BREAST CANCER SUSCEPTIBILITY IN PATIENTS WITH SPINAL BULBAR MUSCULAR ATROPHY. A CASE REPORT

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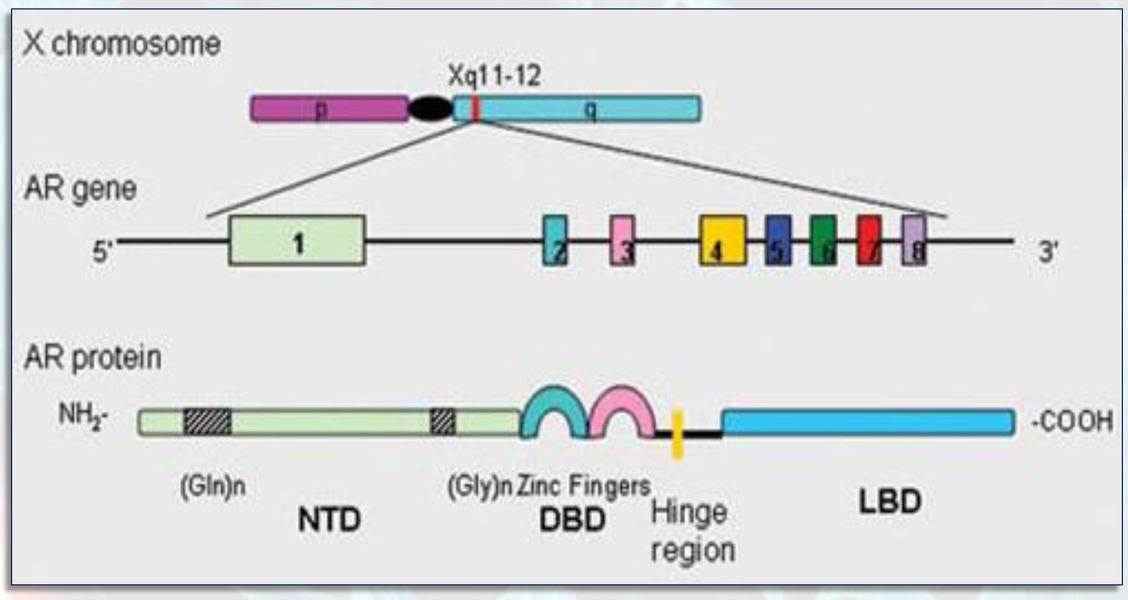
XLVII Congresso Nazionale SIN, 22-25 Ottobre 2016, VENEZIA

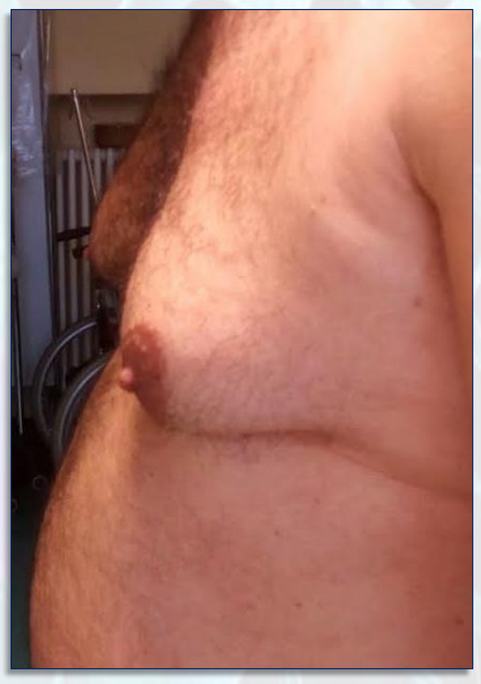
BACKGROUND

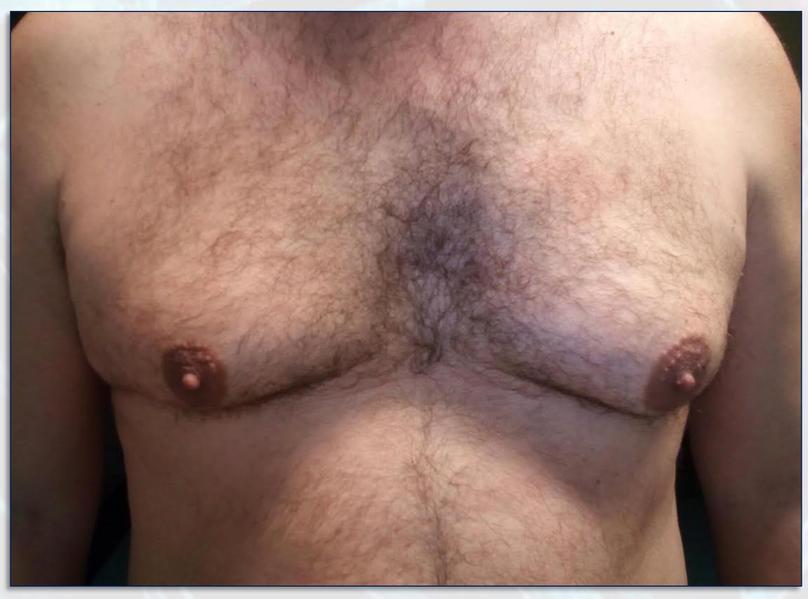
Spinal and bulbar muscular atrophy (SBMA), also known as Kennedy's disease (KD), is a rare, X-linked neuromuscular disease caused by a mutation in the first exon of androgen receptor (AR) gene: an expansion of CAG triplet, that encodes for an expanded polyglutamine (polyQ) tract. Male breast carcinoma (MBC) is an uncommon disease, accounting for less than 1% of all cases of breast carcinoma. There are increasing evidence that polymorphic AR CAG-repeat length could play a role in carcinogenesis. A relationship between breast cancer in general both sex population and the number of CAG repeats in AR gene has been reported, but it is still controversial.
Here we report a 55-year-old SBMA patient with 45 CAG repeat expansion in the AR gene who has developed breast cancer.

CASE REPORT

A 55-year-old male was admitted to our Department of Neurology complaining muscle weakness, fasciculations, cramping, and tremor since age 34. These clinical features had slowly progressed over the following 15 years. A gynecomastia was noted since young age.
Since genetical analysis showed 45 CAG repeats in AR receptor gene, SBMA diagnosis was made.
For cosmetic reasons, he underwent excision of left breast tissue because of an enlargement of the breast occurred after a moderate trauma of the chest. During the operation an incidental nodule was detected.
Histological analysis revealed ductal carcinoma in situ, micropapillary cribriform type. No evidence of metastatic repetition was detected in lymph nodes. The immunohistochemistry highlighted an Estrogen Receptor positivity in 95% of neoplastic cells and a Progesterone Receptor positivity in 60%.
Extensive hormonal analyses were within the physiological range.







DISCUSSION

AR CAG-repeat length and carcinogenesis

The androgen receptor belongs to the superfamily of nuclear receptors that binds to androgen response elements (AREs) and regulates their transcription.

The transactivation of the AR is inversely correlated to CAG repeat length.

Since hormonal factor could be important in cancer development, several studies investigated the potential relationship between AR activity) and carcinogenesis.

AR CAG-repeat length and breast carcinogenesis in both sex population

Data from several types of studies suggest that androgens are protective against breast cancer: women with AR-positive breast cancers have better response to hormone therapy.

The difficulty to assess the role of CAG comes from:

> genetic-hormonal background

- Variable AR gene expression due to random X inactivation in female cells.

AR CAG-repeat length and breast carcinogenesis in male population

Although some susceptibility genes have been described in MBC, the role of androgens is still unclear. Risk factors are Klinefelter syndrome, gynecomastia, diabetes, obesity.

In SBMA patients, along with the risk secondary to gynecomastia and metabolic syndrome, several studies investigate the potential molecular link between breast cancer and androgen hyposensitivity caused by long CAG-repeat in AR gene.

CONCLUSIONS

Extensive data indicate that the correlation between polymorphic poliQ repeat length and carcinogenesis in general population is controversial.
CAG repeat polymorphism in AR gene, through alterated interaction with co-activators and transcriptional factors, could be involved in dysregulation of cell growth, differentiation, apoptosis, adhesion and migration that can lead to cancer development.
Breast cancer has not been assessed as a common occurrence in SBMA.
Beside of the increased risk due to gynecomastia and metabolic syndrome in SBMA, there are several studies that demonstrate a potential molecular correlation between breast cancer and androgen hyposensitivity caused by long CAG-repeat in AR gene.
This case report supports the hypothesis that long AR CAG-repeats could have a role in male breast carcinogenesis.
More evidence is necessary to assess if a systematic screening is required to identify promptly breast male cancer in SBMA patients.