**Case Report**

**CARCINOMA URINARY BLADDER WITH SYNCHRONOUS GRANULOSA CELL TUMOR OVARY- A RARE CASE PRESENTATION**

**ABSTRACT-** The incidence of secondary primary malignancies (SPM) has been reported to range from 1.33% to 5.8% according to the location of the primary cancer and follow up duration. The term 'Synchronous Malignancy' is used when two or more malignancies appear within 6 months whether presenting in same or different organ with a different histology or morphology .

 Here we present a case of 56 year old female , known case of Urinary Bladder presenting with synchronous Granulosa Cell Tumor Ovary. To the best of our knowledge ,this is the first case of Urothelial carcinoma of the Urinary bladder presenting with synchronous malignancy of Granulosa cell tumor of the Ovary.

**INTRODUCTION**- The term 'Synchronous Malignancy' is used when two or more malignancies appear within 6 months whether presenting in same or different organ with a different histology or morphology [1].The frequency of synchronous malignancies or multiple primary tumors is around 2-17%[2-6].The presentation of such tumors include various risk factors ,exposure to chemicals, immunosuppression ,mutations in blood line,etc.[7,8].

Urothelial carcinomas presenting with synchronous Granulosa cell tumor is not yet presented in females and one such case on open acess is presented in males by Espejo et al.[9].They presented yolk sac differentiation in urothelial carcinoma of the urinary bladder and AFP(Alphafetoprotein ) determination in such cases[10].

Urinary bladder carcinomas in females have various epidemiological risk factors such as menopausal status,chronic urinary tract infections,obesity, smoking, family history ,etc.[11]

The risk factors of GRANULOSA cell ovary include obesity, family history,genetic alterations such as FOXL2,Oral contraceptives, BRCA1 AND 2 mutation[12].Their presentation as a Synchronous malignancy is a rare scenario.There remains a therapeutic deliemma in management of these SPM( second primary malignancies) due to possible drug- drug interactions,CYP enzymes in metabolism and morbidity related to treatment via combined modalities.

**CASE PRESENTATION - CARCINOMA URINARY BLADDER WITH SYNCHRONOUS GRANULOSA CELL TUMOR OVARY**

56 year old female presented with complaints of pain abdomen and occasional blood in urine . PET CT scan showed 3\*3 cm polypoidal lesion in the urinary bladder with FDG avid 7\*9 cm adenexal mass. TURBT showed low grade papillary urothelial carcinoma and adenexal deposit Biopsy and IHC showed Granulosa cell tumor**[FIGURE 1,2]** .

IHC confirmation of both specimens was done and at last a diagnosis of synchromous malignancy was made.TURBT sample was positive for CK20, P53 and E-Cadherin indicating low grade papillary urothelial neoplasm. Ovarian Sample stained positive for FOLX2, CD56,GATA 4 and SMAD 3 indicating Granulosa cell tumor ovary .

She was treated with 6 weekly cycles of intravesical BCG and 6 monthly cycles of intravesical BCG.

Now she is on maintenance Inj. Leuprolide 22.5 mg q3 monthly and Tab Tamoxifen 20 BID for GCT ovary.

Follow up PET CT scan showed complete resolution of UB lesion with decrease in size (now 3\*2 cm) and activity of adenexal mass **[FIGURE 3]**.

Biochemical response was also seen with decreasing trend of AFP(200 baseline to 15current) ,BetaHCG( now unrecordable) ,LDH (800 baseline to 126).

The patient is on regular follow-up with subjective as well as objective response.

**DISCUSSION -** Synchronous malignancies are in rising trend ,reasons may be the aggressive diagnostic techniques, extensive drug abuse,Oncoviruses ,host and genetic factors, environmental factors etc. [7].

 Espejo et al.[9] presented a case of 76 year old male presenting with yolk sac tumor differentiation in a case of carcinoma Urinary baldder. Most relevant histological characteristic of the solid-neoplasms with YST differentiation is the identification of variouspatterns, which can be grouped in two classes: the classical ones, which comprise reticular-microcystic, polyvesicular patterns, and the special ones, which comprise glandular, hepatoid and sarcomatoid patterns. Their case showed the described immunohistochemistry profile, in agreement with the diagnosis of YST differentiation.

Chromosome 12 abnormalities, either as an i12p or as 12p overrepresentation, are the hallmark cytogenetic alteration of Granulosa cell tumors.

AFP serum levels should be determined in patients with urothelial neoplasms exhibiting infrequent histological patterns (e.g. glandular or hepatoid), because the elevation of these levels support the diagnosis of YST differentiation. Moreover, these determinations may be used to control the postsurgical evolution, and to detect tumor relapse among these patients [10].

According to a recent studies, instillation of a chemotherapy agent significantly reduces the recurrence rate in patients included in a low-risk group (level 1 evidence )[13] as in the present study , the patient was treated with intravesical BCG post TURBT.

In a large cohort study of patients with granulosa cell tumors, the 6-month clinical benefit rate was seen with Leuprolide acetate treatment and progression-free survival was comparable to patients treated with chemotherapy[14]. In the present study , the patient was treated with leuprolide acetate monthly injections. She is doing well with subjective as well as objective response.

There remains a therapeutic deliemma in management of these SPM( second primary malignancies) due to possible drug- drug interactions,CYP enzymes in metabolism and morbidity related to treatment via combined modalities .Only case reports are available for these entities in giving a guiding path for treatment . Through immuno Histological and radiological workup is a must for developing diagnosis and biochemistry plays no less role in supporting ongoing systemic chemotherapy.

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**Figure 1- TURBT Biopsy specimen showing low grade papillary urothelial carcinoma.papillary core is seen with mildly dysplastic epithelium and mild loss of polarity of the nucleus.**



**Figure 2- GRANULOSA CELL TUMOR SHOWING CALL EXNER BODIES -COFFEE BEAN NUCLEI SHOWING GROOVING WITH CENTRAL PAS POSITIVE HYALINE MATERIAL**

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**Figure 3- CARCINOMA URINARY BLADDER WITH SYNCHRONOUS GRANULOSA CELL TUMOR OVARY - FOLLOW UP PET CT SCAN POST TREATMENT SHOWS NO METABOLICALLY ACTIVE LESION IN URINARY BLADDER AND ONLY 3\*2 CM RESIDUAL IN LEFT ADENEXA SHOWN WITH RED ARROW**

