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Pure Primary Ovarian Adult Rhabdomyosarcoma in A Male Hermaphrodite Patient

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Abstract: *Adult pure primary rhabdomyosarcoma of the ovary is a rare neoplasm. It has a poor prognosis. Treatment options include chemotherapy, surgery and radiotherapy. True hermaphrodite gonads degenerate in rare cases. We report the first case of pure primary ovarian rhabdomyosarcoma in a true hermaphrodite patient.*

Keywords: *Chemotherapy, Hermaphrodite, Ovarian tumors, Rhabdomyosarcoma*

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I. Introduction

Rhabdomyosarcoma (RMS) is a malignant tumor developed from skeletal muscle cells. It typically arises in or near muscle beds and can appear almost anywhere. It's very uncommon in adult:there are only about 400 cases of adults RMS seen in large published series (1, 2). The most common localizations are head and neck (25%) , gynecological and urinary tract (22 %) and limbs (18%) (3,4)**.**Only about 6,2 % of primary tumors are found in the retro peritoneum and primary ovarian RMS (PORMS) is exceedingly rare (5)**.** RMS of the ovary usually arises as a component of a complex tumor such as mixed mesodermal tumor, adenocarcinoma, teratoma and Sertoli-Leydig cells tumors (6). Pure primary ovarian adult RMS (PPORMS) is reported in 34 cases in the literature. We report in our paper a case of PPORMS in a male hermaphrodite patient and a review of all published cases. To our knowledge this is the first case of PPORMS in male.

II. Case Report

A 39-year-old male patient presented in December 2015 with a deep vein thrombosis of the lower right limb and urinary symptoms made of total hematuria, burning urination and dysuria. He was in a good general condition. Abdominal examination showed a hypogastric mass. The patient had a normally formed penis with normal urethral opening at the tip. We also discovered an empty scrotum. Digital rectal examination showed a large fixed pelvic masswith abdominal venous collateral circulation and edema of the right lower limb. Abdominal ultrasound and computed tomography (CT) scan revealed a large lower abdomen solid mass 15 cm in size, of mesenchymal appearance, invading the prostate, lumbar right urethra, pelvic left urethra and right external iliac artery .Work up made of whole body CT scan and bone scan did not show metastases. A CT scan guided biopsy of the pelvic mass revealed a pleomorphic rhabdomyosarcoma.

The pelvic mass was considered unresecable and neoadjuvant chemotherapy was indicated to achieve downstaging of the tumor. The patient received 4 cycles of " MAID" chemotherapy regimen (Doxorubicine 20 mg /m2 d1 to d3 ,Dacarbazine 300 mg / m2 d1 to d3 , Ifosfamide 2500mg /m2 d1 to d3 ,Uromitaxan3g/m2 d1 to d3 and Granulocyte colony-stimulating factor) .Evaluation CT scan showed partial response of the tumor according to RECIST 1.1. Tumor size decreased from 15cm to 8cmwith increase in necrotic component. Also, the CT scan showed regression of the external iliac artery and the left urethra involvement but a non-functional right kidney. Surgery was then indicated.

At intra-operative exploration, we discovered in the pelvis, a uterus measuring 5 cm with a long cervix and a vagina connected with the urethra. We also found a pelvic normal left testis connected to the uterus by a fallopian tube. The right ovary showed a tumor of 7 cm in size connected to the uterus by a fallopian tube ,adjoined to the external iliac pedicle and the right urethra. The tumor was in a contact with the right internal iliac vein. We did not observe peritoneal carcinomatosis. After careful dissection of the right ovary, we

performed a hysterectomy and bilateral salpingo-oophectomy, omentectomy, pelvic and para-aortic lymphadenectomy and right nephrectomy . No macroscopic residual tumor was left.

Final pathology, showed a complete pathological response in the right ovary., a normal left testicular tissu and a normal atrophic uterus with endometrial mucosa and a myometrium (Fig 1). Due to the large initial size of the tumor, adjuvant radiation therapy consisting of 45 Gy on the pelvis with a boost of 15 Gy on right iliac region was delivered. The study of the karyotype revealed a normal 46,XY male chromosomic formula. Those findings are consisting with a RMS of the ovary occurring in a true hermaphrodite patient with male phenotype. After six months of follow-up the patient has no evidence of recurrent disease. The patient was addressed to an endocrinologist for hormonal treatment.

III. Discussion

Our case represents an extremely rare case of a true hermaphrodite male patient, with malignant evolution of ovarian tissue into RMS, treated with neoadjuvant chemotherapy and surgery with good outcome. RMS is usually a pediatric neoplasm that counts for 1% of adult cancers and 3% of adult sarcomas (7)**..**

Adult RMS is often described as having a worse prognosis than the pediatric forms (8) . Nevertheless some authors suggest that this poor outcome is due to the more advanced stages at diagnosis and the type of chemotherapy regimen used (9)**.** Pediatric RMS were evaluated at five larges series of randomized trials under the supervision of the International Rhabdomyosarcoma Staging Group (IRGS) consisting on IRS I to V (10). In this classification, the patients are categorized to different clinical groups depending on surgical findings, resection, and pathological results.

Treatment protocols associating surgery, radiation therapy (RT) and chemotherapy (CT) are indicated according to prognostic scales. The rarity of the disease in adult explains the difficulty of designing large prospective trials. Adult RMS is usually **treated** by polychemotherapy similar to the one used in soft tissue sarcomas using a combination of ifosfamide plus doxorubicin (11). Recent small retrospective series suggested that pediatric chemotherapy regimen may improve outcome (12) as in our case report, the use of MAID regimen resulted in complete pathological response . In a phase II trial, William G et al assessed neoadjuvant treatement based on MAID regimen with neoadjuvant RT (44Gy). In their study, 87,7 % had Ro resection. They estimated 5-year rates of disease-free survival, distant disease-free survival, and overall survival as 56.1% , 64.1%, and 71.2% respectively (13). Esnaola and al reported that complete response to chemotherapy in adult RMS improved 5-year overall survival (OS) (57% vs 7%; p=0,002) (9).

Lymph node involvement in PPORMS is not reported in the literature. Whereas, a review of 1,415**(7)** patients in IRS-I and IRS-II revealed 10% incidence of clinical nodal disease at diagnosis and a 14% incidence of pathologic lymph node metastasis at resection. Nodal involvement was the most common with genito-urinary tract tumor (41%). Patients with nodal proven disease had worse prognosis on 3-year overall survival (68% vs 83%; P=0,003)(14). Neville et al. reviewed nodal status in limb RMS patients treated in IRS-IV. Fifty percent of the surgically evaluated patients and 17% of the patients who were clinically negative, had lymph node involvement (15). A SEER data base study investigating lymph node status in para-testicular RMS was conducted by Dang et al and reported that 40% of patients who had lymph node dissection had nodal disease (16) . Lymph node dissection improved 5-year overall survival in patients more than 10 years old (86% vs 64% ; P=0,028) . This therapeutic effect may be explained by the adjunction of RT which improved OS in positive nodal patients.

Use of post-operative **RT** is well established in pediatric population using the IGRS grouping system. By analogy to the RMS of the children our patient was classified IRSG-IIA and received adjuvant external beam radiation.

In **litterature PORMS** are often a part of a complex tumor and only 35 cases were reported so far (17-33). Although, pleomorphic rhabdomyosarcoma is the most common subtype in adult patient, embryonal subtype is the most frequent (16 cases) followed by pleomorphic (9 cases) and alveolar (2 case). All cases were women aging from 17 to 86 years old. Usually, diagnosis was made at a late onset with large pelvic tumors (5 to 40 cm) and had extension to the adjacent tissues. According to FIGO classification, tumors were classified stage I in 9 cases, stage II in 7 cases, stage III in 10 cases and stage IV in 5 cases. FIGO stage was missing in the other observations.Treatment was not detailed in most of the PPORMS publications. It usually consists in removing the tumor when feasible often associated with external beam radiation. Chemotherapy was used in only 4 cases

Prognosis seems to be worse than other localizations of RMS and is usually limited to few months after diagnosis. To our knowledge, this is the first published case of ovarian RMS occurring in a **true hermaphrodite** male patient. Risk of malignancy of the gonads in true hermaphrodites is rare and ranges from 2,6% to 4,6% (34). Usually, the most common tumor subtype is a germ-cell tumor. In male phenotype hermaphrodites, there is an increased incidence of seminomas, gonadoblastoma and teratomas. This enhanced risk is explained by the ectopic location of the gonads. In our patient, surgical removal of the controlateral gonad was performed and a hormone replacement therapy was mandatory to avoid losing secondary sexual characters.

IV. Conclusion

PPORMS is a rare neoplasm with a poor outcome. Our current observation emphasize the latest findings that adult pleomorphic rhabdomyosarcoma is a complex disease which should be managed through a multidisciplinary approach with particular use of more intensive chemotherapy to induce complete histological response and enhance prognosis.

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