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A Middle Age Woman with Renal Cell Carcinoma

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HISTORY

Mrs. S.S., 50 years, a house wife from Model Town Lahore, presented in Surgical Out Patients Dept. with complaints of

Pain left flank ——— 18 months
Mass left flank ——— one year

She started pain in left flank 18 months back. It was dull ache, present off and on and was associated with heaviness and dragging sensations. There was no eipsode of colic. The pain had no radiation, no relation with meals or exertion.

She noticed a a mass in left flank one year back. It gradually increased in size. She didn't have any gastro-intestinal complaints.

There was no history of haematuria or any other urinary symptoms. No history of fever, loss of weight, nausea or vomiting.

She has been known hypertensive for the last one year. It was controlled by tablet. Inderal and moduretic.

She was married and had four children. She was allergic to sulfa drugs and pencillin.

EXAMINATION

On examination, she was found to be obese middle aged lady wth pulse 80 /min regular, B.P. 120/80 and normal temperature..

Regional examination of abdomen revealed a protuberant, soft, non-tender abdomen with a mass in left lumbar region. It was 12 x 10cm with smooth surface and ill defined margins. It was mobile, bimanually palpable and tender on deep palpation. No other viscra were palpable.

Examination of her cardio-vascular system, central nervous system and chest was unrevealing.

INVESTIGATIONS

Her haemoglobin was 14.2 gm/dl, TLC 10,600/cu mm, DLC P–78%, L–20%, M–2% blood urea 36 mg/dl, serum cratinine 1.2 mg/dl, serum calcium 9.5 mg/dl, & serum phos. 4.5 mg/dl. Her blood glucose and liver function tests were within normal limits. Urine examination was also normal. It didn't show any RBCs.

Ultrasound examination of abdomen showed enlargement of left kidney due to a solid mass at middle and lower poles. There was no calculus or hydronephrosis.

X-ray chest PA view showed slight elevation of left hemidiaphragm but no lung lesion, while plain X-rays of abdomen outlined a large soft tissue shadow in left renal area. I.V.U. showed a large mass involving middle and lower poles of left kidney with indentation of left lower pole calyces. C.T. Scan abdomen revealed a large necrotizing tumour of left kidney without involvement of renal vein or inferior vane cava. There was no enlargement of para-aortic lymphnodes (Fig 1, 2, 3).

OPERATION

A pre-opeerative diagnosis of left renal tumour was made. She was scheduled for cystoscopy,left retrograde studies followed by left radical nephrectomy on Oct. 14, 1987.

Cystoscopic examination of urinary bladder was unremarkable and retrograde studies again showed indentation of lower pole calyces & medial displacement of left ureter.

Left paramedian incision was made and trans-peritoneal approach was used.

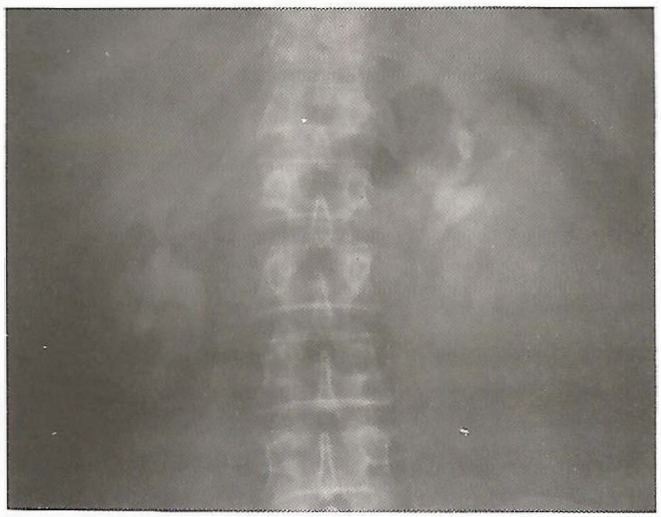

Fig: 1. X-ray abdomen showing large soft tissue mass in left renal area.

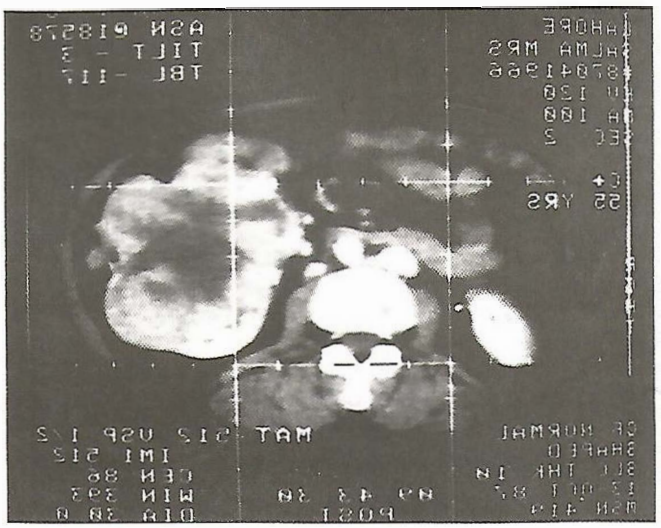

Fig: 3. C.T. Scan showing large renal tumour on left side.

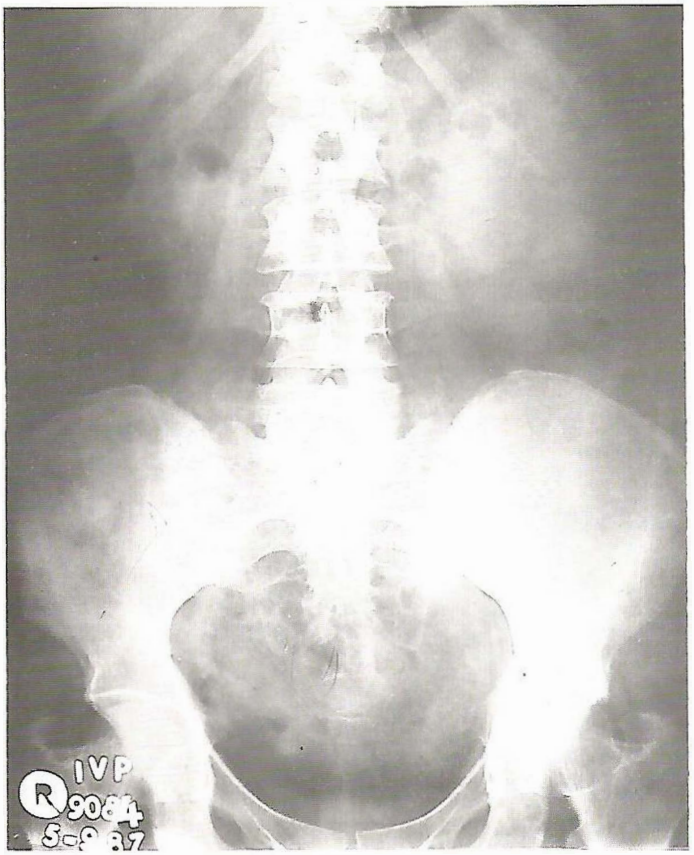

Fig: 2. I.V.P. Indentation of pelvocaleceal system on left side I.V.P. showing large mass involving middle and lower pole of left kidney with indentation of lower pole calyces.

There was a large solid left renal mass with indentation of pelvi-calyceal system. The necrotic tumour was eroding the renal capsule and involving the whole of middle and lower poles. There was no involvement of left renal vein and inferior vena cava. The Gerota's fascia and fat were spared. Also, there were no palpable secondries in liver and para-aortic lymphnodes (Fig 4).

The small bowel was isolated by packs. Left renal vein identified, isolated doubly ligated and divided, as it was hindering the dissection of the Left renal artery. Left

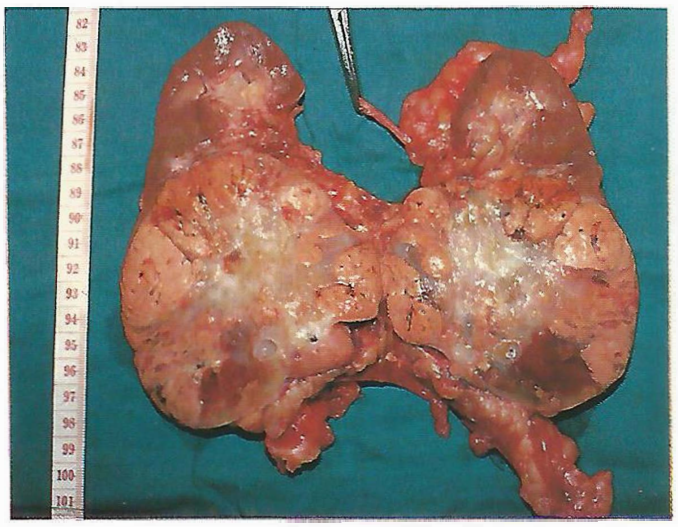

Fig: 4. Cut section of Lt. kidney showing large necrotic tumour at lower pole.

renal artery identified, isolated, doubly ligated and divided. The descending colon and splenic flexure were mobilized. Finally, left kidney was mobilized alongwith perinephric fat Gerota's fascia, left supra-renal gland, para-aortic lymphnodes were removed in toto. Left ureter divided at pelvic brim. Haemostsis secured and suction drain placed. Abdominal wall repaired in two layers.

Post-operatively, she was given inj. heparin 5000 units s/c as prophylaxis for deep venous thrombosis. Her blood pressure was closely monitored. On the third post-operative day she had mild episode of haematemesis. She vomited 30–40 ml of coffee coloured blood. She was put on inj. Tegamet 200mg T.I.D. Thereafter she made an uneventful recovery. Her stictches and drain were removed on 9th post-operative day. She was discharged on next day and advised follow-up in out patient dept.

DISCUSSION

Carcinoma of the kidney was first described by Grawitz, a German pathologist in 1883. There is no place for term hypernephroma. The universally accepted term is renal cell carcinoma of kidney.(RCC)

It accounts for 2–3% of all malignancies. It has world-wide distribution. Male to female ratio is 2:1

The exact etiological factors are unknown. It is common in smokers and tobacco chewers. The genetic factor is worth mentioning e.g. increased incidence in patients with Von Hipple Lindau Syndrome. Wide variety of agents produce RCC in experimental animals i.e. di-methyl nitrosamine found in tobacco smoke, stiesterol, cadmium, lead, asbestos and aromatic hydrocarbons.

CLASSIFICATION

1. Primary Tumours
   - a. Nephroblastic tumours
     Wilm's (Nephroblastoma)
   - b. Epithelial tumours
     Adenocarcinoma
   - c. Epithelial tumours of renal pelvis
     Transitional cell carcinoma
   - d. Non-epithelial tumours
     Fibroma, angioma, sarcoma, angiomyolipoma
2. Secondary Tumours
   From lungs, breast and uterus

PATHOLOGY

Most RCC are advanced when diagnosed. Local spread into retro-peritoneal fat is common. Venous extention is a characteristic feature. It is associated with distant metastases in majority of cases. Tumours less than 3 cm in diameter may have identifiable metastases. The tumour cells can by pass regional lymphnodes, so called skip metastases (Fig 5)

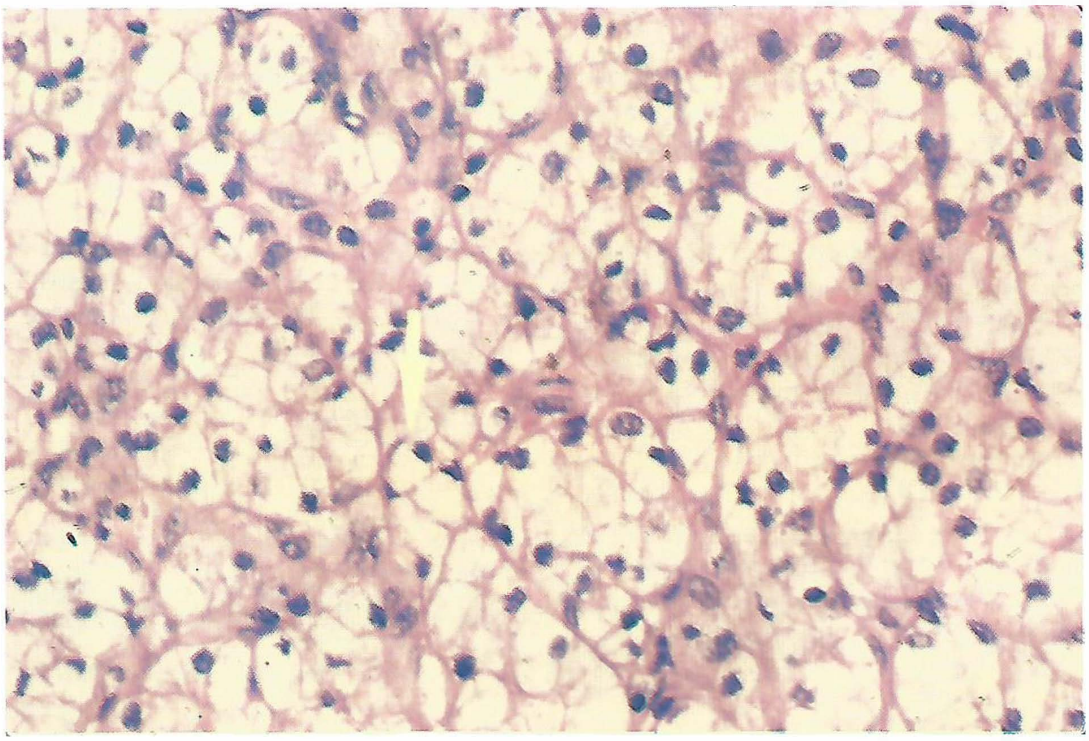

Fig: 5. Microscopic view of tumour.

PRESENTATION

80% present with classical triad of haematuria, pain and flank mass. A varicocele appearing in middle aged man especially on Rt. side should be examined with RCC in mind. 20% present with constitutional symptoms like Stauffer's syndrome (hepato-splenomegaly with abnormal liver functions), hypercalcaemia, erythrocytosis, anaemia, pyrexia, hypertension, neuropathy and amyloidosis.

The presentation may be due to one of the hormones produced by RCC i.g. renin, erthropoiten, gonadotrophins, placental lactogens, prolactin, entero- glucagon, insulin, parathyroid hormone and prostaglandins.

INVESTIGATIONS

Urine examination is very important. 50–70% of patients present with haematuria, When there is involvement or renal vein or inferior vena cava, proteins are present in urine.

Most of the patients with RCC are anaemic but haemoglobin might be above normal due to production of erythropoiten by the tumour..

An I.V.U. is essential, the plain film may show bowel displacement by a large mass. Calcification may occur in benign and malignant lesions. After contrast injection, space occupying lesion in kidney can be out lined.

Renal ultrasound can distinguish between solid and cystic lesions in 97% of cases. Needle aspiration can be carried out under ultrasound control to get a cytological evidence. Good ultra sound can also demonstrate venous involvement. If ther is any doubt, inferior and superior venacavogram may be obtained. Ultrasound also provides information about hepatic involvement.

C.T. Scan have replaced arteriograms as a most useful investigation. Chest radiographs and isotope bone scans are of great use in determining the presence of metastases.

MANAGEMENT

Once the diagnosis is established and the extent of disease is outlined by various investigations the patient is put on mini heparin therapy for prophylaxis of pulmonary embolism. The surgical procedure is planned.

TREATMENT OF PRIMARY TUMOUR

The kidney is approached by an abdominal incision (midline or para-median or lumbar incision) and radical nephrectomy is performed. At some centres, abdominal lymphadenectomy is also combined with radical nephrectomy.

In patients with multiple metastases, or severe bleeding an alternative to surgical procedure is renal artery embolization. It is also used for devascularization of very large tumours before surgery. It is not helpful in routine cases. Renal artery embolization followed by nehprectomy leads to regression of lesion in 14% of case. [1]

ROLE OF ADJUVANT RADIOTHERAPY [2]

As an adjuvant to primary surgical treatment, radiothreapy may be given pre-operatively to reduce tumour size and cell viability or post-operatively to destroy residual cancer cells. it is also indicated when there is lymphnode metastasis or residual tumour in renal bed.

In a randomized study in Rotterdam [3] in 141 cases, there was no difference in 5 year survival rates given pre-operative radiotherapy and surgery compared to surgery alone. But in Rafla's study of 244 cases [4] the survival rates were

Surgery and Radiotherapy	56% in 94 patients
Surgery alone	37% in 96 patients

Local recurrence rates were

Surgery and Radiotherapy	7%
Surgery alone	25%

At the present state of our knowledge, we would advocate pre-operative radiotherapy for patients with large tumours of borderline operability and post-operative radiotherapy for patients with evidence of lymphnode metastases or residual tumour in renal bed.

CHEMOTHERAPY

No significantly effective chemo therapeutic agent has been discovered so far. In one study, the objective response in 243 cases was 10%. The multiple drug regimen has been unsuccessful to date.

IMMUNOTHERAPY

It has a role in control of minimal residual disease but has not proved effective in causing regression of advanced metastatic disease.

Provera, adriamycin, vincristin and BCG given together has an objective response of 33% but it is only short lived.

HORMONE THERAPY

In a study with hormone therapy in 80 patients, with advanced RCC, at Royal Marsden Hospital London, reported in 1971 [7] which was based upon terminal or

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seriously ill patients with multiple metastases. There was subjective improvement in 55% of patients and objective improvement in 50% by reduction of tumour volume, disappearance of tumour metastases and some patients were stable for up to 20 months. The principal hormones which have been used are Medroxy Progesterone Acetate (Provera) 100 mg t.i.d. orally or Testosterone Propionate 100 mg I/M daily , 5 days per week for progesterone failure.

PROGNOSIS

A recent collective review of all published series [8] at Institute of Urology London revealed that nephrectomy produced a remarkable range of 5 year survival rates in patients whith RCC as follows

Disease confined to kidney	56–82%
Extension to perinephric fat	43–80
Involvement of renal vein or regional lymphnodes	8–51%
Distant metastases	0–13%

Ten year survival rates were[9]20–72%, 0–38% and 0–7% respectively.

Survival rates in patients of RCC with renal vein and inferior vena cava involvement are as follows[10]

	Survival		
	1 Yr	2 Yr	3 Yr
Group 1 Subhepatic V.C	50%	40%	40%
Group 2 Intrahepatic V.C.	60%	50%	17%
Group 3 Atrial extension	33%	0%	0%
All patients	52%	40%	28%

Dr. JAVID *(Consultant Urologist)* : Most of the patients present in very advanced stage. It is true even in U.S.A. where medical care is so easily available. Majority present with classical triad of haematuria, mass, and flank pain. One should not confuse it with renal stone and all suspected cases should be properly investigated. A renal cyst especially if complicated by infection should always be kept in mind.

Angio-myolipoma, by all classical signs resembles RCC, even all findings of arteriogram are present but on C.T. Scan, one can see large content of fat. So C.T. Scan is the most important workup of this patient.

Radical nephrectomy is the most important modality in the management of RCC. If combined with pre-operative radiotherapy, the survival rates are improved by 20%.

Dr. ANWAR *(Consultant Gastroenterologist):* Patients with stress ulcers, if put on heparin for prophylaxis of deep venous thombosis, have increased chances of bleeding. I think, if signs of DVT appear in these patients, it is better to insert an umbrella or a filter in inferior vena cava for aprophylaxis of pulmonary embolism.

Dr. SHAHZAD *(Consultant Urologist)* : In all patients who are prone to DVT and pulmonary embolism. we usually start heparin pre-operatively, 5000 units S/C 12 hourly. I don't think it is a contra indication even if patient has mild episode of haematemesis. The prophylaxis of pulmonary embolism is extremely important for the life of patient. Once we found haematemesis in our patient, she was covered with cimetidine and she improved.

Dr. IQBAL : I wonder, if there is any role of needle biopsy in the diagnosis of renal cell carcinoma.

Dr. SHAHZAD *(Consultant Urologist)* : Yes; fine needle aspiration has been advocated in recent literature espacially in doubtful cases like angiomyolipoma.

Dr. JAVAID *(Consultant Urologist)* : There are minimal chances of spreading tumour in tract with needle biopsy. With the help of C.T. scan and angiography, the diagnosis is correct in more than 99% of cases. So needle biopsy has practically no role in diagnosis. I think it should be done in doubtful cases.

Prof. M.A.Z. MOHI-DIN (*Chair Person*) : This lady developed dragging pain 18 months back and a mass one year back. Usually these patients develop pain when tumour is pressing certain viscera like the ureter.

Although she carried this cancer for 18 months but her Hb was 14.0 gm/dl which is again not an unlikely feature of RCC because in some patients tumour itself produces erythrpoitin.

Before the advent of C.T. Scan, Cannon Ball appearance in the lungs along with characteristic findings on I.V.P. were considered as diagnostic features of RCC.

Till today, the treatment of choice is surgery. Radiotherapy has a limited role. Repearted injections of tumour extracts in patients circulation can stimulate immune response and it is still under trial at various centres.

Renal cell carcinoma is a condition in which the physicians should be on their guard. We should not ignore a few RBCs in urine, considering it due to a stone. All patients with haematuria must be throughly investigated.

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