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RESEARCH ARTICLE

THYROID-LIKE FOLLICULAR CARCINOMA OF THE KIDNEY IN A CHRONIC DIALYSIS PATIENT: ONE CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Thyroid-like follicular carcinoma of the kidney (TLFCK) is an extremely rare subtype of renal cell carcinoma (RCC) that histologically mimics primary follicular carcinoma of the thyroid gland. This new entity has not yet been integrated into the current WHO classification of renal tumors due to the limited data available. We report a further case of this rare histological entity, discuss the clinical, histological and immunohistochemical findings and provide an update on the review of the literature. A 73-year-old woman was found to have a left renal mass during her annual medical checkup. Her past medical history included high blood pressure and renal failure at hemodialysis stage. The patient underwent a nephrectomy with simple postoperative course. The tumor was described as being round, well circumscribed and dark brown in color. Histologically, the tumor showed follicular architecture with macro and micro follicles containing eosinophilic secretions or colloid-like material. Immunohistochemical studies demonstrated that the tumor cells exhibited no immunoreactivity for thyroid transcription factor-1 and thyroglobulin. The tumor cells showed intensive staining for cytokeratin 7 (CK7). The tumor cells were completely negative for CK20, WT1 and PAX8. Molecular biology was not carried out for lack of means. These findings are dissimilar to previously classified renal neoplasm. Thyroid-like follicular renal cell carcinoma represents a unique histologic subtype of renal cell carcinoma of low malignant potential and its primary importance is to distinguish it from metastatic carcinoma from the thyroid. A correct histopathologic diagnosis has important clinical and therapeutic implications. The current consensus from ISUP is not to recommend TLFCK as a new WHO histologic classification due to the small number of cases; therefore, documentation of all cases available seems to be important to gain additional knowledge.

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Introduction:-

Thyroid-like follicular carcinoma of the kidney (TLFCK) is an extremely rare subtype of renal cell carcinoma (RCC) that histologically mimics primary follicular carcinoma of the thyroid gland, but TLFCK is characteristically negative for thyroid immunohistochemical markers. [1]

This new entity has not yet been integrated into the current WHO classification of renal tumors due to the limited data available.

The first case of TLFCK was reported in 2004 [2] and since then, to our knowledge, an additional 41 cases have been reported in the literature.

We report a further case of this rare histological entity, discuss the clinical, histological and immunohistochemical findings and provide an update on the review of the literature.

Case Report:

A 73-year-old woman was found to have a left renal mass during her annual medical checkup. Her past medical history included high blood pressure and renal failure at hemodialysis stage.

Computed tomography of her abdomen revealed a relatively homogeneously enhancing mass (3 cm in greatest dimension) of the right kidney. No metastatic lesions or lymph node enlargement were noted.

Physical examination of the thyroid, abdomen and pelvis was normal. Biological data, including thyroid function tests, were within the normal ranges.

The patient underwent a nephrectomy with simple postoperative course.

Materials and Methods:-

Surgical specimens were sampled according to the current protocol of nephrectomy. Formalin-fixed, paraffin-embedded tissue samples were obtained, and 4-µm sections were stained with hematoxylin and eosin (H&E) before microscopic examination.

Results:-

After a radical laparoscopic nephrectomy, the pathological examination showed a 3x2.5x2-cm mass in the upper pole of the left kidney.

Macroscopically, the renal parenchyma was atrophic with fatty involution. The tumor was superior polar and measured 3x2.5x2cm. The tumor was described as being round, well circumscribed and dark brown in color.

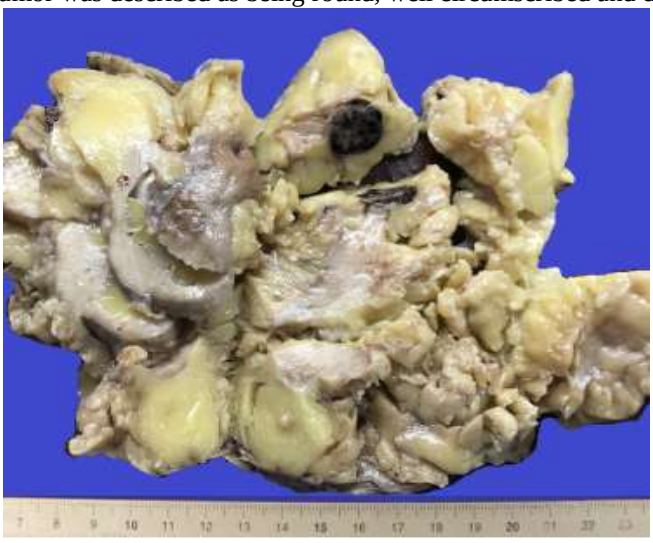

Fig. 1:- Gross image.

Histologically, the different samples taken from the tumor showed follicular architecture with macro and micro follicles containing eosinophilic secretions or colloid-like material.

Follicular cells had moderate eosinophilic cytoplasm, round nuclei and inconspicuous nucleoli corresponding to ISUP(Fuhrman) nuclear grade 2.

The tumor was confined within the kidney parenchyma andthere was no capsular invasion or extension into perinephric adipose tissue.

Significant mitotic activity was not seen.

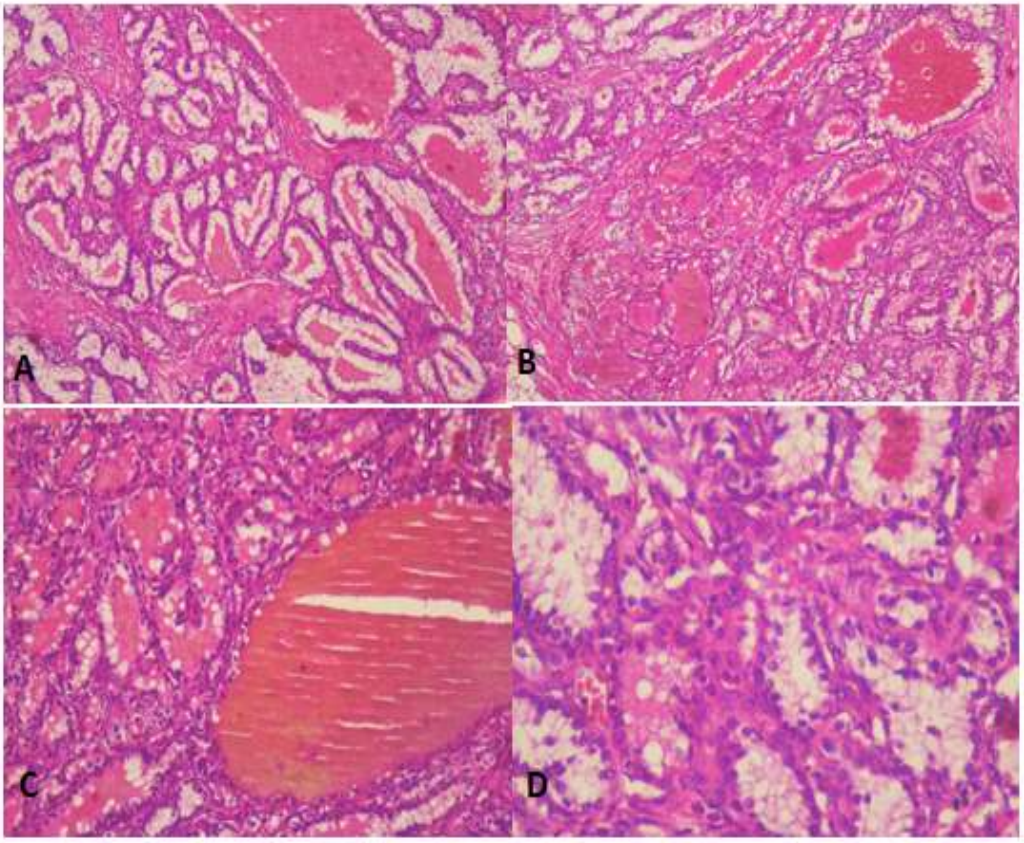

Fig. 2:- Histological image of TLFCK showing follicular architecture with macro and micro follicles containing eosinophilic secretions (A, B: HEx10; C: HEx20; D: HEx40).

Immunohistochemical studies demonstrated that the tumor cells exhibited no immunoreactivity for thyroid transcription factor-1 and thyroglobulin. The tumor cells showed intensive staining for cytokeratin 7 (CK7) (figure 3). The tumor cells were completely negative for CK20, WT1 and PAX8.

The diagnosis of primary thyroid-like follicular carcinoma of the kidney was retained.
Molecular biology was not carried out for lack of means.

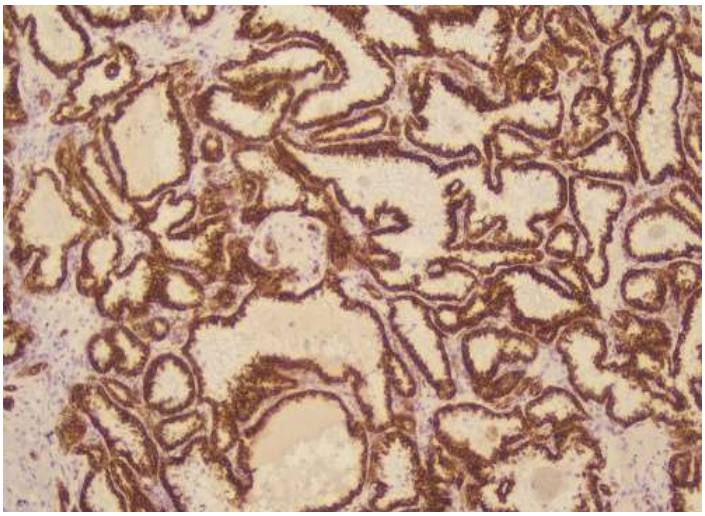

Fig. 3:- Intensive staining for CK7.

Discussion:-

Primary TLFCK is a rare and recently described entity that has low malignant potential. The first case was reported by Amin et al. in 2004, and since then, 41 more cases have been described. The patients' ages ranged from 19 to 83 years with median age of 35 years and mean age of 41 years. A slight predominance in women was noticed (2:1)

In 70% of the patients, including our case, the tumors were incidental findings. The rest of the patients were symptomatic at presentation with hematuria, flank pain or abdominal pain.

TLFCK have a higher incidence in the right renal unit. One patient presented with bilateral tumors. In our case, the tumor was located in the left kidney.

Approximately 20% of the patients had a history of malignancy: Two patients had Hodgkin lymphoma, one patient had lymphoblastic leukemia, one patient had myeloid leukemia, two patients had prostatic adenocarcinoma, one patient had a history of urothelial carcinoma, one patient had an ovarian teratoma and one patient had a history of thyroid cancer. In our case, the patient was a chronic dialysis and had no history of malignancy.

The majority of the cases appear to have low malignant potential, including our case, while 10% of the patients developed metastases, and all of them were women and older than the median age.

40% of the metastases were pulmonary [24], 40% were to lymph nodes, while 10% were to the skull and 10% were to the meninges [4, 19, 21].

These latter cases provide evidence that this rare variant of RCC has a low but distinct malignant potential and can be clinically aggressive.

In no patient did the carcinoma cause death.

On gross examination, most tumors have been unifocal and surrounded by a thin fibrous capsule, with or without areas of cystic changes [5, 8, 9, and 13] or necrosis. [25, 5, 26, 13] However, in some cases, the tumors were nonencapsulated. [27]Like in our case, the tumor tissue was generally confined within the kidney parenchyma and rarely presented capsular invasion or extension into perinephric adipose tissue.

The diameter of the tumors ranged from 11 mm to 130 mm with a median diameter of 35 mm and a mean diameter of 43 mm. The tumors were described as being homogeneous, dark brown in color.

Areas of hemorrhage or necrosis, or both were mentioned for about half the tumors. In our case, hemorrhage or necrosis were not seen.

Cysts, often small, were also seen in about half the tumors. In our case, there was no cystic areas.

Central areas of fibrosis were observed in only two tumors.

Gross or microscopic invasion of perinephric tissues was found in 13% of the cases. No mention was found of vascular invasion nor extension into the renal pelvis.

Microscopically, the most striking feature was the strong resemblance to thyroid tissue or thyroid neoplasia with follicular architecture.

The tumor shows follicular architecture with micro and macrofollicles containing eosinophilic secretions or colloid-like material that mimics follicular carcinoma of the thyroid. In follicular carcinoma of the thyroid, the composition of this material is thyroglobulin, while in TLFCK, the colloid like material is periodic acid–Schiff positive and diastase resistant and resembles the intraluminal proteinaceous casts of Tamm-Horsfall glycoprotein usually identified in thyroidization of the renal tubules. [29]

The follicles were lined by cuboidal or flattened epithelial cells with amphophilic to eosinophilic cytoplasm.
The nuclei were of modest size, and almost always quite uniform, with uniform distribution of chromatin. In only a few cases, reference was made to nuclear grooves or 'ground glass' nuclear appearance.

In five cases, subtle but distinct nuclear membrane irregularities were present.

In all but two tumors, including our case, the nucleoli were inconspicuous corresponding to ISUP (Fuhrman) nuclear grade 2.

Significant mitotic activity was only seen in one case.

Lymphocytic infiltrate may be present intratumoral or around periphery and macrophages may be present in background. [9]

Calcifications may be seen, including abundant microcalcifications; some cases resemble atrophic thyroid tissue [3].

To some authors, these tumors resembled atrophic renal cortex.

Cytological features were only described in one case [6]. An intraoperative smear preparation of the tumor revealed a hypercellular smear with cells arranged in sheets without any follicular, papillary, or acinar arrangement.

Individual tumor cells may be oval, round and plasmacytoid with mild nuclear pleomorphism, finely stippled nuclear chromatin and inconspicuous nucleoli with moderate amount of eosinophilic cytoplasm and rare nuclear grooves.

Presence of acellular eosinophilic material is associated with the neoplastic epithelial cells in the background of the smear.

Antibodies to a wide variety of antigens have been applied to the 41 thyroid-like follicular carcinomas.

Immunohistochemical stains to exclude the possibility of metastasis were performed in all the reported cases.

Immunohistochemistry for thyroid transcription factor-1 (TTF-1) was undertaken with negative results in all 41 cases. Immunohistochemistry for thyroglobulin was performed in 40 cases and all of the reactions were negative.

Based on the immunohistochemical findings in conjunction with clinical presentation, metastatic follicular thyroid carcinoma to the kidney was easily excluded as well as metastases from struma ovarii.

Immunohistochemistry for PAX8 was performed in 16 cases with positive results in 13. However, this is not helpful in the differential diagnosis with thyroid carcinoma since immunohistochemistry for PAX8 is positive in the nuclei

of nearly 100% of normal thyroid epithelial cells, papillary carcinomas, follicular adenomas, and follicular carcinomas. [31, 32, 33]

Immunohistochemistry for PAX2 was performed in 17 cases, with positive results in nine which 3 were weak. However, Immunohistochemistry for PAX2 is also positive in the nuclei of 50–100% of primary and metastatic clear cell renal cell carcinomas and papillary renal cell carcinomas. [34]

In the other hand, reactions for PAX2 in thyroid epithelial tumors have consistently been negative. [35, 36] Thus, a positive reaction for PAX2 weighs in favor of renal origin and heavily against thyroid origin.

Immunohistochemistry for vimentin was performed in 25 cases and gave a positive reaction in 18 which one was focal. However, this is not useful for differentiating these tumors from metastases of thyroid cancer because in normal thyroid follicles, follicular adenomas, follicular carcinomas and papillary carcinomas immunohistochemistry shows 50–100% of the cells to be positive for vimentin in more than 90% of cases. [37]

Immunohistochemistry for CD10 was performed on 31 cases, with eight giving positive reactions and 23 giving negative reactions. CD10 also known to be positive in about 80% of follicular thyroid carcinomas and follicular variants of papillary thyroid carcinoma, but it is negative in normal thyroid tissue and papillary thyroid carcinoma other than the follicular variant. [38]

Immunohistochemistry for CD117 was performed in 23 cases and the reactions were positive in only four of these.

Immunohistochemistry for cytokeratin 7 (CK7) was performed in 37 cases, with positive results in 27. Immunohistochemistry for cytokeratin 20 was undertaken in 14 cases, with four giving positive results.

Immunohistochemistry for WT1 was performed on a few of the tumors and they were all negative.

Differential diagnosis rests on distinguishing TLFCK from metastatic tumors of the thyroid gland, and thyroid studies must be performed to rule them out. Since the management of metastatic thyroid carcinoma and TLFCK differs greatly, misdiagnosis can result in suboptimal patient management.

A few cases of thyroid carcinoma metastatic to kidney, decades after the thyroid primary was diagnosed, have been reported. [39,40,41]

Another differential is metastases from an ovarian teratoma composed of thyroid tissue (malignant struma ovary). To our knowledge, there are no reports of struma ovarii metastasizing to the kidney. In any case, metastatic carcinoma cells from struma ovarii should disclosed positive immunoreactivity for TTF-1 and Tg [8]. In all reported cases of TLFCK, including ours, the carcinoma cells lacked immunoreactivity for these two markers, and no lesion was found in the ovary.

TLFCK should also be distinguished from kidney thyroidization. Thyroidization of the kidney is a well-known phenomenon characterized by atrophic distal tubules or collective ducts with colloid-like hyaline casts imitating the usual structure of the thyroid gland. It is a benign phenomenon that is typically bilateral and widespread, as opposed to TLFCK which presents as a well circumscribed mass.

It is recognized that different types of renal cell carcinoma have distinct genetic abnormalities.
In TLFCK, genetic analysis has shown variable genetic alterations [25, 42]. Using comparative genomic hybridization analysis, Jung et al. [25] reported losses of chromosomes 1p36, 3 and 9q21-33 and gains of chromosomes 7q36, 8q24, 12, 16, 17p11-q11, 17q24, 19q, 20q13, 21q22.3, and Xp in their case. Using fluorescent in situ hybridization analysis, Sterlacci et al. [24] found losses of chromosomes 1, 3, 7, 9p21, 12, 17, and X in this tumor.

In our case, molecular biology was not carried out for lack of means.

Conclusion:-

In summary, we report the case of an unusual renal tumor disclosing histologic features similar to follicular carcinoma of the thyroid, but lacking typical thyroid markers, and corresponding to TLFCK.

A correct histopathologic diagnosis has important clinical and therapeutic implications. The current consensus from ISUP is not to recommend TLFCK as a new WHO histologic classification due to the small number of cases; therefore, documentation of all cases available seems to be important to gain additional knowledge.

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