

A Rare Coexistence of Uterine Lipoleiomyoma, Leiomyoma, Endometrial Polyp and Early Clear Cell Carcinoma of the Endometrium, Never Described Before

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Abstract

Background: Uterine lipoleiomyoma is a rare and specific type of leiomyoma being composed of benign smooth muscle cells admixed with mature adipocytes. These lesions may have coexistent malignancy in the uterus, ovaries and fallopian tubes, or may have other metabolic disorders and abnormal estrogen status.

Case Summary: Here, we report a case of a 66-year old female patient who was admitted to our hospital with irregular vaginal bleeding, due to atypical adenomatous hyperplasia, diagnosed on D&C (dilatation and curettage). A total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Histopathological examination revealed rare occurrence of coexistent uterine lipoleiomyoma, leiomyoma, endometrial polyp and clear cell carcinoma of the endometrium.

Conclusion: Our findings are in accordance with that of other authors, in that lipoleiomyoma coexists with hyperestrogenic-related conditions and gynecologic malignancies. Clear cell carcinoma of the endometrium has not been previously described among co-existent malignancies. Although lipoleiomyomas have a favorable prognosis, the pathogenesis and clinical significance of these rare neoplasms need more clarification. The principal significance of these lesions is that they may have a coexistent malignancy.

Keywords: *Lipoleiomyoma; Leiomyoma; Endometrial Polyp; Clear Cell Adenocarcinoma; Co-Existence*

Introduction

Uterine leiomyoma is the most common neoplasm of the female genital tract, particularly during the reproductive age. Though secondary degenerative changes are common in existing leiomyoma, microscopic variants are less common. Lipoleiomyoma is a rare variant of uterine leiomyoma, composed of an admixture of mature smooth muscle cells and adipocytes, in different proportions, often with predominance of the adipose tissue [1-4]. Fatty tumors of the uterus are very uncommon and almost invariably benign [5]. The incidence

varies from 0.3% [2] to 2.1% [1] and 2.9% [6]. These tumors are seen in uterus as intramural growths and mostly located in the posterior wall of uterine corpus, but rarely may be seen arising in the cervix, the retroperitoneum and the broad ligament [7].

We report a case of an incidental uterine lipoleiomyoma in a postmenopausal woman, with an incidental finding of a coexistent early clear cell carcinoma developing in an endometrial polyp.

Case Report

A 66-year old, postmenopausal woman, was admitted in our hospital for surgical treatment. She was diagnosed with an endometrial polyp with focal complex atypical endometrial hyperplasia in D&C, after complaints of irregular vaginal bleeding. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy.

The patient was a smoker, with hyperlipidemia, hyperthyroidism, chronic respiratory impairment and psychotic syndrome under treatment (on antidepressants and antipsychotic drugs). In her past medical history she had been diagnosed with laryngeal polyps, gastritis, adenoma of the large bowel and she had been operated on, for GIST of the bowel.

On Ultrasound and MRI examination, a uterine leiomyoma-like neoplasm, of 2,5 cm diameter was revealed. The possibility of degenerative changes were considered in MRI examination. An additional small uterine leiomyoma of 6-7mm, was also mentioned.

Macroscopic examination revealed a well-circumscribed soft mass, with a yellow cut surface, located on the anterior surface of the fundus, of 2.5 cm maximum dimension (Figure 1). In the endometrial cavity there was an endometrial polyp of 2 cm long (Figure 1). An additional small intramural leiomyoma of 0.5 cm (Figure 1) was also found.



Figure 1: Cut surface of the uterus where a lipoleiomyoma with yellowish discoloration, endometrial polyp and small leiomyoma are present.

Microscopically, the intramural tumor proved to be a leiomyoma consisting largely of mature adipose tissue and islands composed of bundles of smooth muscle fibres and fibrous connective tissue among the adipose tissue (Figure 2). The interspersed smooth muscle bundles were stained positively for SMA (Figure 3), desmin and calponin. A non-infiltrating clear cell carcinoma was evident in the endometrial polyp (Figure 4-7). The carcinoma had negative expression for ER (Figure 8) and PR and positive expression in Napsin A (Figure 9). MIB-1 was expressed in approximately 50% of the neoplastic cells (Figure 10 and 11). Areas of adenomyosis were also present.

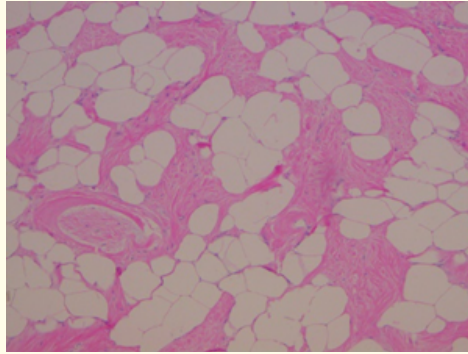


Figure 2: Microscopic appearance of the lipoleiomyoma consisting of mature adipose tissue admixed with bundles of smooth muscle fibres and fibrous connective tissue among the adipose tissue (H&E, X20).

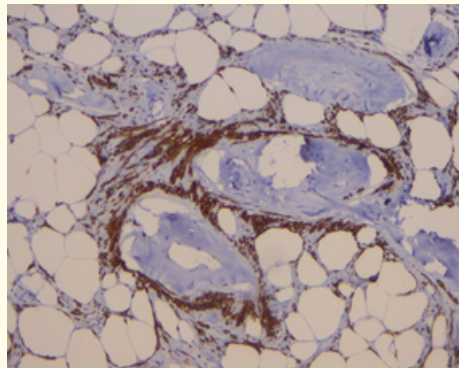


Figure 3: The interspersed smooth muscle bundles in lipoleiomyoma were stained positively for SMA (IHC, X40).

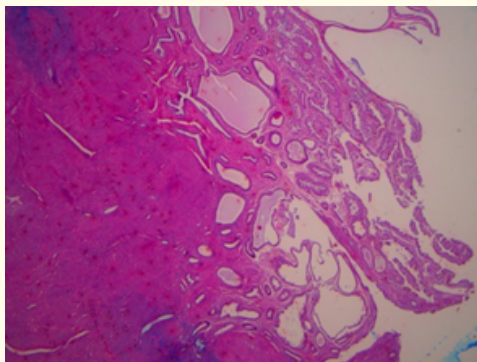


Figure 4

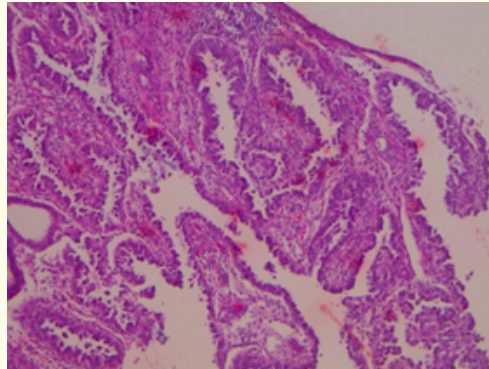


Figure 5

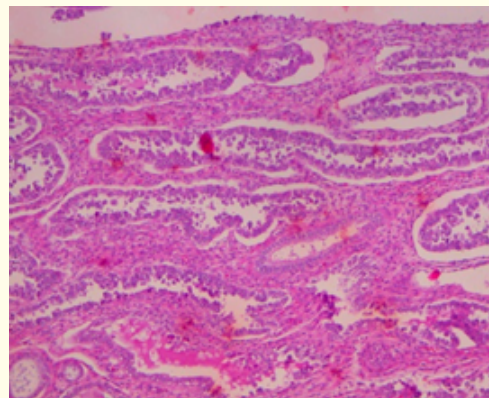


Figure 6

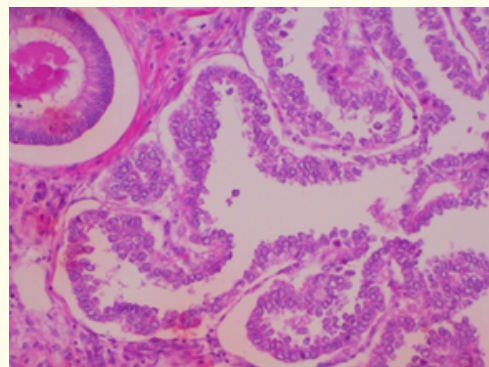


Figure 7

Figure 4-7: A non-infiltrating clear cell carcinoma was evident in the endometrial polyp (different foci and magnifications, H&E, X10, X20, X40).

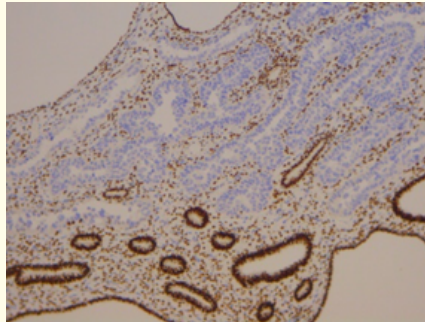


Figure 8: The carcinoma had negative expression for ER (IHC, X20). Evident is the positive ER expression in the rest, non-neoplastic endometrial tissue.

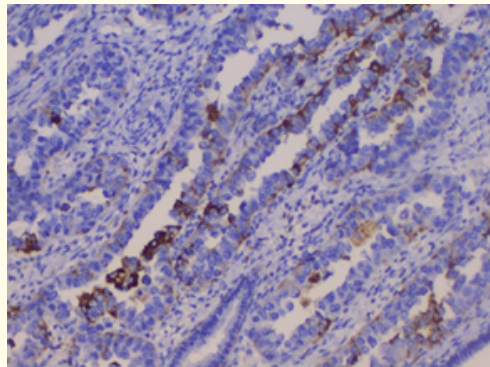


Figure 9: The carcinoma had positive expression in Napsin A (IHC, X40).

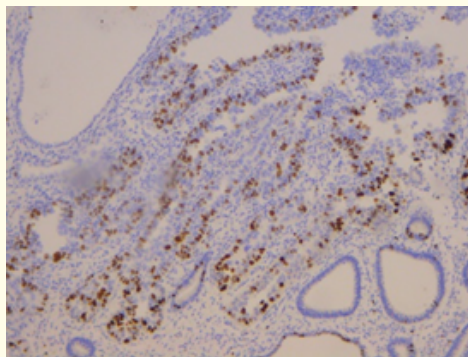


Figure 10: MIB-1 was expressed in approximately 50% of the neoplastic cells (IHC, X20).

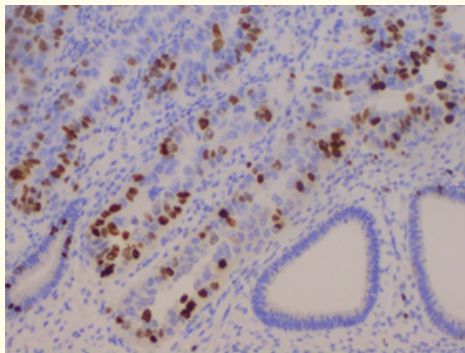


Figure 11: Higher magnification of figure 10 (IHC, X40).

There was no connection between the lipoleiomyoma and the malignancy, macro- or microscopically.

The woman was recovered successfully.

Discussion

Lipomatous uterine tumors are rare neoplasms. Uterine lipoleiomyoma is a benign tumor which is variant of leiomyoma [1,2] which is composed of a considerable amount of adipocytes, it has similar prognosis and clinical presentation like leiomyoma and it is typically found in postmenopausal women. These tumors are usually asymptomatic but may present with typical leiomyoma symptoms, such as abnormal uterine bleeding or abdominal pain. Lipoleiomyomas most commonly present as intramural neoplasms of the uterine corpus. They can also be found in the cervix, retroperitoneum, broad ligament and ovary [4,8]. They are usually solitary, ranging in size from 0.5 to 55 cm, mean 5.5 cm [4].

In most cases, lipoleiomyomas are found incidentally during surgery for other reasons [9], like in our case, where the woman underwent surgery for atypical adenomatous hyperplasia of the endometrium, diagnosed in D&C specimen. In the literature, lipoleiomyomas have been seen more frequently in patients with adenomyosis, endometriosis, endometrial hyperplasia and polyps [4]. In the study by Akubulat, *et al.* [4], the most common associated lesions were leiomyoma (33/70 cases) followed by adenomyosis in 24/70 cases. In our case, concomitant lesions found were adenomyosis, leiomyoma and endometrial polyp.

Although ordinary leiomyomas tend to occur mostly in women of reproductive age and regress after menopause, the lipoleiomyomas are frequently seen in older women, of 50 - 70 years of age. The mean age of the patients with lipoleiomyomas, in the largest two series was 55.4 years (34 - 77) of which 60% were older than 50 [1,6]. Several theories have been suggested regarding the pathogenesis of this tumor, such as: a) metaplasia of immature perivascular pluripotent mesenchymal cells or smooth muscle cells of leiomyoma to adipocytes, b) misplaced embryonic fat cells and c) fatty infiltration of connective tissue [4]. The theory of metaplasia is regarded as the most widely accepted underlying mechanism for the formation of uterine lipoleiomyoma.

Many studies have also postulated that lipoleiomyomas are mostly found in women with a hyperestrogenic status [10]. Therefore, alteration of lipid metabolism associated with menopause may play a role in the development of lipoleiomyoma [4]. A number of various lipid metabolic disorders, possibly promote abnormal intracellular storage of lipids. In addition, some metabolic disorders such as hyperlipidemia, hypothyroidism and diabetes mellitus, seem to occur more commonly in these patients [4].

It is not possible to diagnose uterine lipomatous tumors preoperatively. Although MRI [11-13] may be useful in determining the fatty structure of the lesion, most of these lesions are diagnosed by postoperative histopathological examination.

Histologically, these tumors are composed of smooth muscle tissue admixed with varying amounts of mature adipose tissue. If the adipocytes are evenly distributed throughout the tumor, they are called 'lipomas'. When lipocytes are concentrated in focal areas, they are called lipoleiomyomas.

The origin of lipomatous lesions of the uterus has been the subject of much speculation. In the past, they were reported as hamartomas or choristomas [14]. Later, many theories have been proposed, including 'misplaced embryonic fat cells', origin from 'multipotential undifferentiated mesenchymal cells', 'lipomatous metaplasia of smooth muscle cells', 'perivascular fat cells accompanying the blood vessels into the uterus', 'inclusion of fat cells into the uterine wall during surgery, or fatty infiltration or degeneration of connective tissue' [15,16]. Fukunaga [17] considered that some lipoleiomyomas can result from lipomatous metaplasia of leiomyomas, a hypothesis supported by immunohistochemical findings. The current concept is that lipoleiomyomas may arise from 'perivascular immature mesenchymal cells or direct transformation of smooth cells into adipocytes by means of progressive intracellular storage of lipids'.

In the study by Metin Akbulut, *et al.* [4] 75,7% of patients with lipoleiomyomas had different types of lesions associated with hyper-estrogenic status, such as adenomyosis, endometriosis, endometrial hyperplasia, polyps, complex endometrial hyperplasia, endometrial atypical hyperplasia (4,2%) and gynecologic carcinomas, like endometrioid carcinoma, endometrial carcinosarcoma, ovarian serous carcinoma and breast carcinoma.

There have been additional reports to suggest an association between lipomatous uterine tumors and concomitant malignancies of the uterus, ovaries and fallopian tubes. Several studies have reported simultaneous gynecological malignancy [18-20]. In two large studies, Aung, *et al.* [2] reported two (11%) gynecologic carcinomas in 17 cases and Wang, *et al.* [1] reported 10 cases (20%) of patients with uterine lipoleiomyoma associated with gynecologic malignancies. In Metin, *et al.* [6] report, in 70 patients found 12 cases (17.1%) of gynecologic malignancies: eight endometrial, three ovarian and one breast. This was also a significant observation of the present study, adding an additional type of endometrial cancer, in coexistence with lipoleiomyoma, never described before.

To our knowledge, this is the second case in the literature of a lipoleiomyoma, leiomyoma and endometrial polyp in the same patient [21]. In addition, our findings are in concordance with the ones referred in the literature, of concomitant gynecologic malignancy and estrogen-related lesions, presumably related to estrogenic stimulation, like adenomyosis and endometrial hyperplasia and the first case of clear cell carcinoma in this setting. Although, further studies on larger populations are needed to establish any association with malignancy, estrogenic status or metabolic disorders, our findings suggest that the presence of adipocytes in an otherwise normal leiomyoma should lead to further detailed clinical and pathological evaluation in order not to overlook a coexistent gynecologic malignancy.

It is important for the physicians to be aware of this condition as it presents with clinical symptoms similar to leiomyoma but has distinctive radiological and histological appearance.

The principal significance of these lesions is that they may have a coexistent malignancy.

Conclusion

In conclusion, patients with lipoleiomyomas have been described to coexist with hyperestrogenic-related conditions, such as endometriosis, adenomyosis, endometrial hyperplasia, polyps and gynecologic malignancies. Although lipoleiomyomas have a favorable prognosis, the pathogenesis and clinical significance of these rare neoplasms needs more clarification.

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