MALIGNANT PHYLLODES WITH BILATERAL LEYDIG CELL HYPERPLASIA OF TESTES IN A CASE OF COMPLETE ANDROGEN INSENSITIVITY SYNDROME - A RARE CASE REPORT

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ABSTRACT

Introduction: Complete androgen insensitivity syndrome (CAIS) is an AIS condition that results in the complete inability of the cell to respond to androgens. Individuals with complete androgen insensitivity syndrome are born phenotypically female, without any signs of genital masculinization, despite having a 46, XY karyotype. Case report: We present a case of a 66 year nulliparous female with primary amenorrhea with complaints of bilateral inguinal mass for 5 years and bilateral breast lump for 3 years. The patient developed a sudden increase in the size of a left breast lump. An MRI chest revealed a large 15.4x11.5cm heterogeneous mass in the left breast and a 9.9x6.1 cm lobulated mass in the right breast. MRI abdomen and pelvis revealed soft tissue structures in the bilateral inguinal region near the deep inguinal ring with a blind-ending vaginal tract and absent uterus and ovaries. Karyotyping revealed 46XY. We received specimens of left MRM, right lumpectomy and bilateral inguinal mass. Left MRM measured 32x20x12cm. The cut section showed a large tumour with a variegated appearance. The right lumpectomy showed a tumour with a leaf-like appearance noted. The bilateral inguinal mass measured 5x3x3 cm each, cut section showed yellowish nodules. Histopathological examination reveals malignant phyllodes of the left breast, benign phyllodes of the right breast, and Leydig cell hyperplasia of bilateral testes. Conclusion: This is the first case reported of malignant phyllodes in a case of complete androgen insensitivity syndrome with bilateral Leydig cell hyperplasia of testes.

KEYWORDS malignant phyllodes, CAIS, Leydig cell hyperplasia

Introduction

Complete androgen insensitivity syndrome is a condition that affects sexual development before birth and during puberty.1 People with this condition are genetically male but do not respond to male hormones. Patients have female external genitalia and female breasts. Still, they do not have a uterus or cervix, so they cannot menstruate. Other signs and symptoms may include undescended testes and sparse to absent pubic hair. Complete androgen insensitivity syndrome is caused by mutations in the AR gene and is inherited in an X-linked manner. There are 2 main types of AIS, which are determined by how much the body is able to use testosterone. Complete androgen insensitivity syndrome (CAIS) – where testosterone has no effect on sex development, so the genitals are entirely female partial androgen insensitivity syndrome (PAIS) – where testosterone has some effect on sex development, so the genitals are often not as expected for boys or girls PAIS is usually noticed at birth because the genitals appear different.
Case report

We present a case of a 66 year nulliparous female with primary amenorrhea with complaints of bilateral inguinal mass for 5 years and bilateral breast lump for 3 years. The patient developed a sudden increase in the size of the left breast lump for 3 months with ulceration of the overlying skin and hemorrhagic nipple discharge. An MRI chest revealed a large 15.4x11.5cm heterogeneous mass in the left breast and a 9.9x6.1 cm lobulated mass in the right breast (Figure 1). MRI abdomen and pelvis revealed soft tissue structures in the bilateral inguinal region resembling testis near the deep inguinal ring with blind ending vaginal tract and absent uterus and ovaries (Figure 2), karyotyping revealed 46XY. (Figure 3) The hormone levels were studied, showing normal testosterone levels, DHEA, LH and FSH. Left MRM with left axillary dissection was done along with right lumpectomy with bilateral orchidectomy. We received specimens of left MRM, right lumpectomy and bilateral inguinal mass.

There were multiple foci of benign phylloides adjacent to the malignant component. All the resection margins were free of tumours. Left axillary lymph nodes were negative for malignancy. Hence the diagnosis of malignant phylloides of the left breast was made. The right breast mass showed characteristic histological features of benign phylloides. Sections from bilateral testes showed nests of Leydig cells separated by collagenous bands. These Leydig cells were round to polygonal with abundant eosinophilic cytoplasm and round central nuclei. Renkie crystal and lipofuscin pigment were also seen. The periphery of the tissue showed atrophic seminiferous tubules with Sertoli cells. No nuclear pleomorphism, abnormal mitosis, or necrosis was noted. (Figure 5) Therefore the diagnosis of bilateral Leydig cell hyperplasia was made. IHC for breast showed diffuse cytoplasmic positivity for CD34, and on testes, the positive markers were Inhibin and Calretinin. The post-operative period was uneventful; presently, the patient is receiving radiotherapy for the right breast.

This is the first reported case of malignant phylloides with bilateral Leydig cell hyperplasia in a case of complete androgen insensitivity syndrome.
Discussion

Complete androgen insensitivity syndrome (CAIS) is an AIS condition that results in the complete inability of the cell to respond to androgens. Individual with complete androgen insensitivity syndrome is born phenotypically female, without any signs of genital masculinization, despite having a 46, XY karyotype. Patients with complete androgen insensitivity syndrome are at an increased risk for gonadal germ cell cancer. Residual androgen receptor (AR) activity and abnormal gonadal location influence the survival of atypical germ cells.

The occurrence of germ cell cancer has been reported to be up to 22% in adult patients. Germ cell cancer is very rare in childhood and adolescence; however, non-invasive precursor lesions characterized as intratubular germ cell neoplasia, also termed carcinoma in situ of the testis, have been repeatedly described in this age group. Interestingly, the occurrence of intratubular germ cell neoplasia in pediatric patients, at a maximum of 6% of cases, does not reach the frequency of germ cell cancer in adulthood reported in most literature.

Hannema et al. described that residual activity of AR has a positive effect on the development of Wolffian structures and the enlargement of seminiferous tubules during puberty in patients with complete androgen insensitivity syndrome. Whether residual AR activity also impacts the survival of normal and/or atypical germ cells has not yet been reported.

Phyllodes breast tumour, which accounts for about 0.3-0.5% of all female breast tumours, is extremely rare in men. Very few cases of phyllodes tumour were reported in men. Pathologically, phyllodes tumours are subdivided into three types: benign, borderline and malignant according to mitotic frequency, nature of margins, stromal growth, cellularity and atypia. Malignant phyllodes tumours spread via a haematological route mainly to the lung, then to the bone. Phyllodes tumours, even benign types, tend to recur even after complete excision, with a higher tendency for malignant cases. Therefore, wide local excision is the standard of care for phyllodes tumours with or without adjuvant radiotherapy in malignant lesions. Clinically, phyllodes tumours are usually rapidly growing and painless masses.

Based on single case reports in the literature, gynecomastia seems to be associated with the development of male phyllodes tumours, which suggests hormonal aetiology in the pathogenesis of male phyllodes tumour. Gynecomastia is the most common male breast abnormality with various etiological factors which are potent in affecting the estrogen/androgen imbalance.

Conclusion

In conclusion, we present an extremely rare case of complete androgen insensitivity syndrome with malignant phyllodes of the left breast with benign phyllodes of the right breast with Leydig cell hyperplasia of bilateral testes. This is the first case to be reported of bilateral breast malignancy in males with androgen insensitivity syndrome with no primary gonadal malignancy.

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Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

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