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Research Paper

Malignant ovarian germ cell tumour: Literature review about a case

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Summary:
Germ cell tumours of the ovary account for 15-20% of all ovarian tumours. They are fast-growing neoplasms that develop from the primordial germ cells of the embryonic gonad. Malignant germ cell tumours represent 5% of ovarian tumours. Their annual incidence in France is 0.5 per 100,000 women. The diagnosis, suspected on clinical examination, is based on pelvic or endo-vaginal ultrasound evidence of a large ovarian mass responsible for pelvic heaviness. It is only established during the initial surgical procedure (laparotomy). The determination of tumour markers hCG, LDH and alphaFP is also of interest for the diagnosis, prognosis and monitoring of the evolution of the disease. Surgery is the first therapeutic procedure and consists of the removal of tumour masses and should attempt to preserve reproductive function. Malignant germ cell tumours are unique among non-haematological cancers in that they can be cured by cytotoxic chemotherapy, and the introduction of cisplatin in the treatment protocols has been a decisive advance. Malignant ovarian germ cell tumours are linked to the existence of a cytogenetic characteristic common to all ovarian, testicular or extragonadal germ cell tumours in adults and children: the presence of an isochromosome in the short arm of chromosome [12i(12p)], which is not found in any other type of cancer.

Keywords: *Ovarian germ cell tumours, embryonic gonad, chorionic gonadotropin hormone (hCG), lactodehydrogenase (LDH), alpha-fetoprotein FP), isochromosome [12i(12p)*

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I. Definition:

Germ cell tumours of the ovary account for 15- 20% of all ovarian tumours. They are fast- growing neoplasms that develop from primordial germ cells from the embryonic gonad and can grow to large size in a short time. About 95% of germ cell tumours are cystic teratomas The remaining 5% are malignant germ cell tumours. The remaining 5% are malignant germ cell tumours and are the cause of the main diagnostic difficulties encountered, particularly tumours combining several histological groups. Two histological groups are distinguished: dysgerminomas (45%) (equivalent to testicular seminomas) and non-dysgerminomatous (non-seminomatous) tumours.

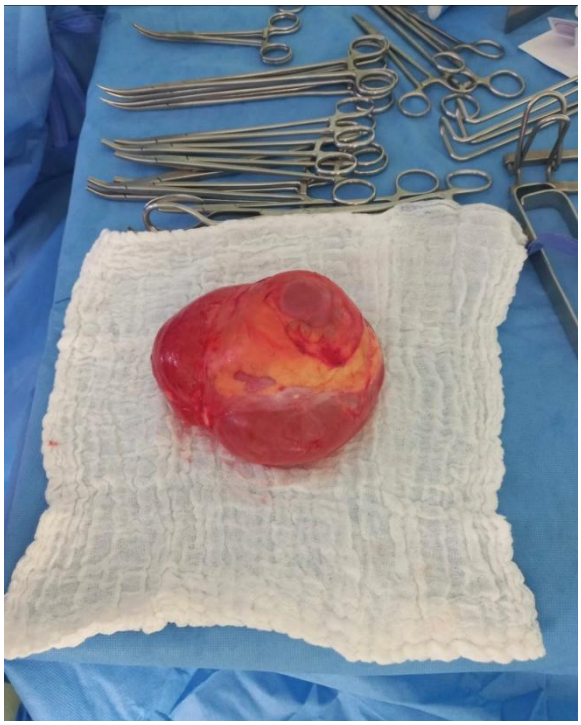
❖ These include:

- Yolk tumours or tumours of the endodermal sinus (20%);
- Teratomas (20%) classified into three grades according to theextension of the immature neuroectodermal parentage (the current trend is to group grades II and III together);
- Rare pure embryonal carcinomas (<5%);
- Pure choriocarcinomas
- Composite tumours (10%) (composed of mature and immature teratoma and/or yolk tumour, embryonal carcinoma associated with a predominantly
- Dysgerminomatous component) (Scully, 1979)

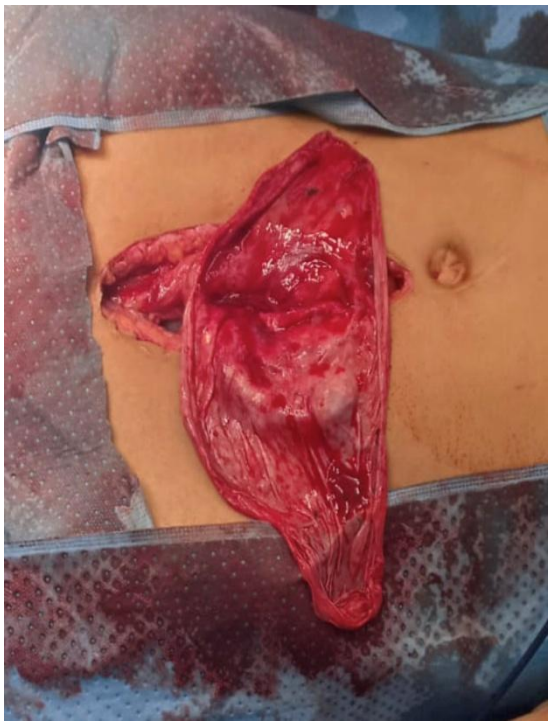
II. OBSERVATION :

Patient aged 14 years, ATCD= operated on 28/05/2020 for germinal tumour of the right ovary measuring 16*17 cm (Anapath in favour of an embryonal carcinoma) having benefited from a right Annexectomy, followed by 10 sessions of chromotherapy (She initially received 5 sessions of chemotherapy according to Protocol TGM 2013 RI risk group and in front of the persistence of a high rate of alpha FP the decision was to add 5 sessions of chemotherapy according to protocol VIP, DDC :01/08/21) The patient presented with an increase in abdominal volume 4 months ago and was then referred to our training centre for treatment. A pelvic ultrasound showed a large pelvic cystic mass (pseudo-peritoneal cyst) measuring 117*81mm, containing a suspicious endocystic vegetation measuring 11*9mm, slight right pyelo-caliceal dilatation with a pyelon measuring 5 mm in diameter without any homolateral morphological impact on the kidneys: Progression in size of the left ovarian lesional process, with a majority triple cystic component, presenting parietal vegetation still measuring 8x13mm, and fatty having increased in size with individualisations of parietal microcalcifications. It currently measures 120 x 100 mm in diameter (transverse and anteroposterior) versus 100 x 97 mm (i.e. an increase of 17%). Appearance of two peritoneal nodules, completed by a pelvic MRI: large pelvic cystic mass measuring 125*120 mm, containing large vegetation measuring 13*08 mm, moulding the douglas cul-de-sac, initially evoking a pseudo-peritoneal cyst. File staffed with Radiologists for feasibility of a puncture of the peritoneal cyst: no indication, Patient benefited from a laparotomy, at exploration: no ascites, no nodules of Carcinosis, uterus of normal size, right adnexa not seen, liver and stomach smooth. Presence of a large mass of the left ovary, with a thin wall and a double fluid and tissue component with visualization of hairs and a bone component, making it possible to first evoke a teratoma, taking a sample for cytological study, performing a left cystectomy without rupture of the cystic wall, multiple biopsies: GPCG and GPCD , ANAPATH

- Histological appearance of a mature, multi-segmented teratoma
- GPCG: Substantially normal fibro-muscular tissue
- GPCD: Substantially normal fibro-muscular tissue
- Peritoneal cytology: Reactive fluid.



Left ovarian mass measuring 9*6 cm



left cystectomy without break ef the wall

Frequency:

Malignant germ cell tumours represent 5% of ovarian tumours. Their annual incidence in France is one per 0.5woman100000, and the number of new cases can be estimated at around one hundred per year (Williams and Gershenson, 1993).

Diagnostic methods:

The diagnosis, suspected on clinical examination, is based on pelvic or endo-vaginal ultrasound evidence of a large ovarian mass causing pelvic heaviness. For some histological subtypes, notably embryonal carcinoma, signs of early puberty are sometimes the reason for consultation.
However, it is the initial surgical procedure (laparotomy) that establishes the diagnosis. The diagnosis can also be made by measuring the following tumour markers (see table1):

- Hormone chorionicgonadotropin (hCG) is a glycoprotein with a molecular weight of 33 kDa, a half-life of 3 days, and a radioimmunoassay. It is secreted by choriocarcinoma, whether pure or part of a mixed tumour, and by isolated syncytiotrophoblastic cells. Moderate elevation of hCG may be seen in pure dysgerminoma. hCG consists of two subunits: an alpha subunit, common with pituitary hormones, and a specific beta subunit which is unique to hCG.

- Alpha-fetoprotein FP) is a glycoprotein with a molecular weight of kDa130, a half-life of days7, and a radioimmunoassay. It is secreted by vitelline tumours and by
some embryonal carcinomas. It is often elevated in mixed tumours and is never increased in pure dysgerminomas.

- Enzymelactodehydrogenase (LDH). Its determination is of interest in particular for dysgerminomas where its level is very often increased (Sheiko and Hart, 1982

***Table 1: Tumour markers of ovarian germ cell* malignancies**

Type of tumour	*aFP*	*hCG*	*LDH*
dysgerminoma	-	+/-	+
Tumour of the endodermalsinus	+	-	+/-
Immature teratoma	+/-	-	+/-
Embryonal carcinoma	+/-	+	+/-
Choriocarcinoma	-	+	+/-
Composite tumour	+/-	+/-	+/-

In cases of suspected germline ovarian tumour, these markers should be measured routinely before surgery, and even before any surgery on the pelvic mass in young women.

Etiology:

Ovarian germ cell malignancies are linked to the existence of a cytogenetic feature common to all ovarian, testicular or extragonadal germ cell tumours in adults and children: the presence of an isochromosome in the short arm of chromosome 12 [i(12p)], which is not found in any other type of cancer (Kurman and Norris, 1976a).

Evolution of the disease

The measurement of the tumour markers hCG, LDH and FP is also of interest for prognosis and monitoring of disease progression. Although their prognostic value is not clearly established, an increase in their levels signifies tumour relapse. Although the specificity of these markers is very high, their sensitivity is not absolute because there are clinical courses in the absence of an increase in tumour markers (Bidart et al. , 1992; Droz et al. , 1992). The age of the patients (over years22) is also described as a prognostic factor to be taken into account (Mayordomo et al. , 1994).

Other tumour markers have been evaluated (CA 125, CA 19-9, NSE, Angiotensin, MCSF) (Kawai et al. , 1991). However, their measurement has only been carried out on a small number of patients, which means that their value outside of a therapeutic trial cannot yet be determined (Suzuki et al. , 1998).

Several studies have attempted to identify prognostic factors capable of establishing metastatic risk. Thus, tumour size (greater than 10 cm), histological type (endodermal sinus, choriocarcinoma) and high histological grade (for immature teratomas) (Kurman and Norris, 1976b; Norris et al. , 1976), are frequently described prognostic factors. Tumour residue after surgery appears to be a prognostic factor

Support:
The treatment of rare ovarian tumours is currently established as follows:

- Surgery is modelled on that for ovarian adenocarcinoma, with one major difference: preservation of genital function in women of childbearing age (which is usual in this type of tumour)
- Chemotherapy based on literature data is identical to that for testicular germ cell tumours
- Surgery, chemotherapy and possible surgery for residual lesions are highly interrelated.

Surgical management:

- The initial surgical procedure is essential in rare ovarian tumours as it allows diagnosis, assessment of the extent of the disease and the first therapeutic act.
- Although many patients underwent initial surgery with maximal removal of tumour masses (total hysterectomy with bilateral adnexectomy , omentectomy , complete abdominal exploration and lymph node dissection), a number of patients underwent conservative surgery (preserving the contralateral ovary and uterus) combined with complete abdominal exploration (Culine et al. 1997a).
- Exploratory surgery after chemotherapy is not indicated:
- For pure dysgerminomas, even if retroperitoneal masses remain, as they often do not contain live tumour cells, they can continue to regress.
- For endodermal sinus tumours and choriocarcinomas, which secrete sufficiently reliable tumour markers (respectively
- FP and hCG).
- For patients with an early stage of disease who have had a complete primary surgery.
- A second surgery is necessary:
- When only biopsies were taken during the first surgery. The surgery then allows the removal of the ovary where the primary tumour was located.
- In embryonal carcinomas or mixed non- secretory germ cell tumours. In these cases, removal of residual lesions after chemotherapy is essential because neither imaging nor tumour markers are sufficiently reliable to know the histological nature of the residue (Gershenson, ;1993 1994).
- In teratomas. Some tumour components, especially neuroectodermal ones, may, on losing their malignant potential, evolve towards maturation. This mature tissue may reach a large volume (growing teratoma) responsible for functional complications (Gershenson et al. , 1985; 1986; Williams and Gershenson, ; 1993Geisler et al. , 1994).
- Simple surveillance after surgery is classically accepted only for pure stage I dysgerminomas or immature stage I and grade I teratomas, for which the risk of relapse is extremely low (Norris et al. , 1976; Thomas et al. , 1987; Dark et al. , 1997). For other cases, such as patients with embryonal carcinomas or yolk tumours, and those with stage II, III or IV tumours, the high risk of relapse leads to the suggestion of adjuvant chemotherapy after surgery.

Chemotherapy:

Malignant germ cell tumours are unique among non-haematological cancers in that they can be cured by cytotoxic chemotherapy. Too rare to allow randomised studies, these tumours have benefited from the therapeutic advances observed in germ cell tumours of the testicle. The introduction of cisplatin in the therapeutic protocols constituted a decisive progress, radically modifying the survival of the patients (Einhorn, 1981). Published studies have focused on the PVB (cisplatin, vinblastine and bleomycin) combination. 1987,Vinblastine has since been replaced by etoposide, with BEP (bleomycin, etoposide and cisplatin) having been shown to be as effective and less toxic than PVB in testicular tumours (Williams et al, 1987). Chemotherapy should be tailored to the histological type and stage of the tumour (Culine et al. , 1997b). Because of the rapid tumour growth, it should be initiated soon after surgery (one week to days10) (Herrin and Thigpen, 1999).
The acute toxicities observed, particularly haematological, are identical to those encountered during chemotherapy of germ cell tumours of the testis (Einhorn, 1990).

Treatment of relapses:

It was observed that 69% of patients treated with a protocol including cisplatin, and being in a relapse situation after treatment In the case of initial surgery and/or radiotherapy, there is a complete remission in the long term (Williams et al. , 1989). In the case of salvage treatment after chemotherapy failure, the indications for surgery at relapse remain debatable and the results of second-line chemotherapy are difficult to analyse. In the case of relapse treatment, the sensitivity of patients to platinum has recently become an important factor. Indeed, patients relapsing more than 6 weeks after the end of cisplatin treatment are defined as platinum

sensitive, whereas patients progressing less than 6 weeks after the end of chemotherapy are considered resistant (Loehrer et al., 1988; Motzer et al., 1991; Gershenson, 1993).

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