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Pathology

CLEAR CELL CARCINOMA OF THE ENDOMETRIUM WITH ADENOCARCINOMA OF THE CAECUM - A CASE OF DOUBLE PRIMARY MALIGNANCY

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ABSTRACT Multiple primary cancers are usually defined as primary malignant tumors of different histological origins in one person . Recently , there has been an increase in the number of patients diagnosed with multiple primary cancers . We report a case of clear cell carcinoma endometrium in a 50 year old female with subsequent development of adenocarcinoma of the caecum , in the absence of any therapeutic intervention

KEYWORDS : synchronous , metachronous , hobnail cells

Introduction - Multiple primary cancers are usually defined as primary malignant tumors of different histological origins in one person . Recently, there has been an increase in the number of patients diagnosed with multiple primary cancers . This trend can be attributed to improved diagnostic techniques , prolonged life span and the increased incidence of long-term survival of patients with malignancy. Most multiple primary cancers are double primary cancers . [1 , 2]

Case report - A 50 year old female was admitted in the gynaecological department with a 1 year history of bleeding per vaginum and anorexia. Biphasic CECT revealed a thick heterogeneously enhancing endometrium and a long segmental intussusceptions with thick edematous caecal wall . On full colonoscopy a growth in hepatic flexure was noted. A radical hysterectomy and radical hemicolectomy was done and finally on histopathological examination , a clear cell carcinoma of the endometrium along with adenocarcinoma of the caecum was diagnosed .

Histopathology -

Specimen 1 -

Grossly ; Received a radical hysterectomy specimen , uterus with cervix measures (10.5 x 10 x 6.5) cubic cm . On cut section of uterus , an ulceroproliferative growth was noted measuring (6 x 4 x 3) cubic cm involving more than half of the myometrium [figure 1] .

Microscopically ; Section studied from tumour proper showed solid, papillary and tubulocystic pattern of tumour cells arrangement. Tumour cells are hyperchromatic, pleomorphic, having abundant clear to eosinophilic cytoplasm , vesicular nuclei with few multinucleated and bizarre nuclei [figure 3]. At places glands are lined by hobnail cells [figure 4] .

Specimen 2 -

Grossly ; Received a radical hemicolectomy specimen 31 cm in length. Caecum measures 8.5 cm in length. On cut section along the antimesenteric border , an ulceroproliferative tumour mass measuring (9 x 6.3 x 4) cubic cm was noted obstructing the lumen of the caecum and infiltrating upto the muscularis layer [figure 2] .

Microscopically ; Sections studied from the tumour mass showed Moderately differentiated adenocarcinoma infiltrating upto the muscularis layer with lymphovascular invasion [figure 5].

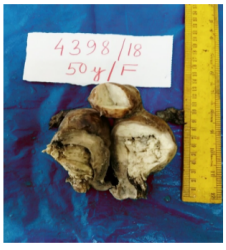

figure 1 - clear cell carcinoma endometrium

figure 2 - adenocarcinoma caecum

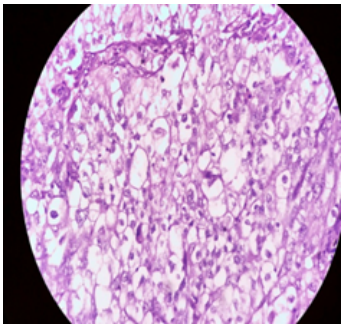

figure 3 - clear cell carcinoma endometrium showing abundant clear to eosinophilic cytoplasm (40x)

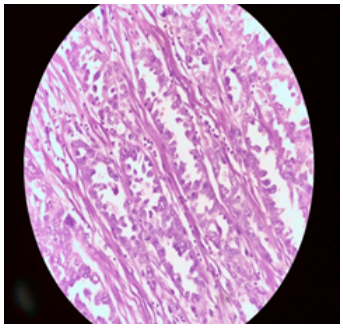

figure 4 - clear cell carcinoma endometrium showing hobnail cells (40x)

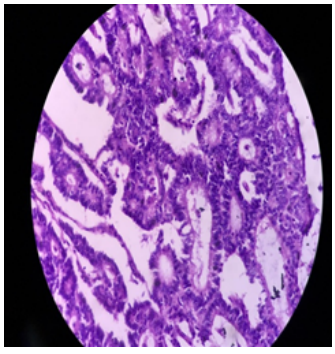

figure 5 - moderately differentiated adenocarcinoma of caecum (40x)

Discussion - Definitions and classifications for multiple primary cancers and multi-centric cancers , proposed by Moertel way back in 1977 hold true even today . [2 , 3] Accordingly , group I includes , multiple primary cancers occurring in organs with the same histology , group II includes multiple primary cancers that originate from

different tissues and group III consists of cancers from different tissues and organs that concurrently exist with group I cancers , and they form multiple primary cancer of three or more cancers . Group I is further subdivided into group A , which includes cancers that occur in the same tissue and organ , group B , which includes cancers that are from the same tissue and different organs , and group C , which includes cancers that occur in bilateral organs. Multiple primary cancers are again classified as synchronous and metachronous . Those malignancies that are observed at the same time or within 6 months are termed as synchronous multiple primary cancers , and those cancers that develop at more than a 6-month interval are termed as metachronous multiple primary cancers . [4] On the other hand , many studies have defined 1 year as the dividing time of these two types of multiple cancers . [5]

Clear cell carcinoma of the endometrium , first described a century ago, received little attention until the publication of two pathological studies by Silverberg and De Giorgi [6] and Kurman and Scully [7] in the 1970s . Clear cell carcinoma is usually detected in postmenopausal women , with a mean age of 62 to 67 years , older than those with endometrioid carcinoma [8 ,9 , 10]. Grossly clear cell carcinomas often form fleshy and soft masses involving most of the endometrial surface [11 , 12] . Microscopically the neoplasm can exhibit different microscopic patterns , namely solid , papillary , tubular and cystic [12] . The solid pattern consists of sheets of clear cells intermixed with eosinophilic cells , whereas papillary , tubular and cystic patterns are mainly composed of hobnail cells with interspersed clear and eosinophilic cells . The clear cytoplasm results from the presence of glycogen , and hobnail cells are cells with a naked nucleus that have discharged their glycogen and lost most of their cytoplasm . Nuclear atypia is usually marked and mitotic activity is high . Clear cell carcinoma also develops in the ovary , cervix and vagina , and displays very similar histological features [13] . The immunophenotypic profile of clear cell carcinoma is not yet well defined . Vang *et al* . [14] analyzed the immunohistochemical expression of cytokeratin 7 (*CK 7*) , *CK20* , low and high molecular weight cytokeratin (*CAM5.2* and *34βE12* , respectively) , carcinoembryonic antigen (*CEA*), Leu-M1 , vimentin , ER , progesterone receptor (PR) , BCL-2 , p53 , HER-2/neu , and CA-125 in 17 cases of primary clear cell carcinoma from different gynecological sites (11 ovary , 5 uterus , 1 vagina) . The characteristic immunoprofile for all sites was positivity for CK7 , CAM5.2 , 34βE12 , CEA , Leu-M1 , vimentin , BCL-2 , p53 , and CA-125 ; variable positivity for ER and HER-2/neu ; and negativity for CK20 and PR . Clear cell carcinoma often shows a higher Ki-67 proliferation index [15] and a greater number of cells expressing the proapoptotic gene *BAX* [16] compared with endometrioid carcinoma of the endometrium .

More than 90% of colorectal carcinomas are adenocarcinomas originating from epithelial cells of the colorectal mucosa [17] . It is apparent that the determination of tumor grade is a subjective exercise . Many studies have demonstrated that a 2-tiered grading system , which combines well and moderately differentiated to low grade (50% gland formation) and defines poorly differentiated as high grade (< 50 % gland formation) , reduces interobserver variation and improves prognostic significance [18 , 19] . Though controversial , tumor grade is generally considered as a stage-independent prognostic variable , and high grade or poorly differentiated histology is associated with poor patient survival [20 , 21 , 22] .

Conclusion - Incidence of multiple primary cancers though uncommon , is being frequently reported now-a-days owing to better diagnostic techniques , the prolonged life span and the increased incidence of long-term survival of cancer patients. Detection of multiple primary malignancies is becoming increasingly common in day-to-day practice . Greater awareness of this is required among both cancer patients and their treating clinicians .

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