Quiz

Correct answer to the quiz. Check your diagnosis

Case report

Ovarian Sertoli-Leydig cell tumour with α-fetoprotein-producing intestinal glandular cells. Clinical case and short review of basic literature

Michał Strus[1], Agnieszka Rajtar-Ciosek[1], Robert Jach[1], Jerzy Hankus[2], Wojciech Szczepański[2]

[1]Clinical Department of the Clinic of Endocrine Gynaecology, Jagiellonian University Medical College, Krakow, Poland
[2]Department of Pathomorphology, Jagiellonian University Medical College, Krakow, Poland

Sertoli Leydig cell tumor of the ovary, is a rare neoplasm from the group of sex cord-stromal tumors of the ovary, accounting for less than 1% of all ovarian tumors. Among the Sertoli Leydig cell tumors, we distinguish a separate group of tumors secreting α-fetoprotein (AFP). The young 24-year-old woman presented to the Clinical Department of Gynaecological Endocrinology at the University Hospital in Krakow due to secondary amenorrhea, hirsutism and worsening abdominal pain for several months. During the admission draws attention was drawn to the abnormal level of testosterone, AFP and the revised structure of the ovary in the ultrasound. After a preliminary diagnosis, expanded pelvic MRI was performed, which found an isolated tumor derived from Sertoli Leydig cells. The patient was enrolled to unilaterally remove the right ovary by laparotomy. Histopathological examination and immunohistochemical staining confirmed the diagnosis of Sertoli Leydig cells tumor, and in pathological examination we found glandular mucosa cells of the colon. Owing to scientific reports on the stromal tumors of the ovary, we decided to perform genetic testing and verify the patient's karyotype. In the follow-up 90 days after the surgery, levels of testosterone and AFP were correct. In case of Sertoli Leydig cell tumors, especially in young women of childbearing potential, special attention should be paid to Anti-Mullerian hormone testing before surgery, as well as genetic diagnostics to exclude disorders of sex development.

Key words: Sertoli-Leydig cell tumour, α-fetoprotein, colonic glandular cells.

Introduction

Sertoli-Leydig cell tumours (SLCTs) are rare, unilateral neoplasms of the stroma of the ovary constituting less than 1% of all ovarian neoplasms. Within SLCTs we may differentiate a separate group of neoplasms that secrete α-fetoproteins (AFP). Histopathogenesis and further prognosis in case of

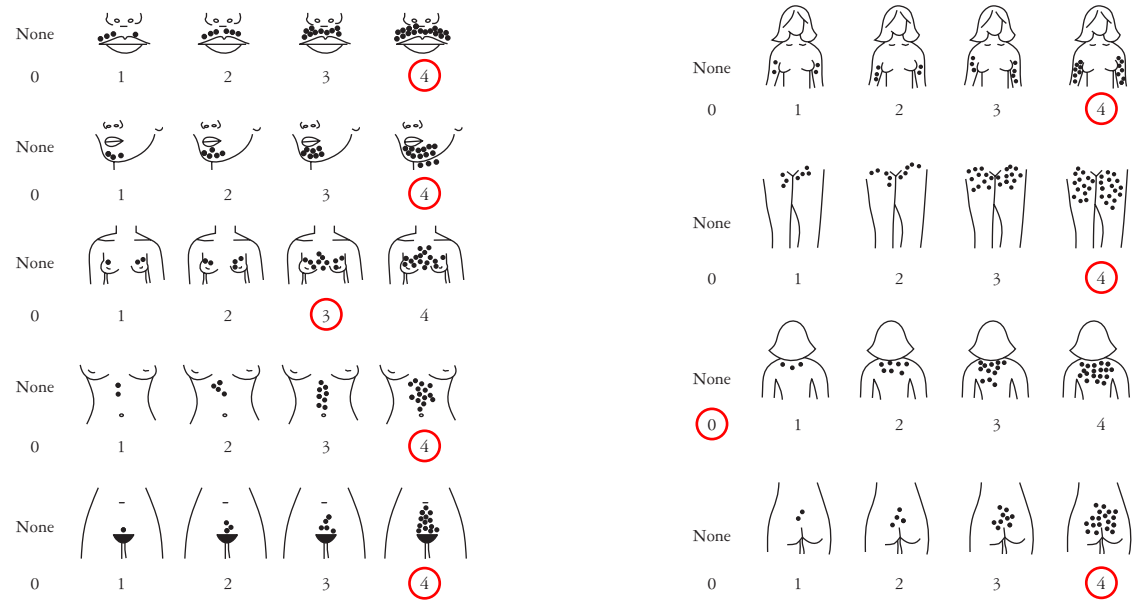

Fig. 1. The patient estimated her symptoms using Ferriman-Gallwey score, before surgery

α-fetoprotein-producing SLCTs were not conclusively investigated, but one has to take into account the potential role of gene mutations (e.g. DICER1 on chromosome Y) in the diagnostics of this inhomogeneous group of neoplasms. To make a correct diagnosis, many factors have to be considered, including clinical signs and symptoms, immunohistochemical analysis and imaging results. The aim of this quiz was to present a case of a young female patient, who presented with hyperandrogenism and secondary amenorrhoea.

Case report

A 24-year old female patient reported to the Clinic of Endocrine Gynaecology at the University Hospital in Krakow with symptoms of secondary amenorrhoea, hirsutism (31 points in Ferriman-Gallwey score) and increasing lower abdominal pains of several months' duration. The last spontaneous menstruation occurred over 3 years ago.

During the first hospitalization, a set of basic diagnostic tests was performed. Detailed analyses of hormonal levels as well as tumour markers pointed to significantly elevated testosterone levels (8.16 nmol/l – with norms between 0.29-1.67 nmol/l) and α-fetoprotein levels (10.02 IU/ml – with norms 0.0-5.8 IU/ml). Values of other parameters such as: cancer antigen 125 (CA-125), carbohydrate antigen 19-9 (CA 19-9) and carcinoembryonic antigen (CEA) were normal.

Furthermore, the extent of hirsutism was evaluated using the 36 degree Ferriman-Gallwey scoring system, where the value below 8 points is correct. The woman self-assessed her symptoms of hirsutism with a score of 31 points and this value confirmed the androgen excess (Fig. 1).

Imaging study results

During hospitalization an ultrasound examination of the abdomen was performed. An echogenically changed structure of the right ovary was noted, measuring 42 × 27 mm (Fig. 2), with no clear demarcation of the tumour, showing signs of increased peripheral vascularisation (Fig. 3).

Owing to low sensitivity of the ultrasound, pelvic magnetic resonance imaging (MRI) was performed. The MRI showed a well demarcated solid-cystic tumour measuring 44 × 32 × 40 mm, with small cystic spaces of 5 mm in diameter, localized in the posterior part of the right ovary. The lesion was adherent to the uterine cervix, bulging into the Douglas pouch and partially abutting the rectal wall. Considering the imaging study results and the clinical data, there was a high probability for the lesion to be a Sertoli-Leydig cell tumour or thecoma or fibroma or granulosa cell tumour.

Surgical procedure

The patient was qualified to undergo a laparotomy and unilateral removal of the right ovary (Fig. 4). Owing to the young age and nulliparity, it was of highest concern to preserve patient's fertility – so it was necessary to perform ovary reserve testing, which before the procedure was 6.0 ng/ml. On the day of the procedure, the control value of testosterone was 10.81 nmol/l (normal values: 0.29-1.67 nmol/l),

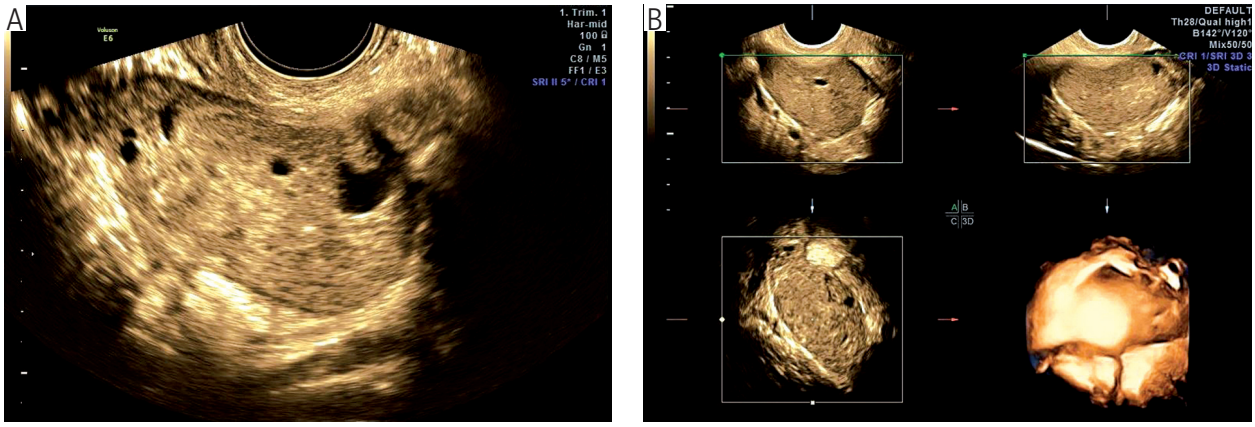

Fig. 2. Echogenically changed structure of the right ovary

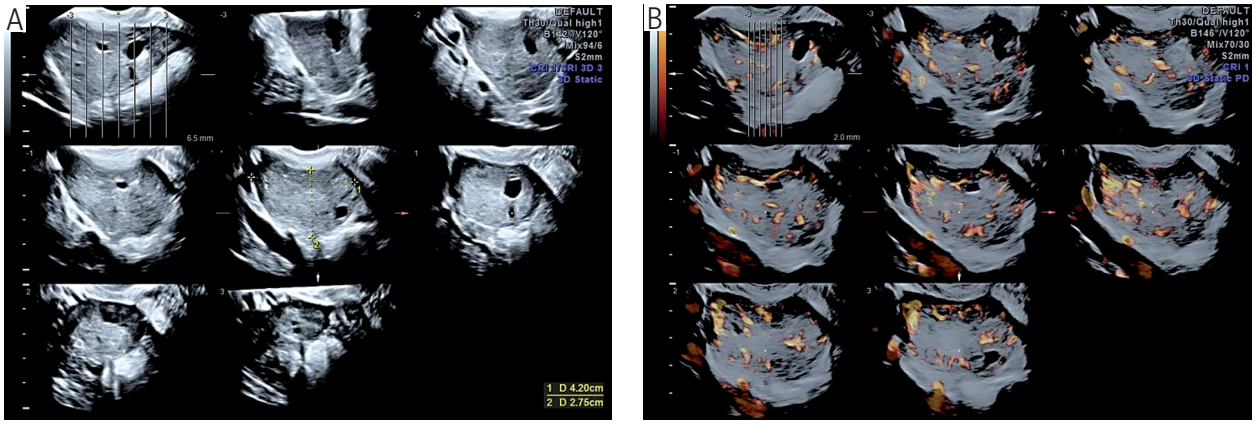

Fig. 3. Increased peripheral vascularisation of tumour

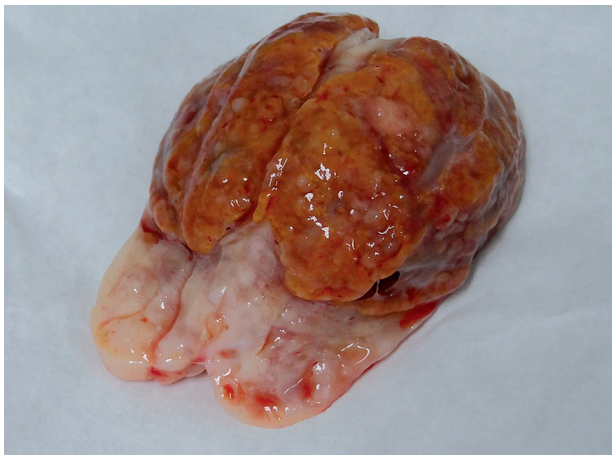

Fig. 4. Intraoperative images showing tumour of the right ovary

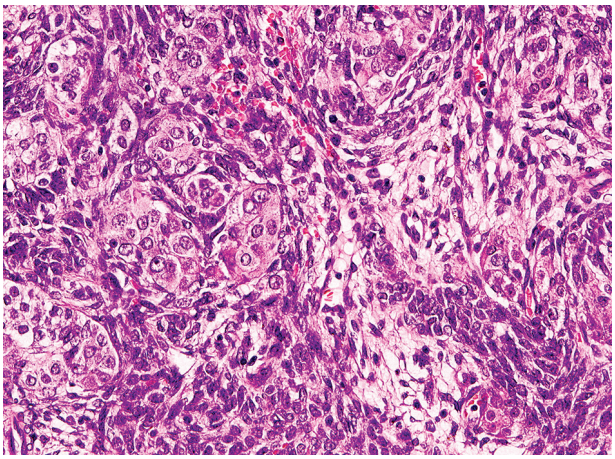

Fig. 5. Nests of Leydig cells (pale cells with abundant cytoplasm) are surrounded by poorly differentiated, sarcomatoid-like Sertoli cells. HE (magnification information is lacking on the microphotographs)

which meant an increase of about 2.65 nmol/l over 30 days, since the first hospital admission.

During the procedure, the right ovary was removed using a classical approach and then a frag-

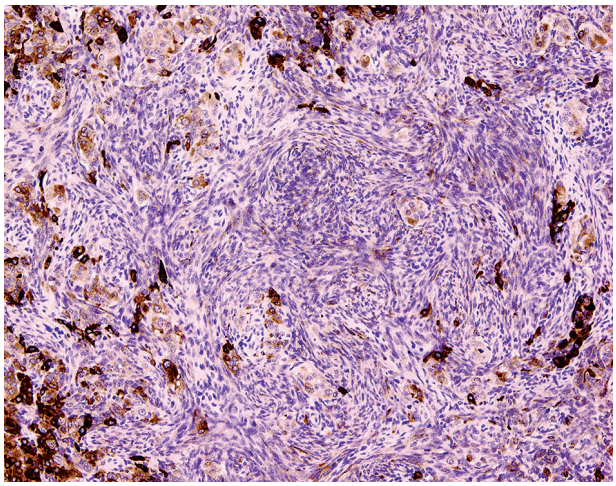

Fig. 6. Positive inhibin stain is seen in the sex cord elements

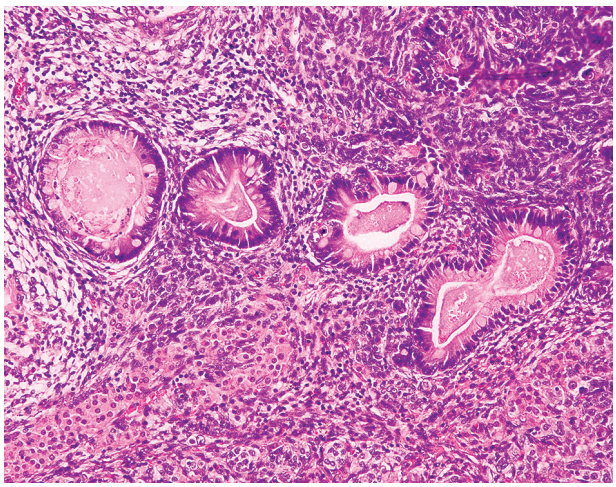

Fig. 7. Heterologous elements conform to glands lined by intestinal type epithelium

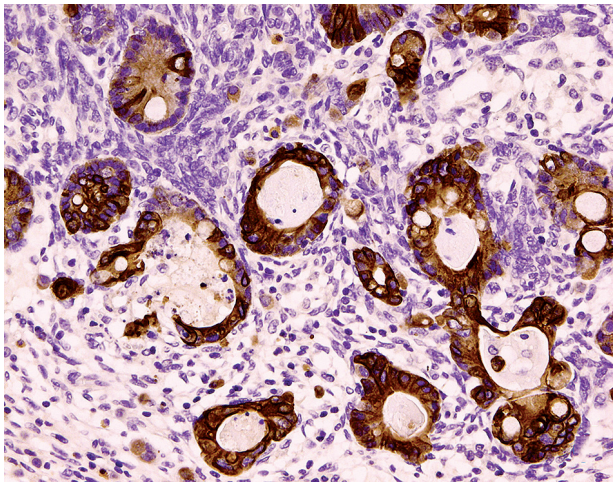

Fig. 8. Positive CK20 stain in the intestinal epithelium

ment of the left ovary and peritoneum were collected for further pathological examination.

The procedure and postoperative period were tolerated well and the patient was discharged home on the fifth day of hospitalization.

Results of histopathological studies

Histopathological and immunohistochemical studies confirmed the initial diagnosis of Sertoli-Leydig cell tumour (Figs. 5 and 6). Such neoplasms may be divided basing on histopathological examination into three main subtypes: well, intermediately and weakly differentiated. Two last categories may additionally include ~20% of heterologous elements, most of them being glands and cysts lined with intermediately or well differentiated gastric or intestinal epithelium. In the presented case, next to Sertoli-Leydig cells, the structure of the tumour included glandular cells from of the colonic epithelium (Figs. 7 and 8). The fragment from the left ovary did not show any pathological finding.

Follow-up visits

During the first follow-up 10-days after the surgical procedure, biochemical laboratory test results normalized, with testosterone 0.50 nmol/l (norms: 0.29-1.67 nmol/l) and AFP 3.12 IU/ml (norms: 0.0-5.8 IU/ml). The patient was in good general condition and had no complaints. The last follow-up visit was 90 days after the procedure. Laboratory test results were still normal for her age and sex, with testosterone value of 0.53 nmol/l and AFP at 0.98 IU/ml. Additionally the patient reported spontaneous menses. During the last follow-up visit, hirsutism was again evaluated using Ferriman-Gallwey score reaching 13 points with results shown in Figure 9 and anti-Müllerian hormone (AMH) level after removal of the right ovary was 4.7 ng/ml.

Discussion and conclusions

We presented a case of Sertoli-Leydig cell tumour with heterogeneous elements of glandular colonic cells producing α-fetoprotein. So far the medical literature lists approximately 30 similar cases [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. Sertoli-Leydig cell tumours most commonly (75%) occur in young females up to 30 years of age [26, 27]. The significant majority of them are unilateral and at the time of diagnosis they are limited to the stroma of the ovary [26, 27, 28]. 30-50% of SLCTs produce androgens (testosterone and other androgen precursors), which are responsible for signs and symptoms of androgen excess, such as oligo or amenorrhoea, hirsutism

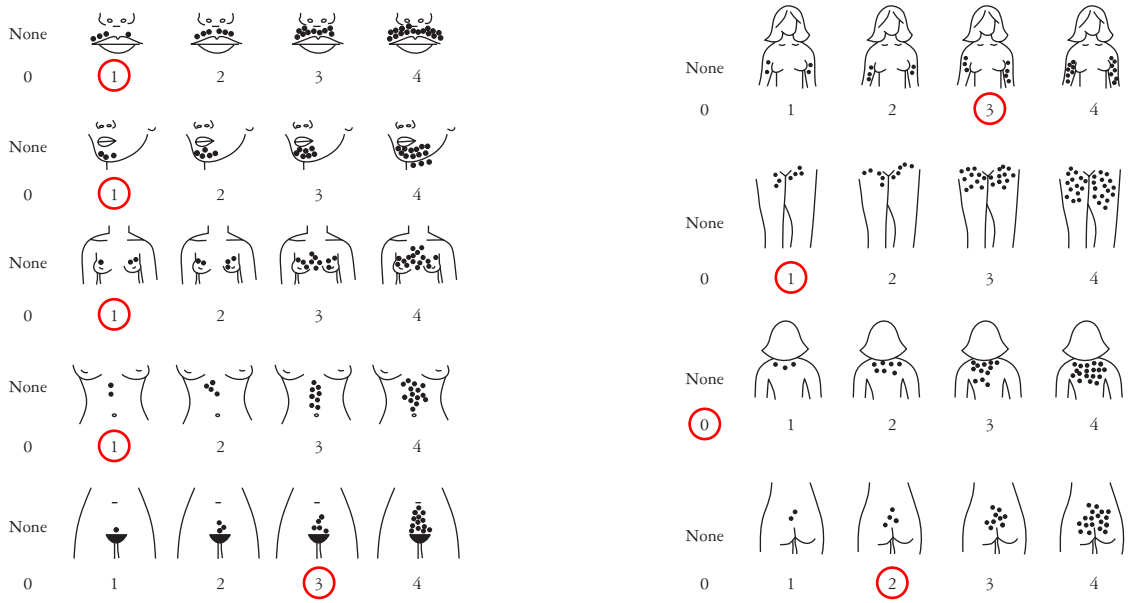

Fig. 9. The patient estimated her symptoms using Ferriman-Gallwey score, 90 days since the procedure

or acne [27, 28]. The patient described in this case had both testosterone and AFP significantly elevated during the first admission.

Moreover, there were some unspecific symptoms such as lower abdominal pains as well as normal cancer marker values. There are no uniform recommendations when it comes to Sertoli-Leydig cell type tumours and the surgical approach depends on the age of the patient, the operator's preferences and the degree of tumour differentiation [29]. In most cases, these neoplasms at the time of diagnosis are localized unilaterally and are limited to the ovary, and for patients in their reproductive age, who would prefer to stay fertile, the method of choice should be unilateral excision of the ovary with simultaneous collection of the fragments of the opposite ovary and peritoneum for pathological examination [30]. In patients with early diagnosed and excised tumorous ovary, Sertoli-Leydig cell tumours usually have a good prognosis. There are not many information on the follow-up strategy for patients after unilateral removal of the ovary, but according to The National Comprehensive Cancer Network (NCCN) guidelines related to sex cord-stromal tumours, it is recommended to perform physical and laboratory examination of tumour markers every 2-4 months in the first 2 years after the surgical procedure and every 6 months thereafter [31, 32]. There are not enough data which would stand behind periodic evaluation using imaging techniques, but in case of suspicion of recurrence, the method of choice should be computed tomography [31, 32]. In case of Sertoli-Leydig cell tumours, especially in young women of reproductive age, special emphasis should be placed on ovarian reserve testing before surgery, and also genetic diagnostics to exclude disorders of sex development.

The authors declare no conflict of interest.

References

1. Gut P, Waligórska-Stachura J, Czarnywojtek A, et al. Management of the hormonal syndrome of neuroendocrine tumors. Arch Med Sci 2017; 13: 515-524.
2. Horta M, Cunha TM, Marques RC, Félix A. Ovarian Sertoli-Leydig cell tumor with heterologous elements of gastrointestinal type associated with elevated serum alpha-fetoprotein level: an unusual case and literature review. J Radiol Case Rep 2014; 8: 30-41.
3. Jashnani KD, Hegde CV, Munot SP. Alfa-fetoprotein secreting ovarian sex cord-stromal tumor. Indian J Pathol Microbiol 2013; 56: 54-56.
4. Shu H, Yang Xh, Gao AF. Ovarian Sertoli-Leydig cell tumor in a 9-month-old infant with special histologic pattern. Fetal Pediatr Pathol 2012; 31: 388-393.
5. Poli UR, Swarnalata G, Maturi R, Rao ST. Recurrent alpha-fetoprotein secreting Sertoli-Leydig cell tumor of ovary with an unusual presentation. Indian J Cancer 2009; 46: 64-66.
6. Watanabe T, Yamada H, Morimura Y, et al. Ovarian Sertoli-Leydig cell tumor with heterologous gastrointestinal epithelium as a source of alpha-fetoprotein: a case report. J Obstet Gynaecol Res 2008; 34: 418-421.
7. Jang KT, Park HR, Kim DH, Kim CM. Alfa-fetoprotein producing Sertoli-Leydig cell tumor of the ovary: A case report. Korean J Pathol 2002; 36: 128-131. Available at: www.koreanjpathol.org/upload/journal/2002/2002_0128.pdf.
8. Mooney EE, Nogales FF, Tavassoli FA. Hepatocytic differentiation in retiform Sertoli-Leydig cell tumors: distinguishing a heterologous element from Leydig cells. Hum Pathol 1999; 30: 611-617.

9. Golbang P, Khan A, Scurry J, et al. Cervical sarcoma botryoides and ovarian Sertoli-Leydig cell tumor. Gynecol Oncol 1997; 67: 102-106.
10. Singh ZN, Singh MK, Chopra P. Sertoli-Leydig cell tumor with malignant heterologous elements and raised alpha-fetoprotein: a case report. J Obstet Gynaecol Res 1996; 22: 595-598.
11. Hammad A, Jasnosz KM, Olson PR. Expression of alpha-fetoprotein by ovarian Sertoli-Leydig cell tumors. Case report and review of the literature. Arch Pathol Lab Med 1995; 119: 1075-1079.
12. Amato G, Izzo G, Izzo A. A paradoxical inhibition of androgenic hyperproduction by a Sertoli-Leydig cell tumour ovary. Hum Reprod 1995; 10: 2967-2969.
13. Farley JH, Taylor RR, Bosscher JR. Late presentation of an alpha-fetoprotein secreting isolated large upper abdominal retroperitoneal Sertoli-Leydig cell tumor recurrence. Gynecol Oncol 1995; 56: 319-322.
14. Larsen WG, Felmar EA, Wallace ME, Frieder R. Sertoli-Leydig cell tumor of the ovary: a rare cause of amenorrhea. Obstet Gynecol 1992; 79 (5 Pt 2): 831-833.
15. Ohyama N, Yamamoto Y, Tanaka K, et al. A case of ovarian Sertoli-Leydig cell tumor associated with high serum alpha-fetoprotein (AFP) concentration. Nihon Sanka Fujinka Gakkai Zasshi 1990; 42: 637-640.
16. Motoyama I, Watanabe H, Gotoh A, et al. Ovarian Sertoli-Leydig cell tumor with elevated serum alpha-fetoprotein. Cancer 1989; 63: 2047-2053.
17. Gagnon S, Têtu B, Silva EG, McCaughey WT. Frequency of alpha-fetoprotein production by Sertoli-Leydig cell tumors of the ovary: an immunohistochemical study of eight cases. Mod Pathol 1989; 2: 63-67.
18. Taniyama K, Suzuki H, Hara T, et al. An alpha-fetoprotein producing Sertoli-Leydig cell tumor – a case report. Gan No Rinsho 1989; 35: 107-113.
19. Chadha S, Honnebier WJ, Schaberg A. Raised serum alpha-fetoprotein in Sertoli-Leydig cell tumor (androblastoma) of ovary: report of two cases. Int J Gynecol Pathol 1987; 6: 82-88.
20. Tiltman A, Dehaeck K, Soeters R, et al. Ovarian Sertoli-Leydig cell tumour with raised serum alpha fetoprotein. A case report. Virchows Arch A Pathol Anat Histopathol 1986; 410: 107-112.
21. Tetu B, Ordóñez NG, Silva EG. Sertoli-Leydig cell tumor of the ovary with alpha-fetoprotein production. Arch Pathol Lab Med 1986; 110: 65-68.
22. Mann WJ, Chumas J, Rosenwaks Z, et al. Elevated serum alpha-fetoprotein associated with Sertoli-Leydig cell tumors of the ovary. Obstet Gynecol 1986; 67: 141-144.
23. Sekiya S, Inaba N, Iwasawa H, et al. AFP-producing Sertoli-Leydig cell tumor of the ovary. Arch Gynecol 1985; 236: 187-196.
24. Young RH, Perez-Atayde AR, Scully RE. Ovarian Sertoli-Leydig cell tumor with retiform and heterologous components. Report of a case with hepatocytic differentiation and elevated serum alpha-fetoprotein. Am J Surg Pathol 1984; 8: 709-718.
25. Chumas JC, Rosenwaks Z, Mann WJ, et al. Sertoli-Leydig cell tumor of the ovary producing alpha-fetoprotein. Int J Gynecol Pathol 1984; 3: 213-219.
26. Benfield GF, Tapper-Jones L, Stout TV. Androblastoma and raised serum alpha-fetoprotein with familial multinodular goitre. Case report. Br J Obstet Gynaecol 1982; 89: 323-326.
27. Tanaka YO, Tsunoda H, Kitagawa Y, et al. Functioning ovarian tumors: direct and indirect findings at MR imaging. Radiographics 2004; 24 (Suppl 1): S147-S166.
28. Outwater EK, Wagner BJ, Mannion C, et al. Sex cord-stromal and steroid cell tumors of the ovary. Radiographics 1998; 18: 1523-1546.
29. Pratt J. Pathology of the Ovary. 1st ed. Germ cell tumours sex cord-stromal tumors. Sounders, Philadelphia 2004; 219-225, 261-262.
30. Bhat RA, Lim YK, Chia YN, Yam KL. Sertoli-Leydig cell tumor of the ovary: analysis of a single institution database. J Obstet Gynaecol Res 2013; 39: 305-310.
31. Gui T, Cao D, Shen K, et al. A clinicopathological analysis of 40 cases of ovarian Sertoli-Leydig cell tumors. Gynecol Oncol 2012; 127: 384-389.
32. Salani R, Backes FJ, Fung MF, et al. Posttreatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations. Am J Obstet Gynecol 2011; 204: 466-478.
33. Morgan RJ, Jr, Alvarez RD, Armstrong DK, et al. National comprehensive cancer networks. Ovarian cancer, version 2.2013. J Natl Compr Canc Netw 2013; 11: 1199-1209.

Address for correspondence

Robert Jach
Clinical Department of the Clinic of Endocrine Gynaecology
Jagiellonian University Medical College
Kopernika 23
31-531 Krakow, Poland
e-mail: jach@cm-uj.krakow.pl