Borderline clear cell adenofibroma of the ovary associated with ovarian endometriosis: a case report

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Summary

Clear cell tumours of the ovary are relatively uncommon. Most of them are clear cell carcinomas. Benign and borderline clear cell tumours are extremely rare and almost always fibromatous. We report a case of a 34-year-old woman. Ultrasound and computed tomography showed a right ovarian mass 8 cm in diameter. The patient underwent right salpingo-oophorectomy. Microscopic examination revealed glands and cysts different in size and shape within an abundant stromal component without evidence of stromal invasion. Many cysts and glands were lined by a single layer of flattened, cuboidal or hobnail cells with mild to moderate cytologic atypia and prominent nucleoli. Psammomatous calcifications were occasionally indentified. Features of endometriosis were also present adjacent to the tumour. Lesional cells were positive for Ker 7 and CA125. Staining for p53 was focally positive. Based on the above characteristic morphologic and immunohistochemical findings a diagnosis of borderline clear cell adenofibroma was made. The patient was free of recurrence four years after surgery.

Key words: Clear cell tumour; Ovary; Adenofibroma; Endometriosis.

Indroduction

Ovarian adenofibromas consist of epithelial and stromal elements with the latter predominating. The epithelium is usually of the serous type. Adenofibromas with endometrioid, clear cell, mucinous and mixed epithelium are unusual [1, 2]. Benign and borderline clear cell adenofibromas are extremely rare. Clear cell adenofibromas of borderline malignancy constitute less than 1% of borderline tumours of the ovary and to date only a few cases have been reported in the world literature [3, 4].

Case Report

A 34-year-old woman presented at our hospital with a month history of lower abdominal pain. There was no family history of malignancy. Laboratory investigation including complete blood count, biochemical examination and tumour markers (CEA, CA19-9, CA125) were normal. Cervical cytology was negative. Ultrasound and abdominal and pelvic computed tomography showed a right ovarian mass 8 cm in diameter and the patient underwent right salpingo-oophorectomy. Gross examination revealed an enlarged right ovary which was replaced by a tumour measuring 8 x 5.5 x 3 cm and the cut surfaces had a fine honeycomb appearance with cysts in different sizes embedded in firm stroma. Microscopic examination revealed glands and cysts that were different in size and shape within an abundant stromal component without evidence of stromal invasion (Figure 1). The stromal component was predominantly fibrotic with an interlacing pattern. Foci of calcifications were occasional indentified. Many cysts and glands were lined by a single layer of flattened, cuboidal or hobnail cells with mild to moderate cytologic atypia and prominent nucleoli (Figures 2, 3, 4). In the tumour clear cells predominated but papillary structures were not seen. Vascular or lymphatic space invasion and necrosis were absent. Features of endometriosis were also present adjacent to the tumour (Figure 6). No significant pathologic findings were present in the fallopian tube.

Immunohistochemical study showed that the lesional cells were positive for Ker 7 and CA125 and negative for CEA and Ker 20 (Figure 5). Stain for p53 was focally positive. Based on the above characteristic morphologic and immunohistochemical findings a diagnosis of borderline clear cell adenofibroma was made. The patient was free of recurrence four years after surgery.

Discussion

Clear cell tumours of the ovary are relatively uncommon. Three main subtypes are recognised: clear cell adenofibroma, clear cell adenofibroma of borderline malignancy and clear cell carcinoma. Most clear cell tumours are clear cell carcinomas which comprise 2% to 3% of all epithelial ovarian neoplasms [3-5]. Borderline clear cell tumours are extremely rare and composed of glands or cysts lined by one or more layers of predominantly clear or hobnail cells showing moderate to marked nuclear atypia set in a dense fibrous stroma. The stromal component is cellular and resembles an ovarian fibroma. Mitotic activity (≤ 3 mitosis/HPF) may be found. Capsular stromal or lymphovascular invasion should always be absent [2-4, 6].

Patients with borderline clear cell tumours may have a similar non specific clinical presentation. They can be asymptomatic until the tumour grows to a certain size and can be palpable on routine examination as a pelvic mass or can be presenting with abdominal enlargement, pelvic pain and vaginal bleeding [2, 3].

Borderline clear cell adenofibromas can be distinguished from typical clear cell carcinomas based on

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Fig. 1

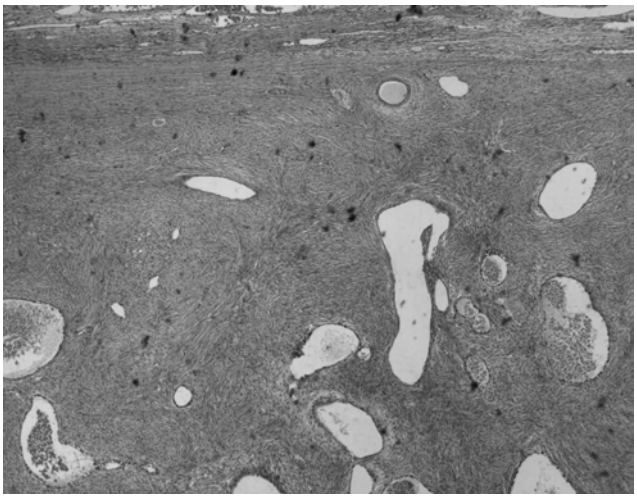

Fig. 2

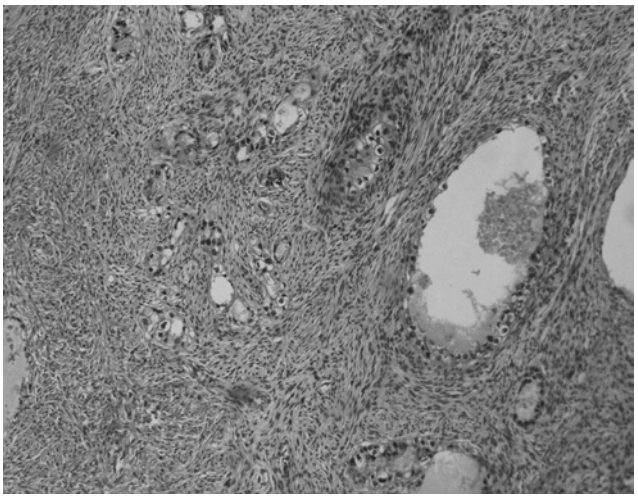

Fig. 3

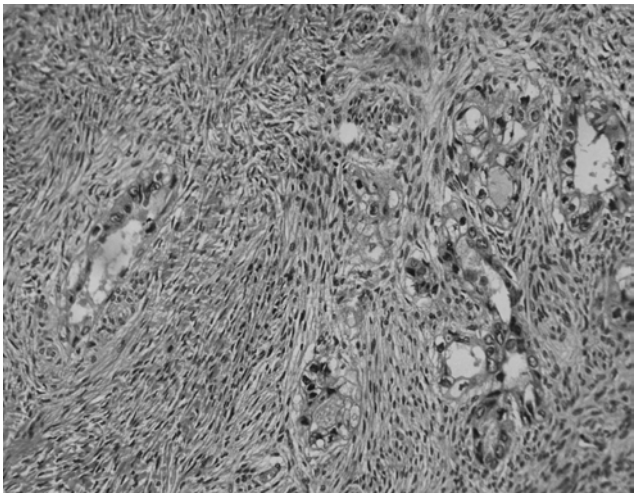

Fig. 4

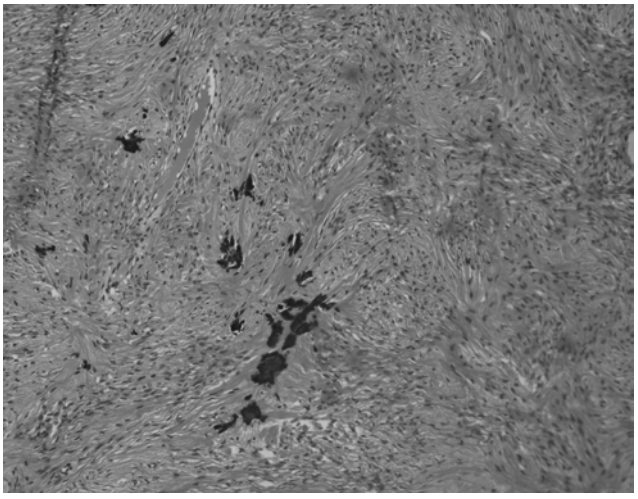

Fig. 5

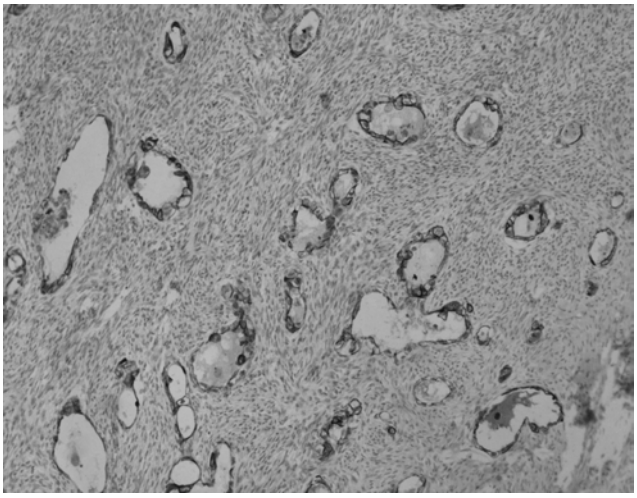

Fig. 6

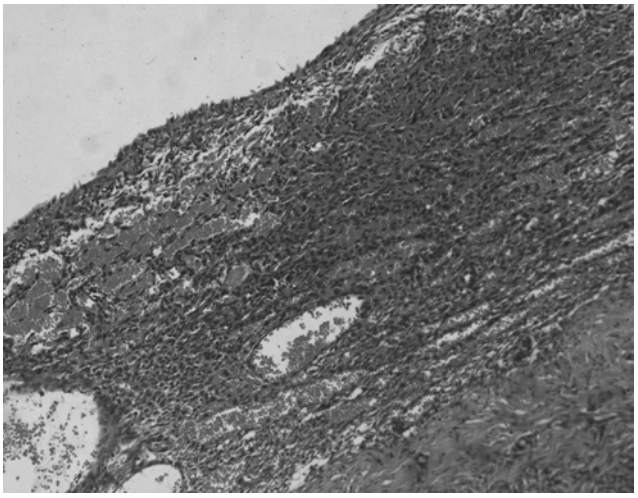

Figure 1. — Borderline clear cell adenofibroma (H&E x 100).
Figure 2. — Tumour cells with clear or oxyphilic cytoplasm and moderate nuclear atypia (H&E x 100).
Figure 3. — Tumour cells with clear or oxyphilic cytoplasm and moderate nuclear atypia (H&E x 200).
Figure 4. — Foci of calcifications (H&E x 100).
Figure 5. — Lesional cells immunoreactive with Ker 7 (Ker 7 x 100).
Figure 6. — Features of endometriosis adjacent to the tumour (H&E x 100).

nuclear features of the epithelium and on the characteristics of the stroma. In a clear cell carcinoma the fibrous connective tissue is usually entirely non specific, does not resemble ovarian stroma and lacks an increased periglandular cellularity [2, 7].

With the exception of two cases borderline clear cell adenofibromatous tumours have a benign course following removal of the ovary [3, 4, 8].

Recently Momotani *et al*. reported a case of ovarian clear cell adenofibroma of borderline malignancy associated with high levels of CA19-9. Postoperatively the serum CA19-9 level decreased to the normal limit [9].

The pathogenesis of ovarian clear cell tumours has yet to be fully elucidated [2, 4].

Clear cell tumours of the ovary are frequently associated with ovarian endometriosis [2, 4, 10, 11]. It has been suggested that clear cell tumours develop from endometriosis but there has been little molecular evidence supporting this speculation [12, 13].

Recently ovarian clear cell tumours, including benign, borderline and malignant lesions showed immunohistochemical expression of hepatocyte nuclear factor-1beta (HNF-1beta) in the nucleus while other types of ovarian epithelial tumours (endometrioid, serous, mucinous and Brenner tumours) rarely expressed it [4, 13, 14]. HNF-1beta is also expressed in ovarian endometriosis of atypical type or of a reactive nature.

Early differentiation into the clear cell lineage takes place in the endometriotic epithelium, and clonal expansion of such cells is probably responsible for the development of clear cell tumours of the ovary [13].

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