

Abstract - ESHRE 2021

Safety of ovarian tissue cryopreservation and transplantation in patients with central nervous system cancers

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1. Abstract title:

Safety of ovarian tissue cryopreservation and transplantation in patients with central nervous system cancers

2. Study question:

Is cryopreserved ovarian tissue transplantation safe in patients with central nervous system (CNS) tumors?

3. Summary answer:

Cancer cell contamination was not detected in any ovarian samples from patients with CNS tumors by histological analysis, immunohistochemistry, molecular biology or long-term xenotransplantation.

4. What is known already:

Frequently encountered CNS cancers in childhood include astrocytoma, medulloblastoma, ependymoma, glioblastoma and germinoma. CNS tumors have the capacity for extraneural metastases in 0.5-18% of cases. There are two publications reporting metastases to patients' ovaries from medulloblastoma.

5. Study design, size, duration:

Prospective experimental study conducted in an academic gynecology research laboratory using frozen-thawed ovarian tissue from 20 patients suffering from 6 types of CNS tumors, including the most common forms mentioned above and primitive neuroectodermal

tumors (PNET). Five-month xenotransplantation was performed to immunodeficient mice.

6. Participants/materials, setting, methods:

Cryopreserved ovarian tissue from 20 patients with CNS cancers was thawed and analyzed for minimal disseminated disease and long-term xenografting to immunodeficient mice. The presence of malignant cells was assessed in both cryopreserved and xenografted ovarian tissue using histological analysis, immunohistochemistry for disease-specific markers (neuron-specific enolase [NSE] and glial fibrillary acidic protein [GFAP]) and reverse transcription droplet digital polymerase chain reaction (RT-ddPCR) for quantification of GFAP gene amplification.

7. Main results and the role of chance:

No malignant cells were detected in frozen-thawed ovarian tissue from any of the patients by histology, immunolabeling for NSE and GFAP, RT-ddPCR for detection of GFAP gene amplification or xenotransplantation to SCID mice. One patient successfully underwent frozen-thawed ovarian tissue transplantation, resulting in the birth of 3 healthy children, but suffered a recurrence of her PNET 6 years after reimplantation and sadly died. Scrupulous analysis of her remaining frozen tissue showed no infiltration by malignant cells, neither after thawing nor long-term xenotransplantation. No relationship was ever established between the patient's relapsed cancer and reintroduction of her

66 cryopreserved ovarian tissue. The risk of reseeding cancer cells when transplanting
67 ovarian tissue in patients with CNS cancers can therefore be considered low.

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69 **8. Limitations, reasons for caution:**

70 The risk of ovarian metastases cannot be completely ruled out for any type of tumor
71 because we cannot analyze the actual fragments that will be reimplanted.

72 **9. Wider implications of the findings:**

73 Our results indicate that the risk of disseminated disease in ovarian tissue from CNS
74 patients is minimal. This is useful information for doctors when counseling women looking
75 to undergo ovarian tissue transplantation.

76 **10. Study funding/competing interest(s):**

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84 **11. Trial registration number:** not applicable

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