and family histories of patients with vulvar leiomyoma generally reveal no abnormal findings (2, 5–7). The genetics of vulvar leiomyoma remain undefined; several possible genes (high-mobility group AT-hook 2 gene (HMGA2), factor gene pleomorphic adenoma gene 1 (PLAG1), RBI-inducible coiled-coil 1 gene (RB1CC1)) might be involved but the mechanism through which any of these genes regulate the aberrant smooth muscle cell development and survival has not been identified (8, 9).

Three principal histological patterns of vulvar leiomyomas have been identified: spindled, epithelioid, and myxoid or myxohyaline, although combinations of these can also be present (10). The management is similar for all histological types. The spindled pattern, present in our case, is a relatively common type of vulvar leiomyoma, in which there is a fascicular proliferation of spindle-shaped cells with ovoid to elongated nuclei and richly eosinophilic cytoplasm (2, 5). The key to histologic differentiation between benign and malignant forms, respectively between leiomyoma, atypical leiomyoma, and leiomyosarcoma are a set of criteria defined by Tavassoli & Norris and later modified by Nielsen et al and Nucci & Fletcher (2, 5, 10, 11). The differentiation criteria between the three forms are presented in Table 1. Both leiomyomas and leiomyosarcomas are positive on immunohistochemistry for smooth muscle cell markers, including smooth muscle actin, desmin, and caldesmon. In addition, leiomyosarcomas are immunopositive for S-100 and cytokeratin. S100 is present in myoepithelial cells (12–14). A recent review shows their importance as markers in cancer (12). Some of these tumors may express oestrogen, progesterone, and androgen receptors (15–18), the significance of which for the development of these tumors is not fully understood (19). Therefore, for our case, we did the smooth muscle cell markers to aid in the differential with malignancy. A relationship between hormonal contraception and growth of such tumors has not been established to date, thus, potential involvement of the contraception used by our

patient to the development and growth of the vulvar tumor, although possible, was not inferred. The hormonal receptors staining was not considered to have played a role in the diagnosis or management of our patient. However, the relationship between hormones and the growth of vulvar leiomyomas warrants further study.

Table 1
Differential histologic diagnostic criteria between benign and malignant neoplasm of smooth muscle cells tumors of the vulva.

<i>Tavassoli & Norris criteria (1979)²⁶</i>
1) ≥ 5 cm in the greatest dimension
2) Infiltrating margins
3) ≥ 5 mitotic figures per 10 high-power fields
<i>Nielsen et al criteria (1996)²¹</i>
4) moderate to severe cytological atypia
<i>Nucci & Fletcher (2000)²⁵</i>
5) coagulative tumor necrosis
Diagnosis:
1 criteria: Leiomyoma
2 criteria: Atypical leiomyoma
≥ 3 criteria: Leiomyosarcoma
any 1 to 4 criteria & criteria 5: Leiomyosarcoma

The differential diagnosis of a solid growth the Bartholin's gland include leiomyoma, primary carcinoma, and leiomyosarcoma and other vulvar mesenchymal lesions such as cellular angiofibroma, angiofibroma and aggressive angiofibroma. (22–24). Leiomyosarcomas of the vulva are very rare, thus frequently mistaken for benign Bartholin's gland lesions, which delays the diagnosis and management. The treatment is complex, generally aiming for complete excision with a goal of pathologic confirmation of negative margins (6). Radical hemivulvectomy with inguinal lymphadenectomy has been reported for some cases (25). Multidisciplinary discussions between oncologists, gynecologist, and pathologists can provide guidance to ensure that adequate surgical excisions are performed and advise on the need for radiotherapy and chemotherapy, as these tumors are aggressive, with high rate of recurrence and distant metastases (25–27). The role of adjuvant therapy is not clear and comparisons between studies are rather difficult to reach a clear consensus.

Other vulvovaginal mesenchymal lesions, such as aggressive angiofibroma and cellular angiofibroma can be distinguished from vulvar leiomyoma through histological evaluation and immunohistochemistry,

specifically the absence of diffuse staining for smooth muscle markers (especially h-caldesmon). Bartholin gland carcinoma is another rare differential, presenting as a painless swelling, which may be clinically confused with a Bartholin gland cyst or abscess. Histologically, these tumors are a heterogeneous group; adenocarcinoma and squamous cell carcinoma each account for approximately 40%, adenoid cystic carcinoma for 15%, and adenosquamous carcinoma for 5%. Their treatment, which is not yet standardized, include either wide local excision or radical vulvectomy and lymphadenectomy followed or not by local radiation therapy, or radiotherapy alone. A study by Balat et al (20) showed no difference between the treatment employed in the rate of primary tumor control or 5-year disease-free survival rate, whereas others found that conventional therapy yielded a 5-year survival of 67%, with two thirds of the patients having a local recurrence in spite of local radiotherapy (21).

In contrast to solid tumors, which often present as gradually enlarging painless masses, the Bartholin's abscess presents as a painful lump, that over time becomes fluctuant, and associates with fever and local inflammation. The Bartholin's cyst is less painful but may cause local discomfort and often associates with history of recurrent Bartholin's abscesses. A recent systematic review found that there is no current randomised trial evidence to support the use of any single surgical intervention for the treatment of a symptomatic cyst or abscess of the Bartholin's gland (22–26).

As our case illustrates, histological evaluation is essential for diagnosis, especially if there are clinical features suggestive of malignancy such as accelerated growth. As such, we support the premise that a biopsy-excision or at least a biopsy should be performed before attempting other procedures such as cyst drainage in cases where the clinical context is not fully relevant of the presumed pathology. Establishment of a full differential diagnosis and correct final diagnosis are essential for optimal clinical management.

Various reports comment on the importance of imaging of vulvar neoplasms, which may confirm the presence, location, size of the tumor, and help with its characterization. Ultrasonography is the most widely used diagnostic tool because of easy access, low costs and being non-invasive. Pelvic computed tomography and pelvic MRI are more sparingly used and employed for rather difficult cases or where malignancy and/or local spread is suspected (2, 19, 27). As with many other reports, we have not employed any of the technologies above. As the tumor was solitary, well circumscribed, asymptomatic for a long time, and clinical evaluation did not find any suspicious features, a benign neoplasm was suspected with a high degree of certainty and thus no imaging investigations were deemed necessary. However, the place of different imaging methods in positive and differential diagnosis of vulvar tumors is not clear. No consensus exist regarding which method should be employed and criteria for positive diagnosis have not been defined.

There is limited reporting of secondary outcomes of vulvar leiomyoma, including hematoma, infectious morbidity, persistent pain, dyspareunia, and risk of recurrence. In spite of careful haemostasis with ligature and diathermy of the blood vessels from the tumor bed, a haematoma did form several days after the surgery in our patient. Non-obstetric vulvar haematomas are not common and there are no guidelines for their management. However, the principle of management in obstetric haematomas can be

applied by analogy to the haematomas post gynecologic surgery (28, 29). Thus, due to size and discomfort symptoms reported by the patient, we opted for drainage in order to reduce the pain, accelerate the recovery, and prevent secondary infection and necrosis.

Regarding the recurrence risk of vulvar leiomyomas, the opinions are controversial. For instance, Nielsen et al. recommend close long-term follow-up because of the high risk of recurrence (5). From 25 smooth-muscle tumors of the vulva analysed in that study, 19 were followed up to an average of 5 years and four had local recurrence and one distant metastasis was found (5). Whereas in several other reports, the patients had one to two recurrences during a median follow up period of 25 months, others found no recurrence at one or two years, as was the case in our patient (2, 30, 31). Complete enucleation or excision of the tumor with surrounding normal tissue decreases the rate of recurrence and increases the five-year survival rate (5, 30). Considering the small number of cases and limited available follow-up data, the long-term clinical behavior of vulvar leiomyoma remains to be established.

Clinical experience with diagnosis and management of smooth muscle tumors of the vulva is scarce. More data is required to improve knowledge on the natural history, diagnostic criteria, optimal management, and prognostic factors of vulvar neoplasms. Because these lesions can present with late-relapse, long-term follow up is advised until more evidence is available.

Abbreviations

IUS, intrauterine system; BMI, body mass index; BP, blood pressure; SpO₂, peripheral capillary oxygen saturation.

Declarations

Ethics approval and consent to participate

This study is compliant with the institutional ethics regulations of the Oxford University Hospitals NHS Foundation Trust and with the Health Insurance Portability and Accountability Act.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal

Availability of data and materials

Interested readers can review the primary data upon request, subject to the data sharing policy of NHS England.

Competing interests

The authors declare that they have no competing interests

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None.

Authors' contributions

AV designed the study, collected patient information, and wrote the manuscript; LI was the designated health care provider and retrieved patient clinical notes; SD provided the figures and their description; HSM provided care to the patient; all authors participated in the clinical care of this patient; all authors provided feedback on the manuscript drafts and read and approved the manuscript in its final version.

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Figures

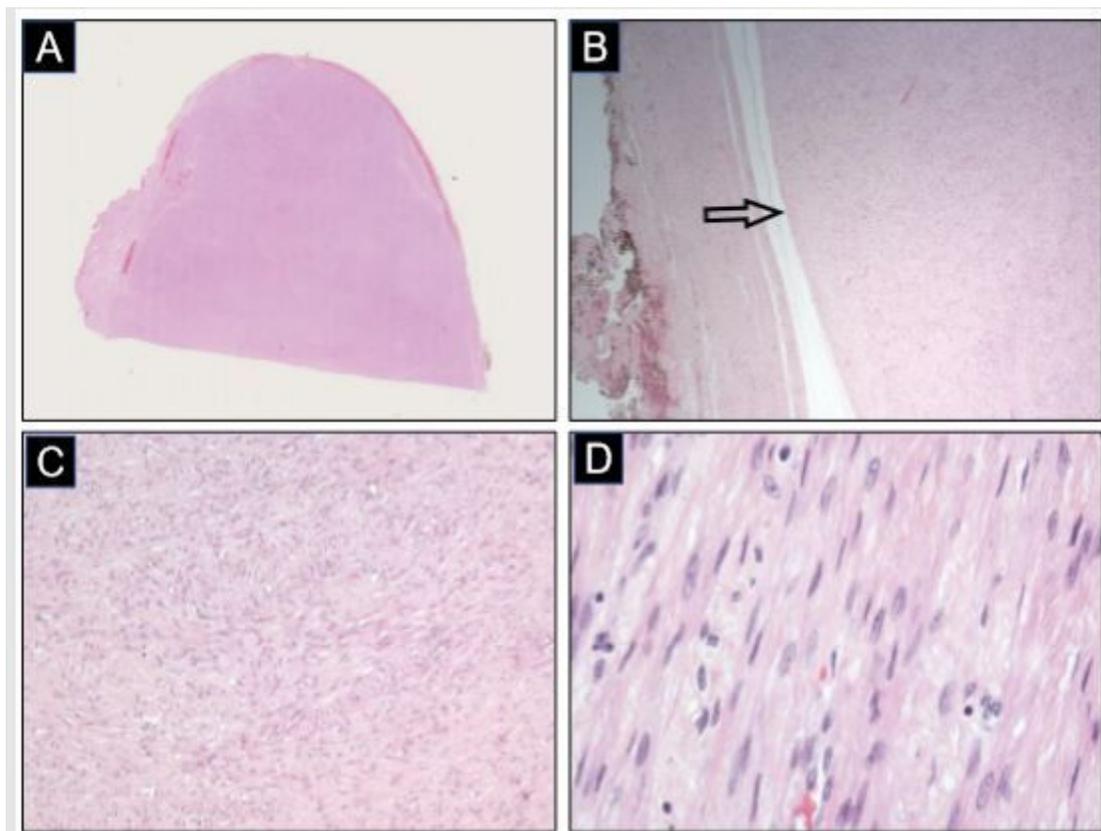


Figure 1

Histopathologic features of vulvar leiomyoma. A-B. The tumour is well circumscribed without any infiltration of the surrounding tissue. The arrow (B) highlights the border of the tumour [haematoxylin and eosin (H&E), whole slide, x20] C. The tumour is composed of intersecting fascicles of uniform spindle-shaped cells [haematoxylin and eosin (H&E), x100] D. The cells have elongated ovoid nuclei and

eosinophilic cytoplasm. There is no significant cytological atypia or mitotic activity [haematoxylin and eosin (H&E), x400].

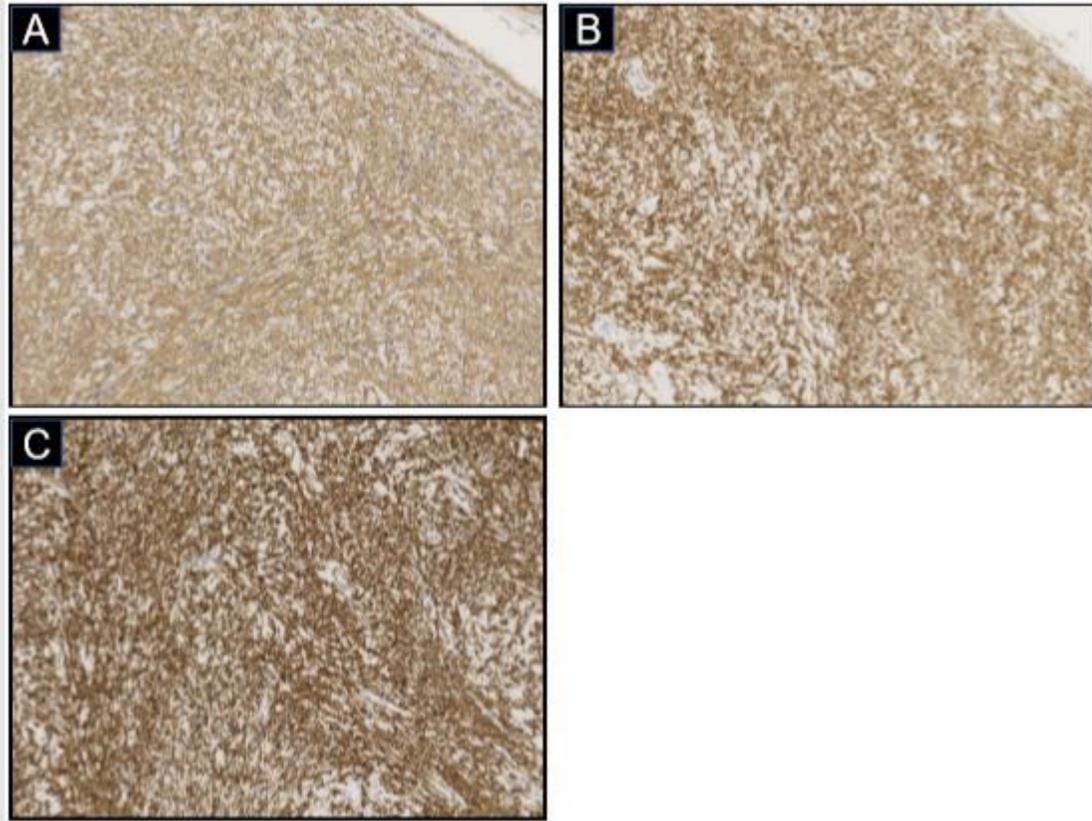


Figure 2

Immunohistochemistry of vulvar leiomyoma. A-C. The tumour cells are diffusely positive for smooth muscle actin (A), desmin (B), and h-caldesmon (C) [magnification x100].