Guidelines for the management of

OVARIAN CANCER DURING PREGANCY

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For optimal management of a suspected malignant adnexal tumour, a multidisciplinary approach involving specialists in oncology, and sometimes in paediatrics is necessary whenever possible, as soon as it is diagnosed. (Grade A)

It should be kept in mind managing cancer and pregnancy always requires a shared decision between the patient and at least a surgical oncologist, an obstetrician, a medical anatomopathologist and a paediatrician;

Transcutaneous and transvaginal pelvic ultrasound imaging is an essential reliable technique which assists the physician in the diagnosis of ovarian tumour during pregnancy. As about 10 % of masses are complex, a second diagnostic test should be performed by a fully trained sonographer. The ultrasound examination should determine the origin of the mass, as well as its location, size, internal structure (existing vegetations or septa) and should classify it into one of the following five categories: unilocular, unilocular-solid, multilocular, multilocular-solid, or solid (grade A). A colour Doppler imaging should also be performed to obtain a vascular road map of the ovarian mass (Grade B).

Pelvic MRI with gadolinium injection can be performed after the first trimester. This second line examination should only be indicated during pregnancy to remove any doubt or to provide additional information if the ultrasound examination is not sufficient or as a tool for the assessment of ovarian cancer (Grade B). Pelvic CT scanning is not indicated during pregnancy, although a thoracic scanner with a leading shield covering the pelvis should be undertaken for the extension assessment of an advanced-stage tumour. As CA 125 is found at high levels during the first trimester and then returns to normal, it is not really useful, but remains interesting for follow up (grade B).

Whatever the term of pregnancy, acute symptoms including pain, defence or trauma, associated with a suspicious ovarian tumour may increase the risk of complications (torsion, haemorrhage or rupture). Surgery should be immediately considered, and the approach should be the same as in a non-emergency context.

<u>For asymptomatic adnexal masses</u>, surgery should only be considered in pregnancy for suspicious masses or obvious malignant tumours.

In patients with suspicious ultrasound appearances of malignant ovarian tumour, the surgical staging procedure is threefold:

- To establish diagnosis: a definitive histological evidence or a reliable extemporaneous evidence should be obtained (epithelial malignant or not, or low malignant potential), without increasing the risk of dissemination (rupture) and harming pregnancy.
- To determine the histopathological grade of the tumour (making the following differentiations: disseminated tumour, infiltrative tumour apparently localised, borderline tumour apparently localised); as a result, it should provide useful information for the management of the disease in a reasonable time, to be discussed depending on the age of pregnancy.
- To perform initial treatment (surgery or chemotherapy) considering the following steps: to set treatment standard for a nonpregnant patient; to evaluate each of the different inevitable or freely accepted changes as a result of pregnancy; it implies a thorough knowledge of proven risk factors for premature birth vs chemotherapy during pregnancy and/or the period when treatment should start whenever the question arises.

Confirmed low malignant potential tumours can be treated conservatively by annexectomy and peritoneal cytology and exploration with biopsies. This diagnosis should never lead to the end of the pregnancy (grade A). The treatment should be performed without rupture by a surgeon/anaesthetist team trained to such oncologic surgical procedure in pregnant patients. It is mostly done by laparotomy, but coeliosurgery may be an option before 24 wk if complete staging is respected and rupture avoided. A super conservative treatment (cystectomy alone) should only be indicated in a patient with one ovary or with a bilateral borderline tumour. If this borderline tumour is revealed by the histology of a surgical specimen, it seems reasonable, considering the good prognosis of these tumours to defer

surgical treatment until after delivery. Surgical staging should be completed 3 to 6 weeks after delivery.

Management of epithelial invasive tumours: surgery, if considered, should be performed or be assisted by a surgeon fully trained for the treatment of malignant ovarian tumours. In the same way, extemporaneous examinations should be performed by pathologists fully trained for the treatment of ovarian pathology. In patients with ultrasound suspicion of stage I malignant tumour, it is recommended to perform a unilateral annexectomy without rupture for stage IA tumours and a bilateral one for stage IB tumours associated with peritoneal cytology and complete abdominopelvic exploration in both cases (grade B). Adjuvant chemotherapy should be indicated according to the extension and histology of the tumour, and should be similar to the treatment recommended in nonpregnant patients. The final decision concerning platinum-based chemotherapy (grade A) should be taken with a multidisciplinary approach involving the opinion of paediatricians and obstetricians and considering gestational age. Treatment should start during or after pregnancy depending on prognosis, multidisciplinary decision and patient preference. The route of delivery should not be an issue. Postpartum secondary surgery should be considered according to multidisciplinary team decisions and patient preference. The surgical procedure should be similar to that of nonpregnant women.

For more advanced-stage tumours (II to IV), it seems preferable to consider termination of pregnancy before 24 weeks, and perform routine surgical treatment for ovarian cancer followed by chemotherapy. After 24 weeks and according to the decision of the multidisciplinary task group, histology is often ordered. A biopsy may be performed by the transparietal route under ultrasound guidance, by laparoscopy or microlaparotomy. Depending on the stage of the tumour and the gestational age, the remaining options should include surgical treatment during pregnancy if possible, or neoadjuvant chemotherapy (grade C). The purpose of this approach is to avoid prematurity and foetal toxicity without deferring the mother's treatment. As a result, dates for the last chemotherapy session and delivery for which a caesarean section is most frequently required should be chosen accordingly. Procedures should take place at a 4-week interval so caesarean section is not planned during a period of aplasia both harmful to mother and child (who may also be diagnosed with aplasia) (grade B). Pre-term birth occurring between 32 to 36 weeks is reasonable. Complete surgical treatment should be performed by a surgical oncologist at caesarean section if possible, or after delivery.

Management of non epithelial malignant tumours: considering the age of patients, malignant adnexal tumours during pregnancy are mostly non epithelial tumours (germinal tumours 30-35%, sex cord tumours 17-20%). Stage 1 tumours are the most frequent. Depending on the gestational age and the size of the tumour, surgical exploration by coelioscopy or laparatomy helps undertake a unilateral adnexectomy for stage IA tumours or a bilateral adnexectomy for stage IB tumours with extemporaneous examination. It is sometimes possible to avoid a bilateral adnexectomy (at the end of pregnancy) because of the good prognosis of some chemosensitive tumours. Peritoneal staging should be performed. Omentectomy is not necessary. Lomboaortic and pelvic lymphadenectomies are not considered anymore (grade B). Postpartum secondary surgery for staging should be discussed according to the histology of disease. Adjuvant chemotherapy should be considered in patients with more advanced-stage tumours during a multidisciplinary meeting involving experts. The term of delivery should be discussed according to the need for chemotherapy or not. The treatment modalities should be adapted to the histology and extension of the tumour, and to the term of pregnancy.

Conclusion

As the incidence of invasive cancers and borderline ovarian tumours diagnosed during pregnancy is low, treatment strategies should ideally be discussed and structured during a "multidisciplinary meeting" involving specialists. The different cases should be recorded into the national database of the CNGOF (French College of Obstetricians and Gynaecologists (cancer.grossesse@tnn.aphp.fr).