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An Infrequent Secondary Location of Renal Carcinoma: About a Case

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Abstract:- Thyroid metastases are an extremely rare secondary location and are generally asymptomatic. It is important to discuss a malignant tumor process such as metastasis to any thyroid nodule found in a patient with a history of renal carcinoma. We describe the case of a 63-year-old patient followed for thyroid nodules, she had a history of left nephrectomy at the age of 48 for clear cell cancer, which had to increase in size of one of the thyroid nodules as well as solids dysphagia, she was able to benefit from a total thyroidectomy.

Pathologic study revealed thyroid metastasis from clear cell kidney cancer, and radiotherapy for her brain metastases combined with systemic treatment for her contralateral and metastatic relapse. In this article on will raise the clinical, paraclinical and therapeutic aspects of this location with a review of literature.

Keywords:- *Thyroid, Renal Cell Cancer, Metastasis.*

I. INTRODUCTION

Early metastatic clear cell kidney cancer (CRC) accounts for 20-30% of cases. Lung, bone, liver and brain are the most frequently affected sites. The scarcity of thyroid metastases, as well as the notion of a prolonged interval between treatment of Primary cancer and its findings can be confusing to diagnose.

Reporting a 63-year-old patient treated with extended nephrectomy 15 years previously and presents with thyroid localization metastases, brain and a recidivism in the contralateral kidney.

II. PATIENT AND OBSERVATION

This is a 63 year old patient with no personal or family medical history individuals, followed since 2005 for clear cell renal carcinoma of the left kidney for which She had a expanded total nephrectomy.

Anatomopathological examination had shown a renal carcinoma with 8 cm long axis lower polar clear cells partially infiltrating theclean capsule of the kidney without crossing it, respecting the hilar region, the adrenal is not invaded, the ureteral section slice is healthy, classified as pT2NxMx. Then regular monitoring was established at her home.

In January 2020, fifteen years later, she noticed solid dysphagia with palpable anterior cervical nodule. Thyroid ultrasound showed thyroid nodule right classified EUTIRADS 5 measuring 43mm, left nodule classified EUTIRADS 3.

A thyroid cytopuncture of the TIRADS nodule was performed and concluded to a lesion carcinomatous which may correspond to either vesicular or medullary carcinoma. The patient was subsequently operated for a total thyroidectomy, the pathological examination revealed thyroid localization of renal cell carcinoma. The immunohistochemistry study showed a positivity of the following antibodies: anti-PAX8, anti-CD10, anti -EMA, with absence of anti-GATA-3, anti-Chromogranine, anti-TTF1, anti-Calcitonine and anti-RE antibodies. In front of these morphological and immunohistochemical arguments, the diagnosis of thyroid localization of renal cell carcinoma was retained.

Then the patient was referred to us two months later. At admission, the patient reported headache with decreased visual acuity which motivated the realization of a brain scan objecting two 20 x 17 mm hyperdense nodules with right occipital parenchyma and 34 x 26mm in left occipital. Supplemented by a cerebral MRI which showed a nodular lesio right occipital in T1 isosignal, raised T2 hyposignal after 14 mm gadolinium injection and the other left occipital oval lesion extended to Left cerebellar hemisphere, in T1 hypersignal T2 hypersignal of 26X16mm.

The CT chest /abdominal /pelvis carried out as part of the extension assessment has 41X40X32 mm hypodense tissue lesion of the right kidney pole top deforming the bypasses external of the slightly heterogeneous kidney quite limited.

The patient was classified poor prognosis according to the IMDC classification. The case was discussed at a multidisciplinary consultation meeting, the collegial decision of which was start a Sunitinub-type anti angiogenic in the first line, followed by surgery in function of tumor response with stereotactic radiotherapy on both metastases brain.

The patient has been on Sunitinib since March 2022, and has received cerebral radiotherapy in 3D conformational radiotherapy without SBRT in our service on the 2 brain metastases at the 45 Gy dose in 15 3Gy fractions for 3 weeks. It is always on Sunitinib with a good clinical evolution, with the last CT Chest/ Abdominal /pelvis regression volume of the right kidney cortical medullary tumour process.

In the context of a suspicion of a hereditary from of renal clear cell carcinoma , the patient benefit of an oncogenetic consultation. The interrogation allowed to find several family history of neoplasia (Figure I), including a son who died at the age of 41 from a colon cancer, the father died at age 70 from prostate cancer, as well as a cousin death at the age of 50 from endometrial cancer. Moreover, the anamnesis has evidence of renal cysts in one daughter and one sister. The clinical examination did not find clinical signs that may suggest a particular syndrome, Also brain MRI and examination of fundus have not identified signs of hemangioblastomas. Subsequently a study of a panel of predisposition genes.

III. DISCUSSION

Clear cell carcinoma represents approximately 2-3% of adult cancers, it ranks 3rd among urological tumours after prostate and bladder cancer. It is a tumor with high histological potential type in 85% of cases clear cell carcinoma. Its incidence is increasing and this is due to advances in early detection imaging. The average age of onset is around 65 years with male predominance. Thyroid metastases of a CCR are rare. They make up 12-34% of all secondary thyroid tumours [1] can be explained by several hypotheses: neoplastic emboli would not be able to settle in the thyroid gland because of the flow of blood which is very important[2], Thyroid metastases are generally observed late in average time of 7 10 years after nephrectomy [3], However, later metastases occurring a few times decades later have also been reported [4] so they usually appear in a metachronous context, the explanation for the late onset of these metastases is not Claire. on the other hand, in a review of the literature related to this subject, Beutner et al reported a single case of synchronous MT [5].

In our patient, thyroid metastases were diagnosed 15 years after the treatment of left kidney CCR, and have been accompanied by brain metastases and recurrence of the contralateral kidney. In this case, two situations are possible: late metastatic recurrence of disseminated CRC in the thyroid, brain and contralateral kidney. Second, a second primary contralateral kidney cancer with synchronous metastases thyroid and cerebral. The distinction between the two situations is difficult.

Clinically the symptomatology is poor however some patients may present symptoms such as, Trouble swallowing, Difficulty breathing hoarseness, changes the voice or palpation of a nodule[6,7].

Imaging test, for example by ultrasound or a thyroid scintigraphy are not specific for diagnosing thyroid metastases [6] which is consistent with the results of our patient's thyroid ultrasound has objectified a thyroid nodule classified as EUTIRADS 5. This may distort the diagnosis that is to say the considered a primary tumour of thyroid origin.

Fine needle tyroid aspiration (FNA) is the key examination to establish suspect nature or not , but it was reported that thyroid metastases have often misdiagnosed as primary thyroid tumours in the preoperative stage, especially when the interval between primary tumor diagnosis and thyroid metastasis is long [7,8,9], including our case in which an aspect of vesicular or medullary carcinoma has cytopuncture. Cytological results may be similar for tumours primary and secondary immunohistochemistry must also always be performed in thesesituations. Immunostaining with anti-thyroglobulin is only positive for lesions primary thyroid and Anti-thyroglobulin immunostaining is generally positive in the case of a primary thyroid, and it will be negative in thryroid metastases[10,11].

In immunohistochemistry the positivity of CD10, renal carcinoma antigen (RCC), and vimentine, and negativity for TTF-1 and thyroglobulin, directed towards the diagnosis of metastasis of a CCR.

However, thyroglobulin positivity or negativity does not confirm or eliminate formally the thyroid origin. Thus, thyroid metastasis can imprison in its in normal thyroid follicles and express thyroglobulin in immunohistochemistry. In Conversely, clear-cell thyroid carcinoma can sometimes express weak thyroglobulin. In these difficult cases, classical and chromosomal cytogenetic analysis targeted by DNA in situ hybridization are useful for determining histological type as well as chromosomal aberrations [12].

For our case the diagnosis was made thanks to immunohistochemistry taking into account overexpression of CD10, PAX8 and negativity of other markers including thyroglobulin.

When thyroid metastasis (MT) is isolated, total thyroidectomy is justified because sustained survival has been reported. Patients with a disease metastatic outside the thyroid were included in some studies. Nakhjavani et al, have reported an average survival of 34 months with thyroidectomy with or without adjuvant treatment, unlike 25 months for non-surgically treated patients [13], however Papi. G and al concluded in their articles that

thyroideectomy may be useful to prevent spread away from the unique thyroid location however it does not help prolong life overall [14]

Total thyroidectomy remains the most appropriate surgical procedure in the majority of cases. Finally, a palliative thyroidectomy in case of disseminated disease may be proposed in front of compressive signs [15].

Due to the scarcity of this situation, it is difficult to make recommendations.

In the case of our patient, a total thyroidectomy was performed, and metastases have been treated with tumoricide dose radiotherapy in the absence of a stereotactic radiotherapy which remains the treatment of choice in the brain disease situation oligomettastatic. A partial nephrectomy will be offered to the patient after obtaining the maximum response.

Since 2006, the interest of targeted therapy has been demonstrated in clear cell kidney cancer metastatic, modifying therapeutic strategies, currently treatment is based on targeted therapy, mTOR inhibitors and immune control point inhibitors. The improvement of SG and the achievement of lasting stability requires a rigorous evaluation of the new therapies.

Concerning the genetic part among hereditary predisposition syndromes for kidney cancer The most common is von Hippel-Lindau's disease. It affects 1/36,000 births. On the renal level, it manifests either by benign cysts or by cell carcinomas clear. It is also characterized by hemangioblastomas of the central nervous system or retina, and is responsible for 24% of cases of hereditary pheochromocytoma. It is a autosomal dominant transmission, by mutation of tumor suppressor VHL gene, localized
3p25[16].

Birt Hogg Dubé syndrome is also another hereditary predisposition syndrome. kidney cancer, autosomal dominant. Its incidence is estimated at 1/100,000. It is genodermatosis, characterized by specific skin lesions on the face and trunk, and also by lung cysts and pneumothorax. Colic cancers are also possible [17], This syndrome is related to mutations of the gene FLCN, suppressor of tumor, localized in 17p11.2[18]. Another hereditary predisposition syndrome to kidney cancer is Cowden's syndrome. It is characterized by the occurrence of malignant tumors including level of the kidney, endometrium and colon. This syndrome is also autosomal dominant [19].

In the case reported in this observation, the panel study of hereditary predisposition genes to kidney cancer has not been done, due to lack of means. Identification of a responsible mutation genetic predisposition is essential to be able to make a pre-symptomatic diagnosis in relatives, thus enabling early surveillance and diagnosis of carriers of genetic mutation.

Generally the prognosis is favourable and it is related to several factors. Uniqueness or multiple metastases is fundamental. Other factors are: complete removal of thyroid metastases, long interval between resection of CRCC and the appearance of MT over 10 years

IV. CONCLUSION

Thyroid metastases of CRC are rare and generally asymptomatic, in any patient with a history of kidney cancer a metastatic relapse to the thyroid level should be reported and confirmed anatomopathological examination of suspected thyoid nodules. The thyroidectomy is justified in case of unique metastasis and appears to improve survival in these patients.

Declaration of Interest: The Submitters did not submit a Declaration of Conflict of Interest.

Consent for publication : The patient agreed that doctors could use and publish her case, including the accompanying pictures. A copy of the writing consents is available for review by the editor of this journal.

REFERENCES

[1]. Medas F, Calò PG, Lai ML, Tuveri M, Pisano G, Nicolosi A. Renal cell carcinoma metastasis to thyroid tumor: a case report and review of the literature. J Med Case Rep 2013; 7: 265
[2]. F. Ménégaux, P. Chigot, Thyroid metastases, Ann. Chir. 126 (10) (2001) 981–984
[3]. RamÃ¬rez Plaza C, DomÃ¬nguez LÃ³pez M, Blanco Reina F. Thyroid metastasis as initial presentation of clear cell renal carcinoma. Int J Surg Case Rep. 2015;10:101-3
[4]. Kihara M, Yokomise H, Yamauchi A. Metastasis of renal cell carcinoma to the thyroid gland 19 years after nephrectomy: a case report. Auris Nasus Larynx 2004; 31: 95-100
[5]. U. Beutner, C. Leowardi, U. Bork, C. Lüthi, I. Tarantino, S. Pahernik, M.N. Wente, M.W. Büchler, B.M.Schmied, S.A. Müller, Survival after renal cell carcinoma metastasis to the thyroid: single center experience and systematic review of the literature, Thyroid 25 (December 10 (3)) (2015) 314–324
[6]. Rosen IB, Walfish PG, Bain J, Bedard YC. Secondary malignancy of the thyroid gland and its management. Ann Surg Oncol 1995;2:252
[7]. Chen H, Nicol TL, Udelsman R. Clinically significant, isolated metastatic disease to the thyroid gland.World J Surg 1999;23:177
[8]. Palazzo FF, Bradpiece HA, Morgan MWE. Renal cell carcinoma metastasizing to the thyroid gland. Scand J Urol Nephrol 1999;33:202–4
[9]. Green LK, Ro JY, Mackay B, Ayala AG, Luna MA. Renal cell carcinoma metastatic to the thyroid. Cancer 1989;63:1810–5.]

ISSN No:-2456-2165

[10]. Harach HR, Franssila KO. Thyroglobulin immunostaining in follicular thyroid carcinoma: relationship to the degree of differentiation and cell type. Histopathology 1988;13:43–54.
[11]. 11. Burt A, Goudie RB. Diagnosis of primary thyroid carcinoma by immunohistological demonstration of thyroglobulin. Histopathology 1979;3:279–86.
[12]. Amo-Takyi BK, Handt S, Gunawan B, Hollweg HG, Fuzesi L. A cytogenetic approach to the differential diagnosis of metastatic clear cell renal carcinoma. Histopathology British Journal of Cancer (2000) 82(8), 1407–1414
[13]. Nakhjavani, M.K., Gharib, H., Goellner, J.R., van Heerden, J.A.: Metastases to the thyroid gland: a report of 43 cases. Cancer 19:574, 1997
[14]. Papi G, Fadda G, Corsello SM, et al. Metastases to the thyroid gland: prevalence, clinicopathological aspects and prognosis: a 10- year experience. Clin Endocrinol (Oxf). 2007;66:565–571
[15]. Sokoloff MH, deKiernen JB, Figlin RA, Belledegrun A. Current management of renal cell carcinoma. CA Cancer J Clin 1996;46: 284–302
[16]. Lonser RR, Glenn GM, Walther M, Chew EY, Libutti SK, Linehan WM, et al. von Hippel-Lindau disease. Lancet. 14 juin 2003;361(9374):2059-67.
[17]. Toro JR, Wei M-H, Glenn GM, Weinreich M, Toure O, Vocke C, et al. BHD mutations, clinical and molecular genetic investigations of Birt-Hogg-Dube syndrome: a new series of 50 families and a review of published reports. Journal of Medical Genetics. 30 janv 2008;45(6):321-31.
[18]. Nickerson ML, Warren MB, Toro JR, Matrosova V, Glenn G, Turner ML, et al. Mutations in a novel gene lead to kidney tumors, lung wall defects, and benign tumors of the hair follicle in patientswith the Birt-Hogg-Dubé syndrome. Cancer Cell. Août 2002;2(2):157-64.
[19]. Bubien V, Bonnet F, Brouste V, Hoppe S, Barouk-Simonet E, David A, et al. High cumulative risks of cancer in patients with PTEN hamartoma tumour syndrome. J Med Genet. avr 2013;50(4):255-63.

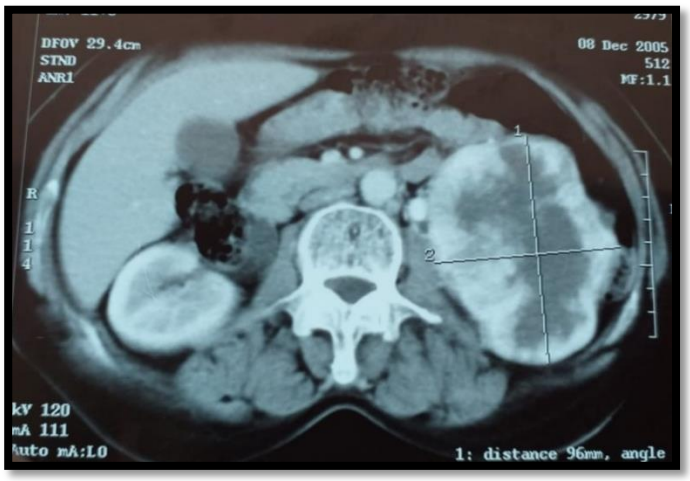

Figure 1: Cross section of a tumor mass of the left kidney necrotic and heterogeneously heightened.

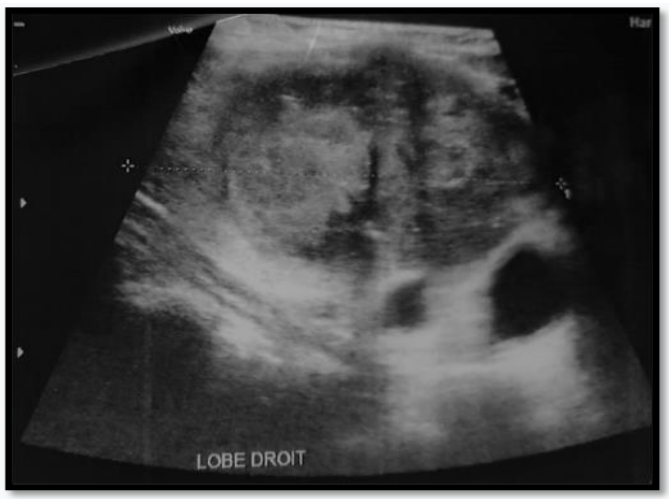

Figure 2: cervical ultrasound showing the right lobe site of a bi-lobar nodule of hypoechoic, heterogeneous echostructure, site of microcalcification measuring 43x35x28mm classified EUTIRADS 5.

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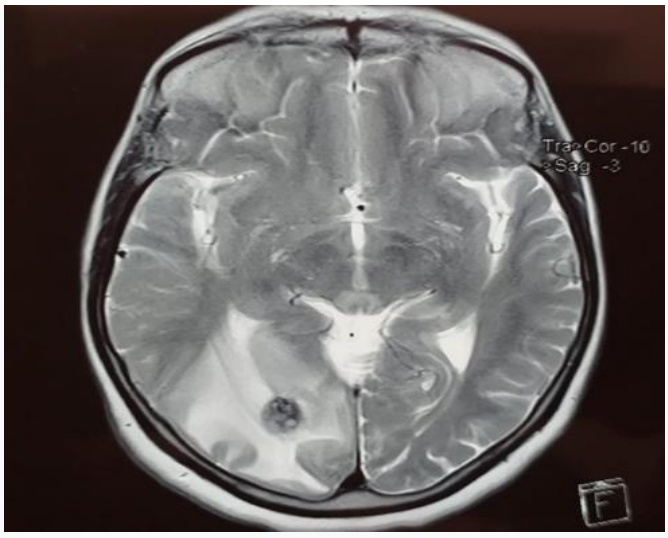

Fig3 : Brain MRI Right occipital nodular lesion in T1 isosignal, T2 hypointensity enhanced after injection of gadolinium measuring 14mm

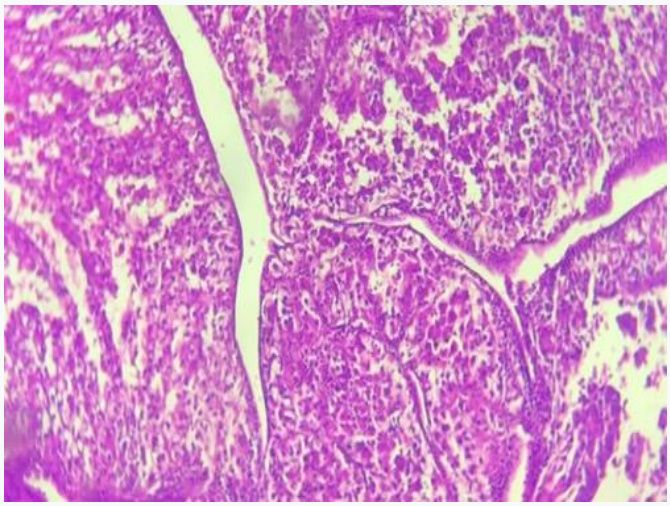

Fig4: Haematein eosin, carcinomatous proliferation solid architecture made of cells with abundant clarified cytoplasm and hyperchromatic nuclei X40 .

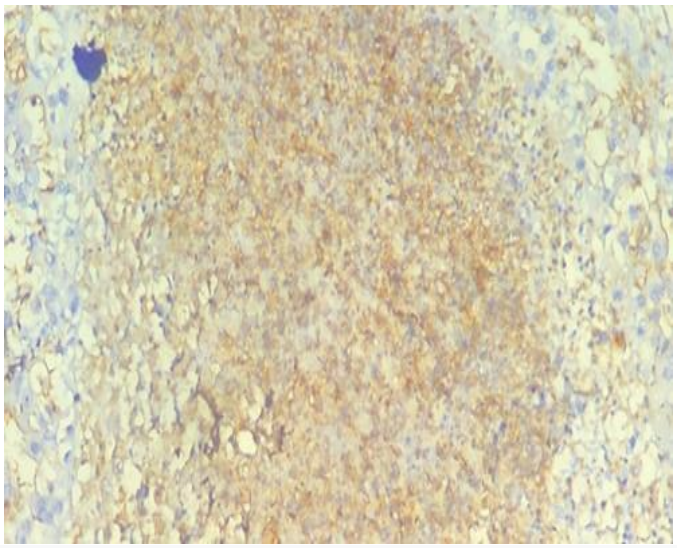

Fig 5: Immunohistochemical study shows expression of CD 10 X40.

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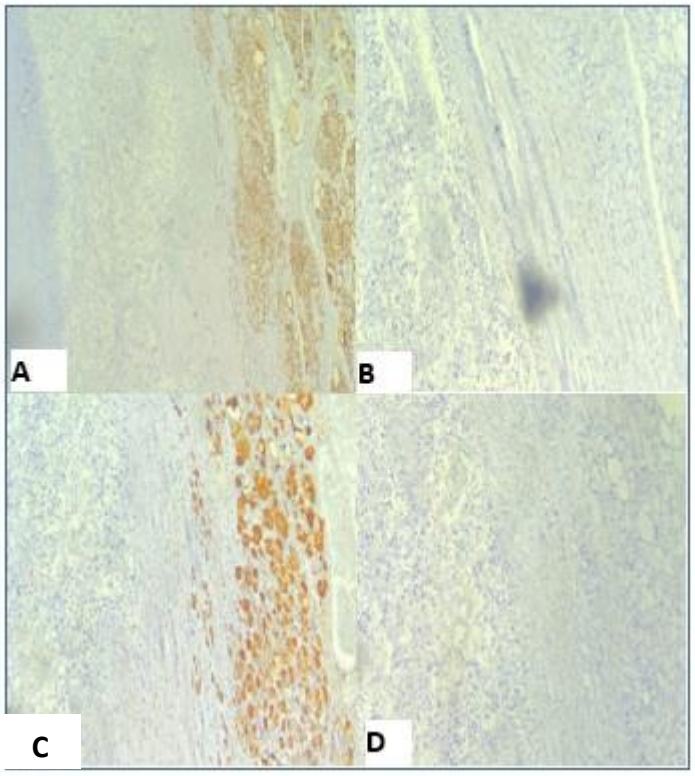

Fig 6: The immunohistochemical study shows: the absence of the expression of cytokeratin 7 (positive internal control) A Cytokeratin 20 B thyroglobulin (positive internal control) C and RCC D X 20.

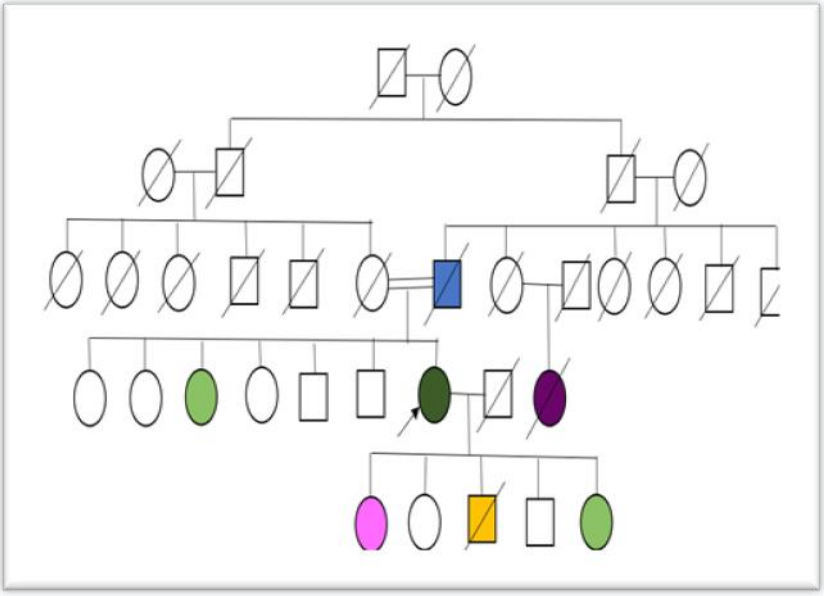

Fig 7: Family tree of the propositus (IV, 7), followed for clear cell renal carcinoma since the age of 57, showing several family history of neoplasms: the father died at the age of 70 a prostate cancer (in blue), a paternal cousin, who died at the age of 50 from endometrial cancer (in purple), and a son who died at the age of 41 from cancer of the colon (in yellow). Note also the presence of renal cysts in a girl and a sister (in green), and in a girl having undergone a hysterectomy for complicated uterine fibroids (in pink).

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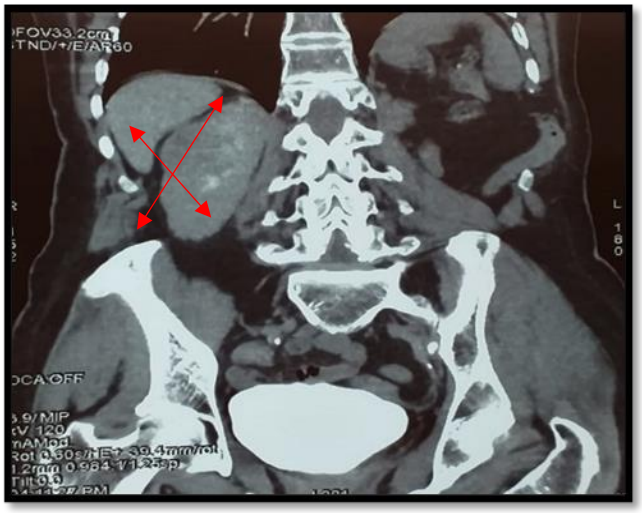

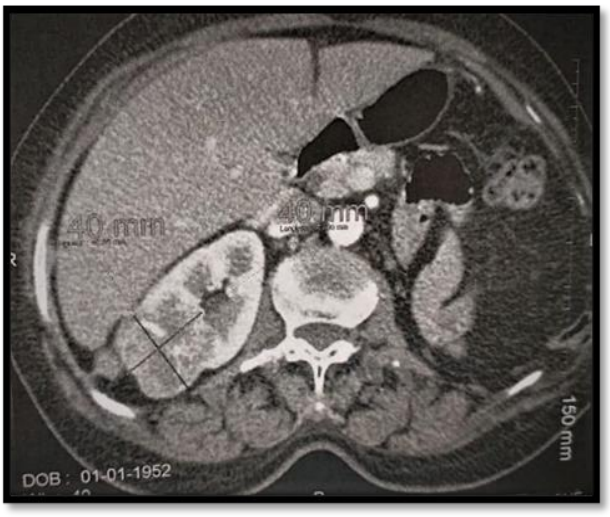

Fig 8 : Thoraco-Abdomino-Pelvic CT performed as part of the extension assessment revealed a tissue lesion of the sup pole of the right kidney of 41X40X32 mm hypodense deforming the external contours of the slightly heterogeneous kidney, which was fairly well limited.