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Advanced stage yolk sac ovarian tumour: clinical approach with cytoreductive surgery upfront

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Summary

The authors report the case of a 21-year-old woman that presented a Pseudo Meigs' syndrome, secondary to a pure endodermal sinus tumour (yolk sac tumour). Fine needle aspiration biopsy was compatible with high-grade carcinoma and the alpha fetoprotein (αFP) was at 13,185 U/ml. Cytoreductive surgery was performed, followed by bleomycin, etoposide, and cisplatin (BEP) chemotherapy.

Key words: Yolk sac ovarian tumour; Endodermal sinus ovarian tumour.

Introduction

Malignant ovarian germ cell tumours (MOGCT) only comprise 2–3% of all ovarian cancers, but are the most common type at childbearing age [1]. These tumours are often divided into dysgerminona and nondysgerminona, being yolk sac tumour (YST) the second most common germinal malignancy, after dysgerminona [2]. YST is almost always unilateral, meaning that fertility- sparing surgery should always be considered [3-5]. Although these are very aggressive neoplasms, their high chemosensitivity confers an excellent prognosis at all stages [6].

In this report the authors describe the case of a young woman with a pure YST advanced stage disease, and discuss the potential benefit of an upfront cytoreductive surgery.

Case Report

A 21-year-old woman with no relevant medical history was admitted in her local hospital with respiratory distress, cough, and abdominal distension. The first suspicion was right lung pneumonia, but the CT scan showed a pelvic mass dependent from the right ovary, ascites, and right pleural effusion (Pseudo Meigs' syndrome). The serum marker αFP was at 3,798 U/ml with normal β-human chorionic gonadotropin (hCG). The aspiration biopsy of the right ovary mass was compatible with high-grade carcinoma, and she was then referred to the present authors' institution.

New analyses of the serum marker αFP was performed and levels were at 13,185 U/ml. Furthermore, after a positron emission tomography (PET-CT) imaging, a heterogeneous pelvic mass with 22×21 cm, with an important cystic component, compromising the ureters (SUV 20.3) was revealed (Figure 1). There were also multiple peritoneal implants, ascites and bilateral pleural effusion, more pronounced at the right side, occupying two-thirds of the right hemithorax (Figure 2). There was no metabolic activity on the pleura.

After discussion in the tumor board, the patient underwent an exploratory laparotomy. Surgical findings included a volume mass arising from the right ovary and centimetre tumour nodules on the omentum, pelvic peritoneum, and right diaphragm, represented Stage IIIB disease. A surgical procedure included right adnexectomy (including the ovarian mass), radical omentectomy, pelvic peritonectomy, and appendicectomy, completing a fertility-sparing and suboptimal cytoreductive procedure (residual disease on the right diaphragm of less than one cm diameter).

The pathological report showed a high-grade malignant neoplasia, with extensive necrosis and haemorrhagic areas, micro- and macro-cystic pattern with solid focal component. Severe atypia and numerous mitotic figures with immunoreactivity for αFP (Figures 3 and 4), and absent immunoreactivity for placental-like alkaline phosphatase (PLAP), cytokeratin 7 (CK7), estrogen receptor (ER) and Wilms' Tumor 1 (WT1) protein, were observed, confirming the diagnosis of a pure YST. There was also tumoral infiltration of the omentum and pelvic peritoneum. The cytological analysis of the ascitic fluid was negative for malignancy.

Two weeks after surgery, the αFP was at 1,150 U/ml and the pleural effusion and ascites were resolved. The approach here described continued with chemotherapy with bleomycin, etoposide, and cisplatin (BEP) regimen plus LHRH analogues, with serologic and clinical complete remission after two cycles. The patient was proposed to receive two more cycles, as consolidative treatment.

Discussion

YST commonly presents with non-specific symptoms as abdominal pain, being pseudo Meigs' syndrome a rare presentation. The authors discussed the case of a pure YST presented with ascites and right hydrothorax, defined as pseudo-Meigs' syndrome, as a way to differentiate it from the conventional Meigs' syndrome. Meigs' syndrome is defined as the triad of benign ovarian fibroma, ascites, and

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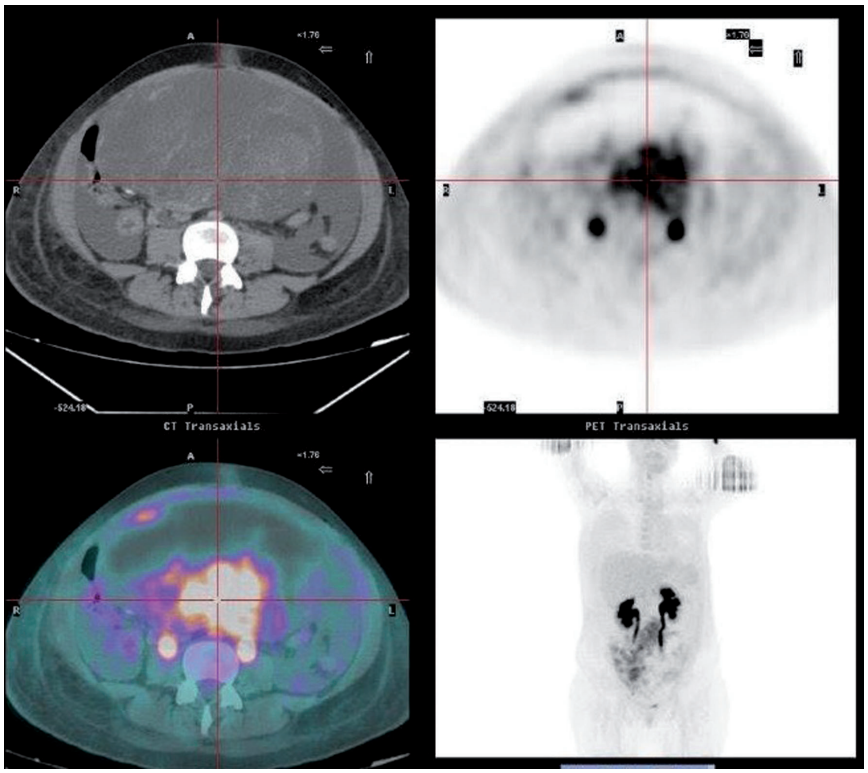

Figure 1. — 18F-FDG-PET and CT transaxial images showing the large pelvic mass with high metabolic activity (SUV 20.3), compressing the ureters.

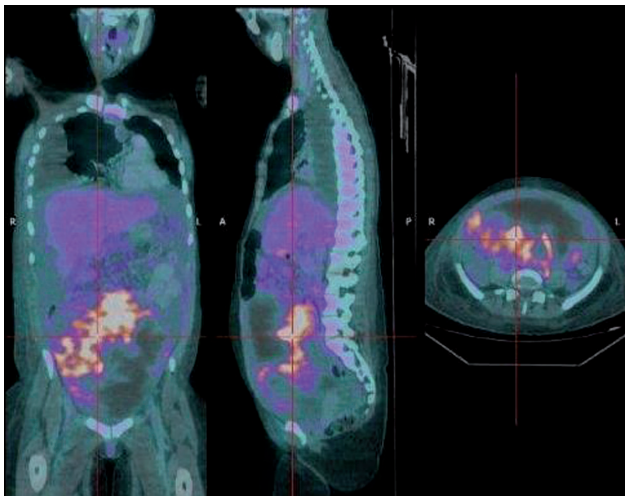

Figure 2. — 18F-FDG-PET-CT coronal and sagittal images revealing the peritoneal carcinomatosis, ascites, and high volume right-sided pleural effusion. The pleura show no metabolic activity.

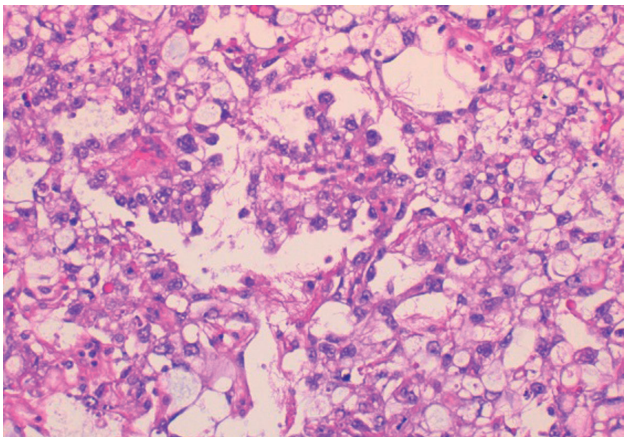

Figure 3. — H&E, ×20. Atypia and mitotic figures with a Schiller-Duval body and hyaline globules.

pleural effusion that resolves after tumour resection. The reason for the pleural effusion development seems to be related with the constitution of the diaphragm, as it has minute foramina and lymphatic channels through which ascitic fluid can pass [7].

In the case here described, the authors identified a malignant ovarian tumour with ascitic fluid negative for malignancy, and right pleural effusion that resolved after surgery, indicating a case of Pseudo Meigs' syndrome. As the patient was so frail at admission, showing respiratory distress due to the large right-sided pleural effusion, she needed a pleural drainage before considering debulking surgery. Upfront debulking surgery instead of neoadjuvant chemotherapy was indicated as the first therapy, based on the evidence listed below and the risk of intestinal obstruction, due to the large pelvic mass described in the PET-CT.

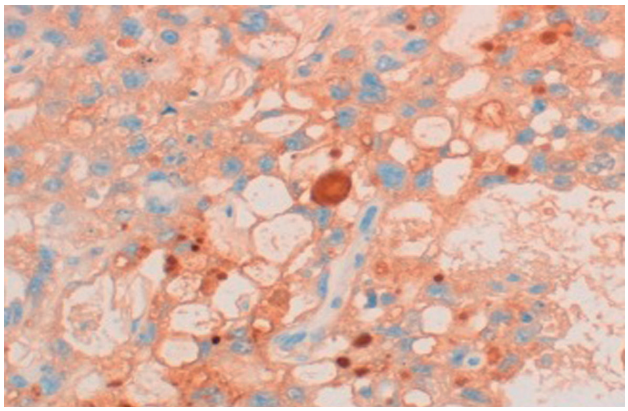

Figure 4. — Positive immunohistochemical staining for αFP.

Two studies with MOGCT reported the benefit from minimal residual disease after primary surgical cytoreduction with platinum-based chemotherapy regimens. Williams *et al.* study in which patients received BEP chemotherapy, patients who had no measurable disease after primary surgery had a greater likelihood of remaining progression-free than those with measurable disease (68% *vs.* 34%) [6,8]. In Lee *et al.* study, the residual tumour after salvage surgery was found to be significantly associated with the risk of primary treatment failure ($p < 0.0001$) [9]. These studies indicate that tumour-reductive surgery strongly affect prognosis, even when cisplatin-based chemotherapy is administered**.**

The prognostic factors of YST have already been reported in retrospective studies, but combining platinum and non platinum chemotherapy regimens. In the study from Nawa *et al.*, 47 YST cases were analyzed. Patients with residual tumour less than two cm had a five-year survival rate of 78% compared to 29.2% if residual disease was > two cm ($p < 0.01$) [10]. In the study of Kawai *et al.*, 29 YST cases were analyzed and the five-year survival rates for patients with no residual disease and residual tumor > two cm were, respectively, 82% and 36% ($p < 0.003$), suggesting that optimal cytoreductive surgery should be performed [6, 11].

As previously referred, MOGCT are highly chemosensitive tumours, being BEP the best chemotherapy regimen. It was found to be active in patients with testicular cancer, and was then experimented in patients with ovarian germ cell tumors, with excellent activity [6, 8, 12].

The best number of chemotherapy cycles is still not defined. The Gynecologic Oncology Group trial considered three cycles of BEP as the gold standard for first line treatment, and four cycles should be considered when there is residual disease after surgery, as in the present case [8, 12].

Although there are many studies that reported regular menstrual cycles and normal pregnancies after chemotherapy, in the present case, LHRH analogues were administered as a way to preserve the fertility potential [13, 14].

In conclusion, although there are no randomized data and the studies report patients treated with different chemotherapy regimens, it seems that the amount of residual disease impact prognosis, even when cisplatin based chemotherapy is administered. In the case here presented, the selected strategy was based on an individualized approach, always taking into account a curative intent, regardless the tumour stage.

References

[1] DeVita V., Lawrence T., Rosenberg S.: "Principles and Practice of Oncology". 9th ed. Philadelphia: Lippincott Williams & Wilkins, 2011 104, 1386.

[2] Fujita M., Inoue M., Tanizawa O., Minagawa J., Yamada T., Tani T.: "Retrospective review of 41 patients with endodermal sinus tumor of the ovary". *Int. J. Gynecol Cancer*, 1993, *3*, 329.

[3] Wu P.C., Huang R.L., Lang J.H., Huang H.F., Lian L.J., Tang M.Y.: "Treatment of malignant ovarian germ cell tumors with preservation of fertility: a report of 28 cases". *Gynecol. Oncol.*, 1991, *40*, 2.

[4] Dällenbach P., Bonnefoi H., Pelte M.F., Vlastos G.: "Yolk sac tumours of the ovary: an update". *Eur. J. Surg. Oncol.*, 2006, *32*, 1063.

[5] Berman M.L.: "Future directions in the surgical management of ovarian cancer". *Gynecol. Oncol.*, 2003, *90*, 33.

[6] Pectasides D., Pectasides E., Kassanos D.: "Germ cell tumors of the ovary" *Cancer Treat. Rev.*, 2008, *34*, 427.

[7] Kazanov L., Ander D.S., Enriquez E., Jaggi F.M.: "Pseudo-Meigs' syndrome". *Am. J. Emerg. Med.*, 1998, *16*, 404.

[8] Williams S., Blessing J.A., Liao S.Y., Ball H., Hanjani P.: "Adjuvant therapy of ovarian germ cell tumors with cisplatin, etoposide and bleomycin: a trial of the Gynecology Oncology Group". *J. Clin. Oncol.*, 1994, *12*, 701

[9] Lee C.W., Song M.J.., Park S.T., Ki E.Y., Lee S.J., Lee K.H., *et al.*: "Residual tumor after the salvage surgery is the major risk factors for primary treatment failure in malignant ovarian germ cell tumors: A retrospective study of single institution". *World J. Surg, Oncol.*, 2011, *9*, 123.

[10] Nawa A., Obata N., Kikkawa F., Kawai M., Nagasaka T., Goto S., *et al.*: "Prognostic factors of patients with yolk sac tumors of the ovary". *Am. J. Obstet. Gynecol.*, 2001, *184*, 1182.

[11] Kawai M., Kano T., Furuhashi Y., Mizuno K., Nakashima N., Hattori S.E., *et al.*: "Prognostic factors in yolk sac tumors of the ovary. A clinicopathologic analysis of 29 cases". *Cancer*, 1991, *67*, 184.

[12] Gershenson D.M., Morris M., Cangir A., Kavanagh J.J, Stringer C.A., Edwards C.L., *et al.*: "Treatment of malignant germ cell tumors of the ovary with bleomycin, etoposide, and cisplatin". *J. Clin. Oncol.*, 1990, *8*, 715.

[13] Gershenson D.M.: "Menstrual and reproductive function after treatment with combination chemotherapy for malignant ovarian germ cell tumors". *J. Clin. Oncol.*, 1988, *6*, 270.

[14] Mitchell P.L., Al-Nasiri N., A'Hern R., Fisher C., Horwich A., Pinkerton C.R., *et al.*: " Treatment of non-dysgerminomatous ovarian germ cell tumors: an analysis of 69 cases". *Cancer*, 1999, *85*, 2232.

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