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Introduction

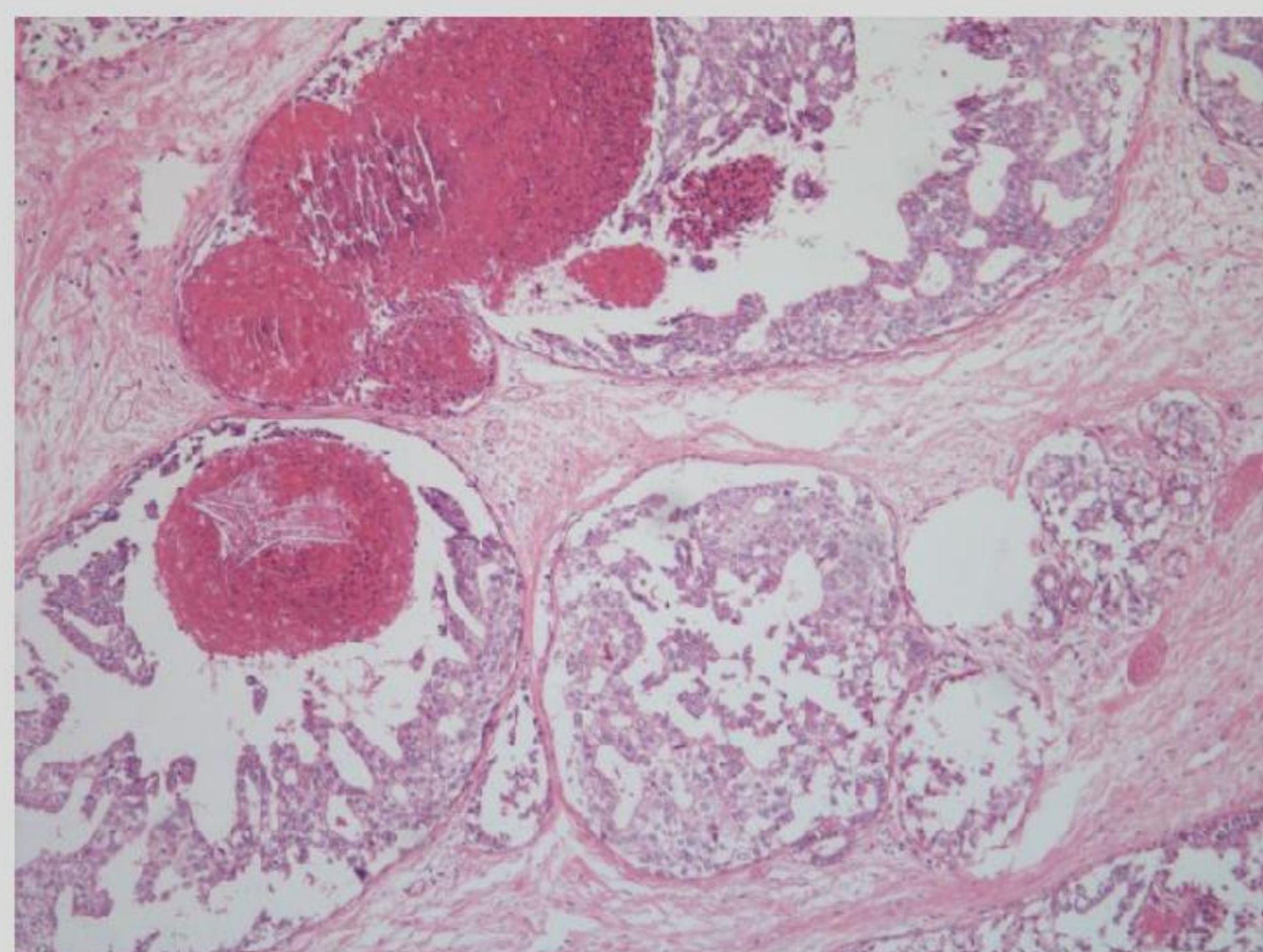
Breast cancer is a rare neoplasia in men, representing <1% of all types of male cancers. However, in case of *BRCA2* mutations, the risk of breast cancer in male patients is 80 times higher than the general population.

Male-to-female transsexualism occurs in ~12 000 males. The secondary sexual characteristics are acquired due to hormonal treatment with anti-androgens and oestrogens, usually used in higher doses and for longer periods of time than in hypogonadal women.

We present here the first case of breast cancer occurring in a male-to-female transsexual patient who was discovered to carry a pathogenic *BRCA2* mutation. The genetic status was not known before diagnosis of breast cancer.

Case report

At the age of 46, the patient was started on cross-sex hormone treatment with anti-androgens associated with estrogens. The treatment was followed for 7 years, after which a routine mammography revealed a suspicious region on the right breast. Biopsy found a high grade ductal carcinoma. Hormone therapy was stopped and the patient was operated – right total mastectomy with sentinel node excision. The histological analysis revealed focally undifferentiated ductal carcinoma without invasion of sentinel node or nipple. Immunohistochemically, the carcinoma was estrogen receptor positive for 100% of cells, progesterone receptor positive for 10% of cells, HER2 negative and had a Ki67 index of 50%.



High grade ductal carcinoma in situ – Hematoxylin Eosin staining

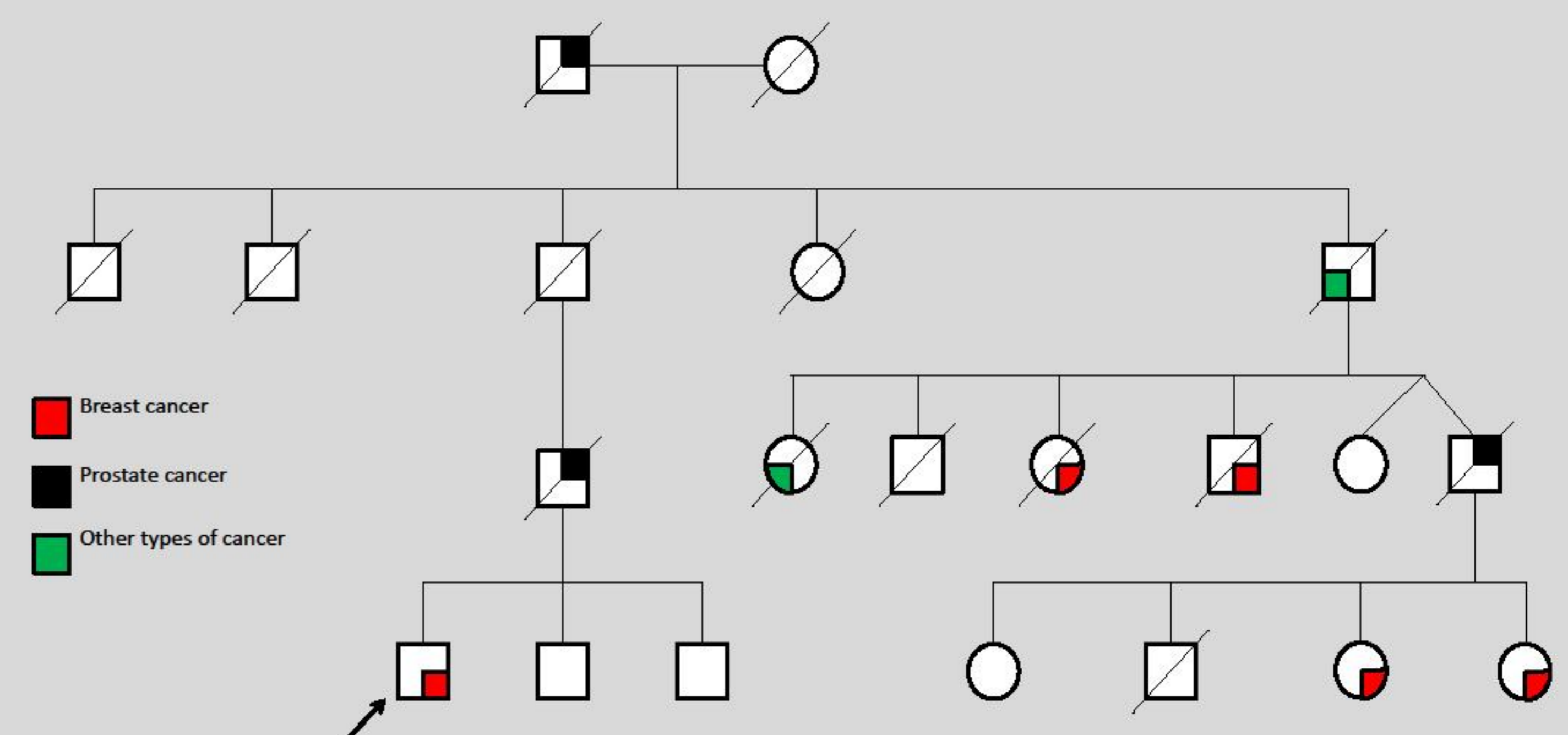
Androgen receptor staining was also performed and found positivity in 80% of cells. SERM treatment was declined by the patient and a follow-up was decided.

30 months after surgery, local recurrence was found at the site of the mastectomy scar. Radiation therapy and chemotherapy were administered.

The patient was tested for mutations in the breast cancer predisposition genes. The heterozygous mutation c. 9117G>A of the *BRCA2* gene was found.

The same mutation was known in a family living in the same region as the patient and bearing the same surname. Several members of this family had been diagnosed with breast and prostate cancer over 4 generations. Further questioning revealed that the patient was related to the aforementioned family.

The mutation found here did not seem to modify the final protein structure (p.Pro3039Pro), but further studies revealed that it lead to splice-site mutations (skipping of one or two exons or deletion of a certain number of aminoacids).



Family tree of the extended family. The patient is marked by an arrow.

Conclusion

This is the first case of a breast cancer occurring in a male-to-female transsexual patient with a *BRCA2* mutation. It raises awareness of the potential effect of cross-sex hormone therapy on breast cancer development in genetically-predisposed patients.

A thorough family history should be obtained for each patient seeking cross-sex hormonal therapy and regular breast and prostate cancer screening organised. Should a genetic predisposition be found, prophylactic management of breast cancer needs to be discussed, but so far there are no protocols available for transgender patients.

Bibliography

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