E-Bulletin – FPSI

ORGANISATION
Secretariat & Regd.Office:
D-59, Defence Colony, New Delhi-110024

Is transplantation of cryopreserved ovarian tissue from patients with borderline ovarian tumors (BOTs) a safe procedure?

This article reviews a recent publication in Human Reproduction (Dec 2017) titled:
Safety of ovarian tissue transplantation in patients with borderline ovarian tumors

By *Rossella Masciangelo, Chiara Bosisio, Jacques Donnez, Christiani A. Amorim, and Marie-Madeleine.*

Key Points:
BOT cells can be found in cryopreserved ovarian tissue from BOT patients, therefore preimplantation analysis plays a key role in decision-making regarding ovarian cortex transplantation in young women with BOT, in whom ovarian cortex cryopreservation is performed.
.
When considering ovarian tissue transplantation, caution is vital if endometriotic glands are found in the frozen–thawed ovarian tissue of patients with BOTs.

Limitations:
Cryopreserved ovarian fragments cannot be tested before transplantation, therefore the preimplantation analysis cannot guarantee that all cryopreserved fragments will be free of BOT cells.

Introduction:
BOTs are typically diagnosed at an early stage and thus usually have an excellent prognosis, but in 2–4% of cases, they can evolve into more aggressive lesions, considerably worsening the prognosis of the patient. The mean age at diagnosis is 45 years, but one-third of the patients are under 40 years of age and therefore potential candidates for fertility-sparing surgery.

Radical surgery with bilateral salpingo-oophorectomy is the gold standard treatment for BOT patients, but conservative surgery, either unilateral salpingo-oophorectomy or cystectomy, can be performed to preserve fertility in the younger patients. The risk of recurrence after unilateral salpingo-oophorectomy is higher than after radical surgery (0–25 versus 0–5%) and even higher in case of cystectomy. Relapses almost always show BOT histology, and they can therefore be safely managed with a second surgical intervention. The disease may recur contralaterally on the spared ovary, or involve both ovaries, necessitating a second intervention with radical Surgery.

In young patients who have yet to consider future childbearing, fertility preservation is of great importance. Ovarian stimulation followed by oocyte or embryo cryopreservation is a

good option for patients who do not wish to conceive immediately, with successful results reported in BOT patients. Ovarian tissue cryopreservation (OTC) has proved to be a valuable strategy in prepubertal patients and those who cannot delay anticancer treatment, and its efficacy has increased over the last 10 years, with more than 110 live births reported to date.

However, the risk of reintroducing malignant cells upon ovarian tissue transplantation has been subject of debate for many years. It is known that reimplantation of cryopreserved ovarian tissue from leukemia patients is unsafe, while results from studies of cryopreserved ovarian tissue from other forms of cancer, such as Hodgkin's lymphoma, are reassuring.

Aim of this study was to evaluate whether transplantation of cryopreserved ovarian tissue from patients with borderline ovarian tumors (BOTs) is a safe procedure.

Study details: This was a prospective experimental study conducted in an academic research unit using ovarian tissue from 11 patients undergoing cryopreservation for BOTs.

Histology, immunohistochemistry (IHC) for mucin 1 (MUC1) and cytokeratin 7 (CK7) and molecular analysis by reverse transcription quantitative polymerase chain reaction (RT-qPCR) for CK7 and MUC1 were performed on frozen-thawed ovarian tissue from 11 patients. Long-term (5 months) xenografting of ovarian tissue in immunodeficient mice was performed. The xenografts were analyzed by histology, IHC and RT-qPCR, furthermore IHC for CD10, a marker of endometriosis, was performed on a selected sample.

The main results showed that all the molecular tests were negative for BOT in ten cases. Xenograft, in the case where molecular tests were positive for BOT showed presence of BOT. In addition, endometriosis was noted in one other case.

Key Conclusions:
BOT cells can be found in cryopreserved ovarian tissue from BOT patients, therefore preimplantation analysis is an absolute prerequisite. Cryopreserved ovarian fragments cannot be tested before transplantation as preimplantation analysis can destroy the tissue itself. Therefore, the ***preimplantation analysis cannot guarantee that all cryopreserved fragments will be free of BOT cells.***

Although considered a benign disease, recent studies have reported an ***association*** between ***endometriosis*** and ***an increased risk of developing ovarian tumors,*** both ***carcinomas*** and ***BOTs.***

In women with ***endometriosis,*** in addition to risk of introducing BOT cells residing within the ovarian tissue, there is the additional ***risk of introducing endometriotic cells with the potential to transform into malignant cells***. Hence, careful evaluation of the disease and comprehensive discussion with patients with endometriosis is needed before ovarian tissue transplantation can be contemplated.

Compiled by:

Dr Anupama Bahadur
Vice Dean (Alumni)
Additional Professor, Department of OBGYN
AIIMS, Rishikesh