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Imaging of gynecological disease (6): clinical and ultrasound characteristics of ovarian dysgerminoma

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KEYWORDS: Doppler ultrasound; dysgerminoma; ovarian neoplasms; ultrasonography

ABSTRACT

Objectives *To describe the clinical history and ultrasound findings in patients with ovarian dysgerminoma.*

Methods *This was a retrospective study of patients with a histological diagnosis of ovarian dysgerminoma who had undergone preoperative ultrasound examination. The patients were identified from the databases of 11 ultrasound centers. The tumors were described by the principal investigator at each contributing center on the basis of ultrasound images, ultrasound reports and research protocols (when applicable) using the terms and definitions of the International Ovarian Tumor Analysis (IOTA) group. In addition, three authors reviewed all available electronic ultrasound images (gray-scale images and color/power Doppler images were available for 18 patients and 14 patients, respectively) and described them using subjective evaluation of gray-scale and color Doppler ultrasound findings (here called pattern recognition).*

Results *Twenty-one patients with ovarian dysgerminoma were identified (including one woman with bilateral masses). Twenty patients had a primary ovarian dysgerminoma (including the one with bilateral masses) and one patient had a recurrence of dysgerminoma in her retained ovary. One of the 21 patients was pregnant. All tumors except one were pure dysgerminomas, one being a mixed germinal cell tumor with 30% dysgerminoma component. Median age was 20 (range, 16–31) years. Information on clinical symptoms was available for 18 patients. In four patients, the tumor was detected incidentally, whereas 14 patients presented with one or more of the following symptoms: acute pain (*n = *4), chronic pain (*n = *8), bloating (*n = *8), menstrual disorders (*n = *5) and infertility problems (*n = *1). One (5%) patient had ascites. Using the IOTA terms and definitions, all but one dysgerminoma were moderately (43%) or very well (50%) vascularized solid tumors. One tumor was multilocular–solid. According to pattern recognition, most dysgerminomas were highly vascularized, purely solid tumors with heterogeneous internal echogenicity divided into several lobules, had a smooth and sometimes lobulated contour and were well-defined relative to the surrounding organs.*

Conclusion *The ultrasound finding of a highly vascularized, large, solid, lobulated adnexal mass with irregular internal echogenicity in a woman 20–30 years old should raise the suspicion of ovarian dysgerminoma.*

INTRODUCTION

Aim

To describe the clinical and sonographic characteristics of ovarian dysgerminoma.

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Background

Epidemiology

Dysgerminomas comprise only 1–2% of all malignant ovarian tumors[1,2]. They are malignant ovarian germ-cell tumors. Malignant ovarian germ-cell tumors are derived from primordial germ cells and are classified into several subgroups: dysgerminomas, endodermal sinus tumors, yolk sac tumors, immature teratomas, choriocarcinomas and embryonal carcinomas. Endodermal sinus tumors and immature teratomas are the most common. According to a survey performed in the USA and comprising 1262 cases of malignant ovarian germ-cell tumors registered from 1973 to 2002, the age-adjusted incidence rate of ovarian dysgerminoma per 100 000 women-years was 0.109[3]. Malignant germ-cell tumors of the ovary occur in young women, 75% being diagnosed in the second and third decades of life[4].

Microscopy

The microscopic appearance of ovarian dysgerminoma is identical to that of testicular seminoma and extragonadal germinoma. Ovarian dysgerminomas are composed of a monotonous population of rounded cells resembling primordial germ cells in a predominantly diffuse or insular arrangement[5] (Figure 1). The tumor cells are polygonal, with discrete cell membranes and abundant eosinophile to clear glycogen-rich cytoplasm. The nuclei are large, central and rounded, and they contain one or a few prominent nucleoli. Mitoses are often numerous. Aggregates of tumor cells are usually separated by thin fibrous septa almost always infiltrated by T lymphocytes[5].

Macroscopy

Ovarian dysgerminomas are characteristically solid and well-encapsulated with an average diameter of 15 cm[5]. In section, they appear to consist of different lobules, are soft and fleshy, and gray–white or light tan (Figure 2). Areas of coagulative necrosis and hemorrhage typically associated with cystic change may be seen. Dysgerminomas may be bilateral: in 10% of cases, gross involvement of the contralateral ovary is present, and in another 10%, microscopic foci of tumor are found in the contralateral ovary[5].

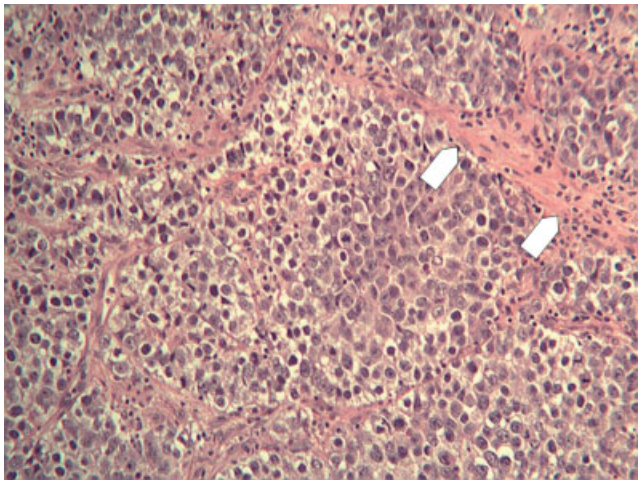

Figure 1 Microscopy of an ovarian dysgerminoma (hemoatoxylin and eosin, original magnification × 100) with nests and nodules of uniform tumor cells separated by fine connective tissue (arrows) containing lymphocytes.

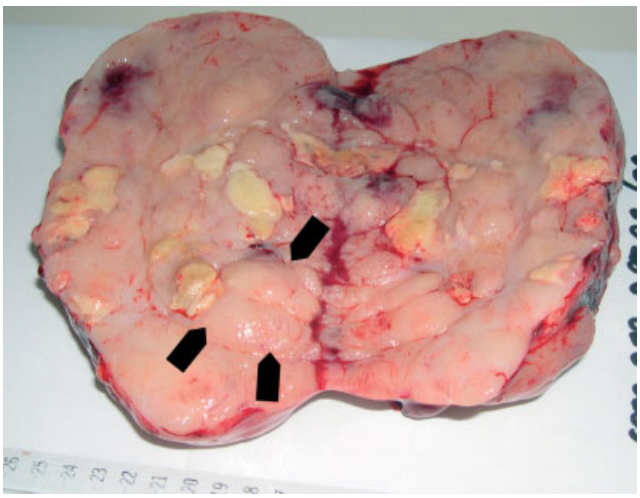

Figure 2 Macroscopy of an ovarian dysgerminoma: the cut surface is solid, uniform, pale, gray–pink and shows areas of necrosis and a lobe-like pattern, including two nodules between the arrows.

Clinical symptoms

Ovarian dysgerminomas may be detected incidentally in women with no gynecological symptoms. The most common symptoms are abdominal enlargement and the presence of a pelvic or abdominal mass felt by the patient herself, sometimes associated with pain. Torsion may cause severe pain. Occasionally, menstrual and endocrine abnormalities may be the presenting symptom. The duration of symptoms is usually short, despite the tumor being large, indicating rapid tumor growth[6]. Dysgerminoma is the most common malignant ovarian germ-cell tumor diagnosed in pregnancy[2], and may also be discovered in patients investigated for primary amenorrhea, in which case it may be associated with gonadal dysgenesis and gonadoblastoma[6].

Ovarian dysgerminoma may produce human chorionic gonadotropin (hCG) simulating a pregnancy, and patients with ovarian dysgerminoma may have elevated serum levels of lactate dehydrogenase (LDH)[2]. Serum levels of CA 125 and placental-like alkaline phosphatase (PLAP) have been found to be elevated in some cases, but CA 125 levels are often not increased in patients with ovarian dysgerminoma[2]. Mixed germ-cell tumors may produce alpha-fetoprotein (AFP) depending on the type and quantity of yolk sac tumor elements in the tumor[2].

Prognosis

Ovarian dysgerminomas have a good prognosis[6]. Gordon *et al.*[7] reported that 72 patients treated by unilateral

adnexectomy for Stage IA pure ovarian dysgerminoma had a 95% 5-year survival. The recurrence rate was 17%. Recurrences usually occur within 2 years of diagnosis and are treatable[8]. Thus, for patients with Stage IA pure ovarian dysgerminoma who wish to preserve fertility, conservative surgery (unilateral salpingo-oophorectomy and careful staging) with close follow-up is the treatment of choice. Biopsy of the contralateral ovary might be considered in patients with dysgerminoma because occult or microscopic tumor involvement occurs in 10–15% of patients[2]. A diagnosis of ovarian dysgerminoma is rarely suspected before surgery. For example, in a series of 129 patients with ovarian dysgerminoma treated between 1983 and 1992, only 29 patients (22%) underwent primary surgery in a specialized gynecological oncology center[9].

METHODS

This was a retrospective study. From the databases of each of 11 contributing ultrasound centers (listed at the end of the article) we identified 21 patients with a histological diagnosis of ovarian dysgerminoma (one patient had bilateral masses) who had undergone preoperative ultrasound examination by an experienced ultrasound examiner between 1997 and 2009: seven patients from Moscow, four from Rome, two from Milan and one from each of the other participating centers. Four (19%) of these patients were included in the International Ovarian Tumor Analysis (IOTA) study 1[10] and two (9%) were included in the IOTA study 2[11] and so had been examined using a standardized examination technique and following a strict research protocol with certain clinical and ultrasound information being prospectively collected. The remaining 15 patients had undergone a clinical ultrasound examination. All women had been examined by transvaginal ultrasound imaging supplemented with a transabdominal scan if necessary. Most examinations had been carried out using high-end ultrasound equipment, the frequency of the vaginal probes varying between 5.0 and 9.0 MHz and that of the abdominal probes between 3.5 and 5.0 MHz. 3D ultrasound was not available in all contributing centers throughout the study period. Therefore, 3D power Doppler volumes were available for three patients only. Information on presenting symptoms was retrieved retrospectively from patient records.

All clinical and ultrasound information was entered into a dedicated Excel file which was used for statistical analysis (Microsoft Office Excel 2003, Redmond, WA, USA).

Each author characterized the tumors from his/her own center on the basis of patient records, ultrasound images, ultrasound reports and research protocols (when applicable) using the terms and definitions published by the IOTA group[12]. The diagnosis suggested by the original ultrasound examiner in his/her ultrasound report was also noted. In addition, three authors (S.G., S.A., J.L.A.) reviewed all available electronic ultrasound images (gray-scale and color Doppler images being available for 18 and 14 tumors, respectively) and described them on the basis of subjective evaluation of gray-scale and color Doppler ultrasound findings in order to determine characteristic findings, if present (the so called pattern recognition)[10,13]. Pattern recognition makes it possible to detect specific ultrasound features should there be any (e.g. the 'Swiss cheese' appearance of granulosa cell tumors[14], or the struma 'pearl' of struma ovarii[15]). The description agreed by the three observers based on pattern recognition is reported. Results of Doppler examinations are reported in terms of a color score[12]. A color score of 1 means that no color or power Doppler signals were detected in the tumor, a score of 2 that a minimal amount of color Doppler signals was detected, a color score of 3 that a moderate amount was detected and a score of 4 that an abundant amount was detected[12]. Three observers re-evaluated the 3D power Doppler ultrasound volumes available to identify the characteristics of intratumoral vessels.

RESULTS

Twenty-one patients with ovarian dysgerminoma were identified (one woman with bilateral masses). Twenty patients had a primary ovarian dysgerminoma (including the one with bilateral masses) and one patient had a recurrence of dysgerminoma in her retained ovary. One of the 21 patients was pregnant. All tumors except one were pure dysgerminomas, one being a mixed germinal cell tumor with 30% dysgerminoma component.

All patients were of fertile age (median age 20 years, range, 16–31). Information on clinical symptoms was available for 18 patients. Four patients were asymptomatic (incidental finding), whereas the remaining 14 patients presented with one or more of the following symptoms: acute pain ($n = 4$), chronic pain ($n = 8$), bloating ($n = 8$), menstrual disorders ($n = 5$), infertility problems ($n = 1$). Results of serum CA 125 measurements were available for 17 patients (median, 67 U/mL, range, 13–332 U/mL), 11 (65%) having values > 35 U/mL and 9 (53%) having values > 65 U/mL. Information on specific biochemical markers of ovarian dysgerminoma (LDH, hCG, AFP) was available in few patients. For these reasons, the data have been not reported.

The sonographic characteristics of ovarian dysgerminoma as reported from each contributing center, and the diagnosis suggested by the original ultrasound examiner are presented in Table 1. The results show that all but one dysgerminoma were purely solid tumors. Half of the patients had fluid in the pouch of Douglas (a common and unspecific ultrasound finding in women of fertile age) and one had ascites. All but one (93%) of the 14 dysgerminomas for which information on the color score was available manifested moderate (43%) or abundant (50%) color content.

The three observers evaluating the gray-scale and power Doppler ultrasound images agreed in their

Table 1 Ultrasound findings in ovarian dysgerminoma ($n = 22$) described using the terms and definitions of the International Ovarian Tumor Analysis (IOTA) group[12] and diagnosis suggested by the original ultrasound examiner

Ultrasound findings/ultrasound diagnosis	*Median (range) or* n *(%)*
Largest diameter (mm)	118 (40–210)
Type of tumor	
Multilocular–solid	1 (5)
Solid	21 (95)
Number of locules	
0	21 (95)
4	1 (5)
Largest solid component (mm)	118 (40–210)
Incomplete septa	0 (0)
Number of papillations	
0	21 (95)
≥ 3	1 (5)
Irregular papillations	1 (5)
Irregular wall	4 (18)
Shadowing	0 (0)
Echogenicity of cyst fluid	
Anechoic	1 (5)
No cyst fluid	21 (95)
Fluid in the pouch of Douglas	11 (50)
Ascites	1 (5)
Doppler findings: color score*	
1	0
2	1 (7)
3	6 (43)
4	7 (50)
Diagnosis suggested by ultrasound examiner: probability of malignancy†	
Certainly benign	2 (9)
Probably benign	1 (5)
Uncertain	0 (0)
Probably malignant	2 (9)
Certainly malignant	17 (77)
Specific diagnosis suggested by ultrasound examiner	
Primary invasive ovarian cancer	5 (22)
Metastatic cancer	1 (5)
Malignant rare tumor	13 (59)
Teratoma	2 (9)
None suggested	1 (5)

*Color score information available for 14 patients. †Information available for all 22 tumors.

descriptions of ovarian dysgerminoma and reached consensus that the 14 dysgerminomas for which both gray-scale and color/power Doppler images were available could be described as follows: 13 were purely solid tumors divided into different lobules with inhomogeneous internal echogenicity (Figures 3–5) richly vascularized at Doppler examination (Figure 6) and well defined relative to surrounding organs, and one mass was a moderately vascularized multilocular solid tumor (Figure 7). Subjective evaluation by the three independent observers of the 3D power Doppler ultrasound volumes available for three tumors revealed densely packed vessels, irregular branching, caliber changes and tortuosity of tumor vessels[16] in all three tumors (Figure 8).

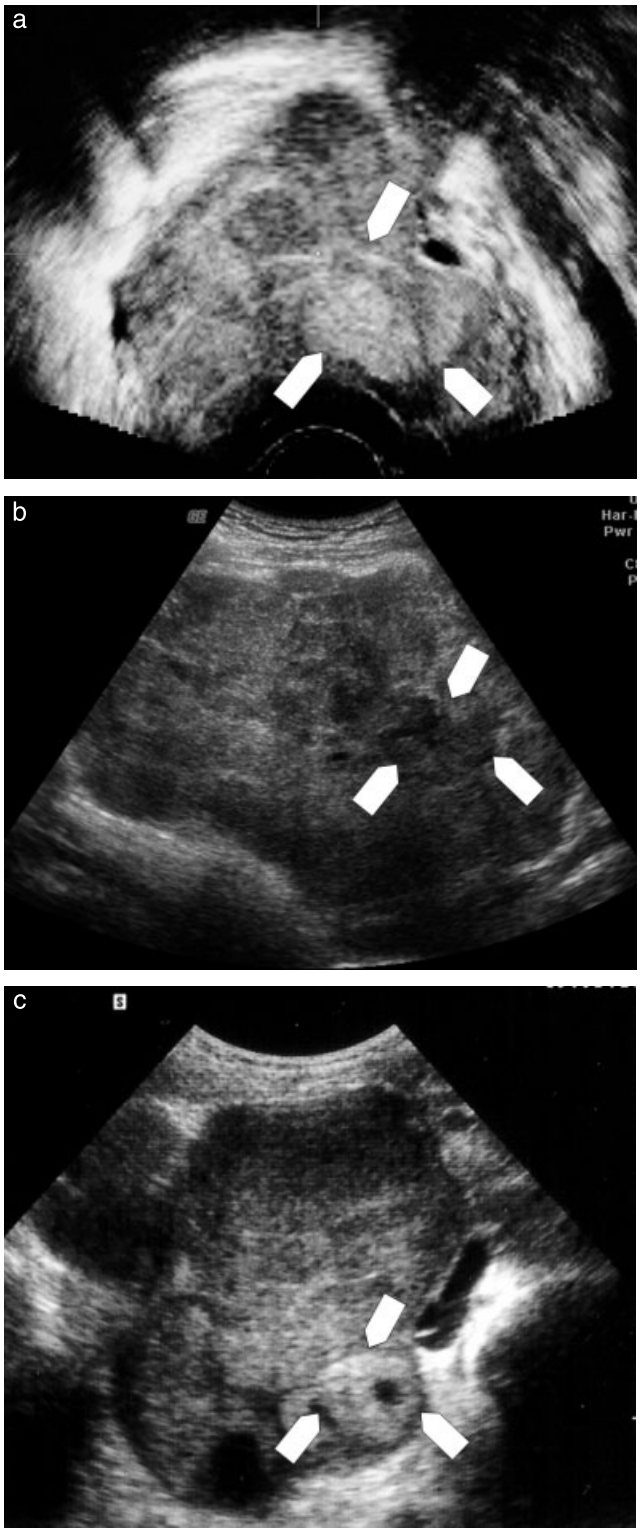

Figure 3 Gray-scale ultrasound images of three different ovarian dysgerminomas (a–c). All three are purely solid with irregular internal echogenicity and a multilobulated appearance, with well-defined lobulated but smooth contours. One lobule in each tumor is depicted between arrows.

DISCUSSION

Our results agree well with the characteristics of ovarian dysgerminoma described in textbooks of pathology and review articles[1,2,5,6], with the exception that fewer than

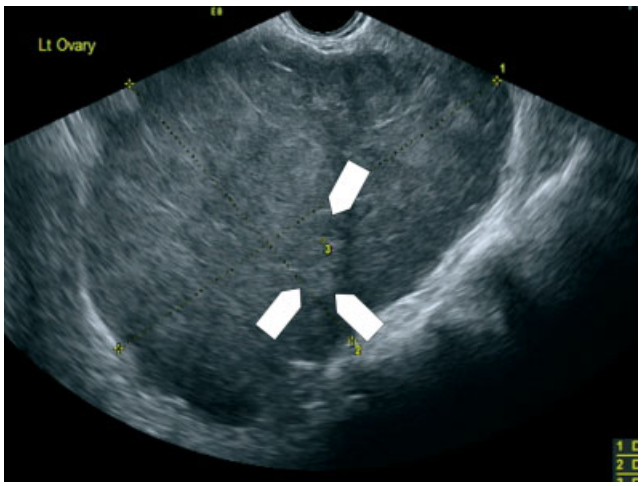

Figure 4 A large solid ovarian dysgerminoma with a less-evident multilobulated appearance (although a lobule is shown between the arrows) and smooth well-defined lobulated contour. The internal echogenicity is less irregular than that seen in many other ovarian dysgerminomas.

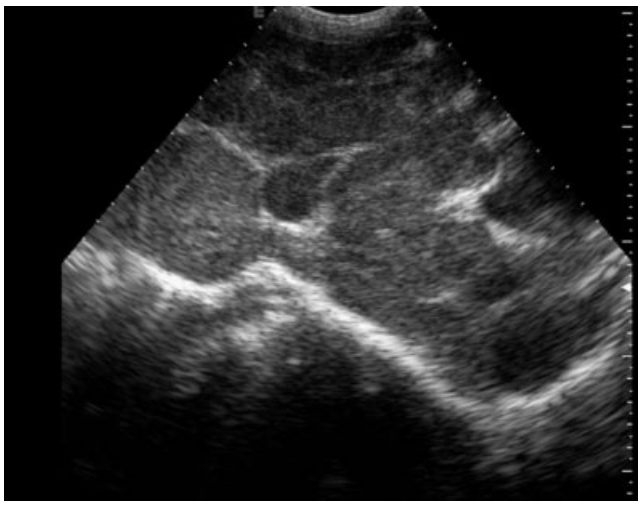

Figure 5 Multilobulated solid dysgerminoma with irregular internal echogenicity but well-defined smooth lobulated contours in a case of recurrent ovarian dysgerminoma.

expected patients had a bilateral tumor (5% vs. the expected 10–20%[5]). All patients in our study were young (16–31 years), and most were symptomatic with pain, bloating and menstrual disorders being the most common symptoms. All except one tumor (Figure 7) were purely solid (Figures 3–5) on ultrasound examination. The most characteristic ultrasound features in our series of ovarian dysgerminoma when using pattern recognition to describe the ultrasound findings was a purely solid tumor divided into different lobules, with irregular internal echogenicity, with smooth lobulated contours and well defined borders, and richly vascularized at color/power Doppler examination (Figure 6). The lobe-like ultrasound pattern of dysgerminomas might be explained by fine connective tissue containing lymphocytes separating nodules of tumor cells as described in textbooks of

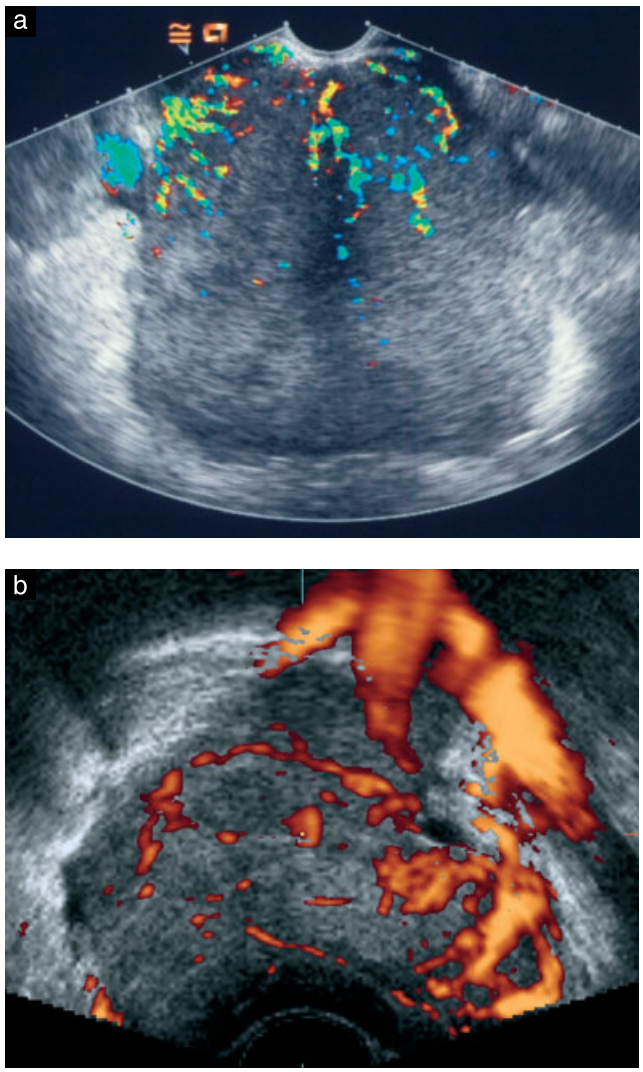

Figure 6 Two different ovarian dysgerminomas (a, b), both solid and well vascularized (color score 4) at power Doppler examination.

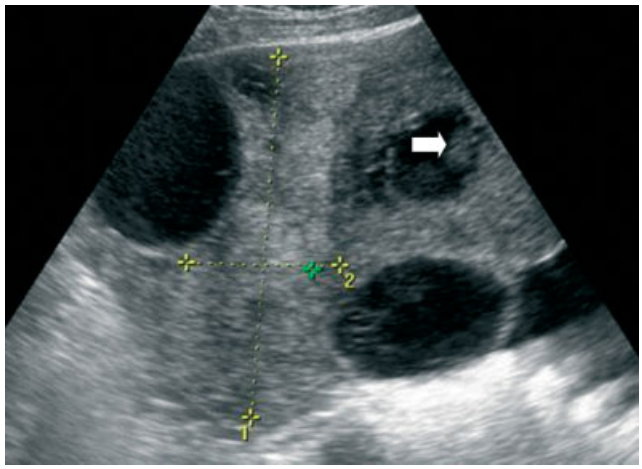

Figure 7 Less typical appearance of an ovarian dysgerminoma. The tumor is mainly solid but contains large cystic areas, some of which have irregular internal cystic borders and even a papillary projection (arrow). The contour is smooth and lobulated and the internal echogenicity is fairly regular.

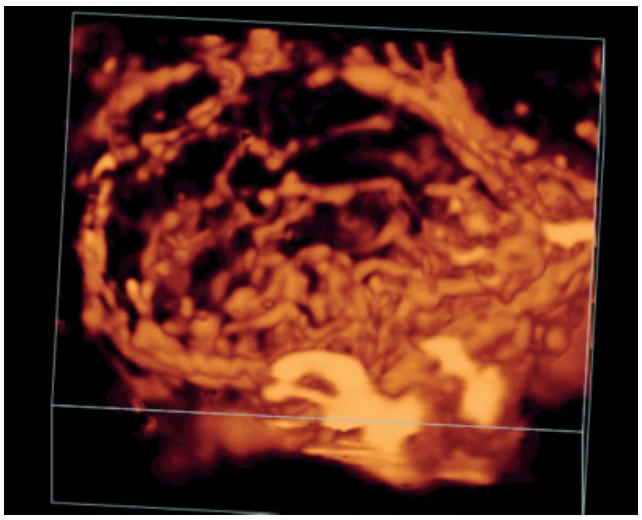

Figure 8 Three-dimensional power Doppler image showing densely packed tortuous vessels with irregular branching and caliber changes in an ovarian dysgerminoma.

pathology[5] (Figures 1 and 2). However, we cannot claim that we have found the ultrasound pattern of dysgerminomas to be distinctly different from that of other solid malignant ovarian tumors such as solid metastases or lymphoma[17]. CA 125 levels were 'normal' (i.e. below the commonly used cut-off of 35 U/mL) in one third of the patients with CA 125 results available. This supports data in the literature that CA 125 is often not raised in patients with ovarian dysgerminoma[2].

The strength of our study is that it is a large series describing the ultrasound features of a very rare type of ovarian tumor. The weakness of our study is that it is retrospective. This resulted in information on clinical data – such as symptoms and clinical findings – being incomplete, and in electronic ultrasound images not being available for all cases. There may also be bias in the retrospectively retrieved ultrasound information. We tried to overcome the limitations by using IOTA terms and definitions to describe the sonographic characteristics of the tumors[12], by using a dedicated Excel file for data entry, and by exchanging and reviewing digital ultrasound images between three independent observers.

In an extensive literature search, we found only two case reports of one and three patients, respectively, describing the sonographic appearance of ovarian dysgerminoma[18,19]. Both described dysgerminomas to be richly vascularized lobulated solid tumors at ultrasound. At magnetic resonance imaging and computed tomography, dysgerminomas also appear as lobulated solid tumors[19,20]. Several studies emphasize the multilobulated appearance of dysgerminomas with the lobules separated by septa[18,20]. The results in our series of 21 patients with ovarian dysgerminoma and those of one case report[19] suggest that it should be possible to suspect a diagnosis of ovarian dysgerminoma preoperatively. The ultrasound finding of a large, solid, lobulated adnexal mass with irregular internal echogenicity and highly vascularized at color or power Doppler ultrasound in a woman 20–30 years old should raise the suspicion of ovarian dysgerminoma: any solid adnexal tumor with ultrasound features suggestive of malignancy – i.e. with irregular internal echogenicity[21] – is more likely to be a rare type of malignancy (e.g. a dysgerminoma) or a metastasis in the ovary than a primary invasive tumor or a borderline tumor[22], and an ovarian dysgerminoma is typically a large lobulated solid tumor in a woman 20–30 years old. Analysis of hCG, AFP or LDH might be helpful for making a correct diagnosis before surgery[2]. The concomitant presence of a positive pregnancy test[18] should increase the suspicion of ovarian dysgerminoma. However, in our series, a preoperative diagnosis of ovarian dysgerminoma was not suggested in any case, but a preoperative diagnosis of 'rare malignant tumor' was made by the original ultrasound examiner in 59% (13/22) of the tumors.

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