General data

- Age ：24 years old
- MARITAL: not married
- Occupation ：student
- Height：160 cm
- Weight：59 kg

Chief complaint

Left lower back pain and intermittent grossly hematuria noted for 2 months

Present illness

- This 24 year-old female was well health before.
- She had the history of left herniated intervertebral disc（HIVD）for 5 years with conservative treatment.
- She complained of left lower back soreness and intermittent flank pain last for 2 months.
- She felt general weakness and anorexia but denied body weight loss.

Present illness（con.）

- Intermittent hematuria was noted for recent weeks.
- Thus she came to the Urology department for help.
- Sonography revealed there was a focal renal heterogeneous mass lesion occupied and she was suggested for further evaluation.

Personal/social history

- Smoking : denied
  Drinking : denied
  Betel nuts use : denied
- Menstruation and pregnancy history : noncontributory
- History of oversea travel : denied
- History of contact with animals or sick people : denied

Past Medical history

- Surgical history (operation, date, hospital): denied
- Hospitalization history : denied
- Medical disease:
  1. **Left HIVD for 5 years under conservative treatment.**
  2. **Scoliosis under regular follow up**
- Drug allergy: denied

Lab data

取様日期	950309
Urea N(血液) [7-18 mg/dl]	20.3
Creatinine(血液)[0.5-1.3 mg/dl]	0.8

取様日期 a	950309
SP.Gr.	1.020
PH	7
Protein	-
Sugar	-
Ketone	-
Bilirubin	-
Occult Blood	**3+**
Nitrite	-
Urobilinogen	0.1
*RBC	**5-10**
*WBC	2-5
*Epithel	5-10
*Cast	-
*Crystal	-
*Bacteria	+
COL	P.YEL
WBC	+/-
other	—

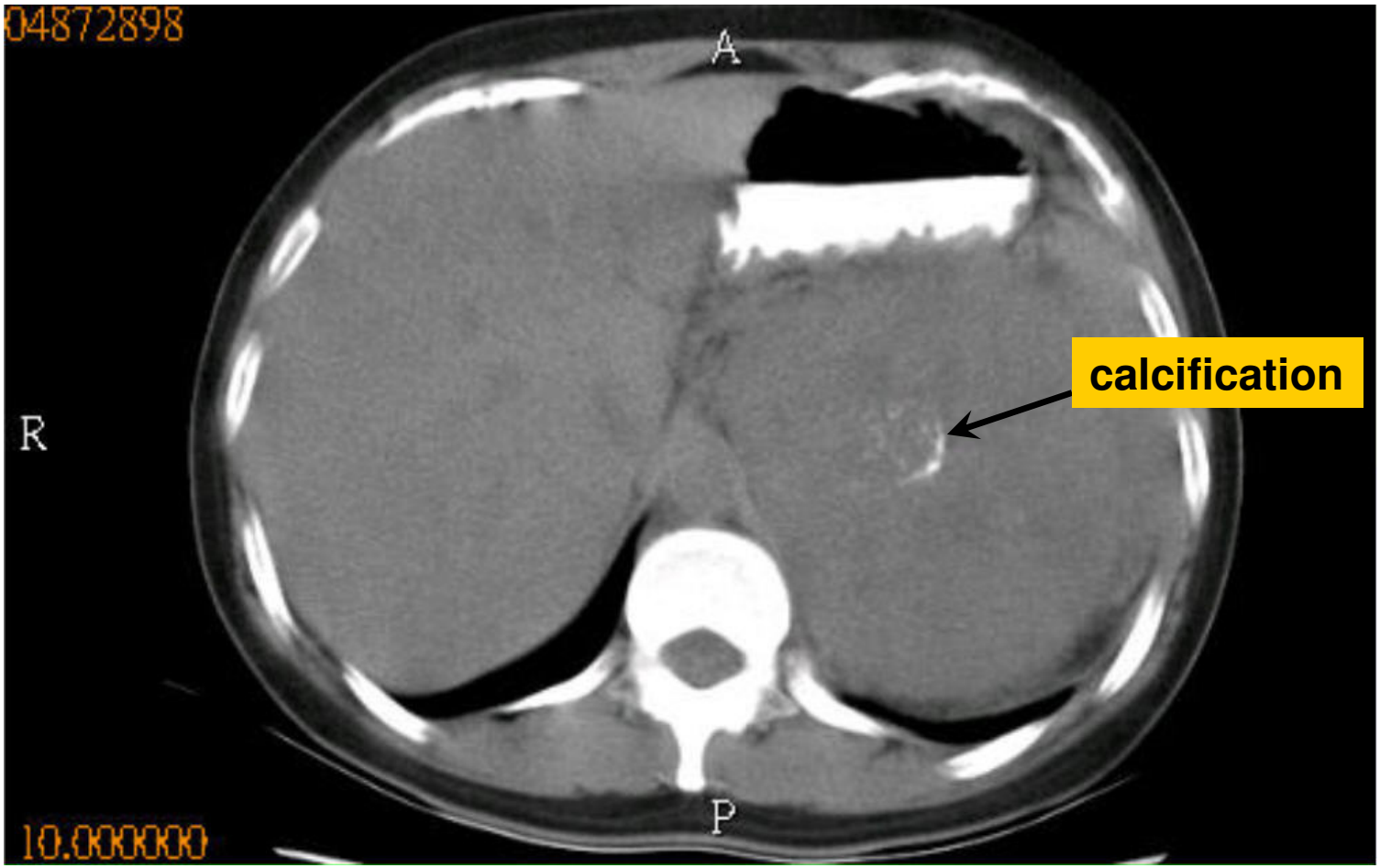
Image study

Ultrasound

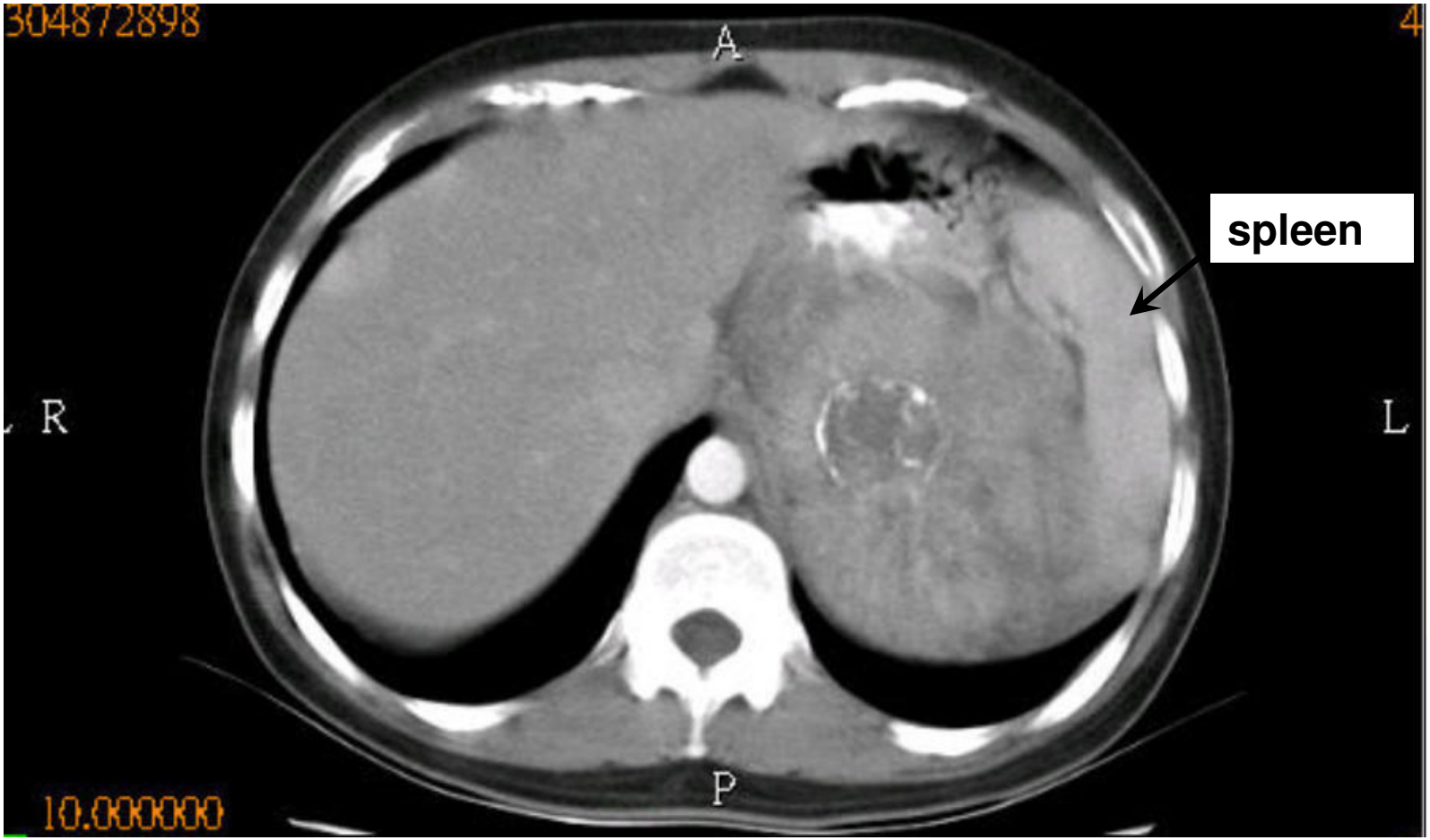
- Renal sonography showed there was a 12x11cm mass lesion occupied.
- Left focal hydronephrosis was also noted.
- Suspected renal tumor or other kidney parenchymal disease.
- CT and MRI was suggested and to be arranged.

KUB

CT scan with pre-contrast enhancement

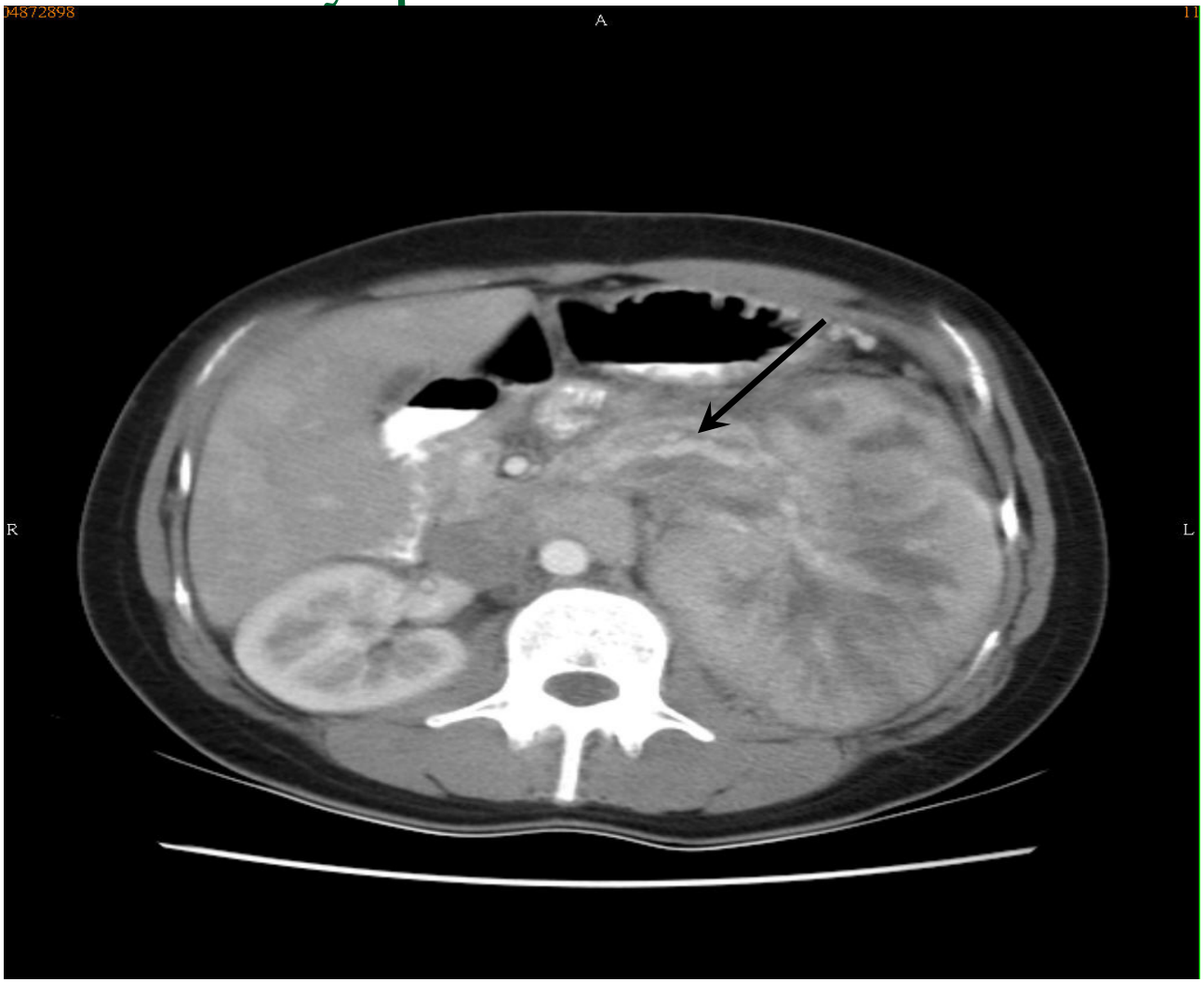


CT scan with contrast enhancement



heterogeneous enhancement is noted on the post-contrast images

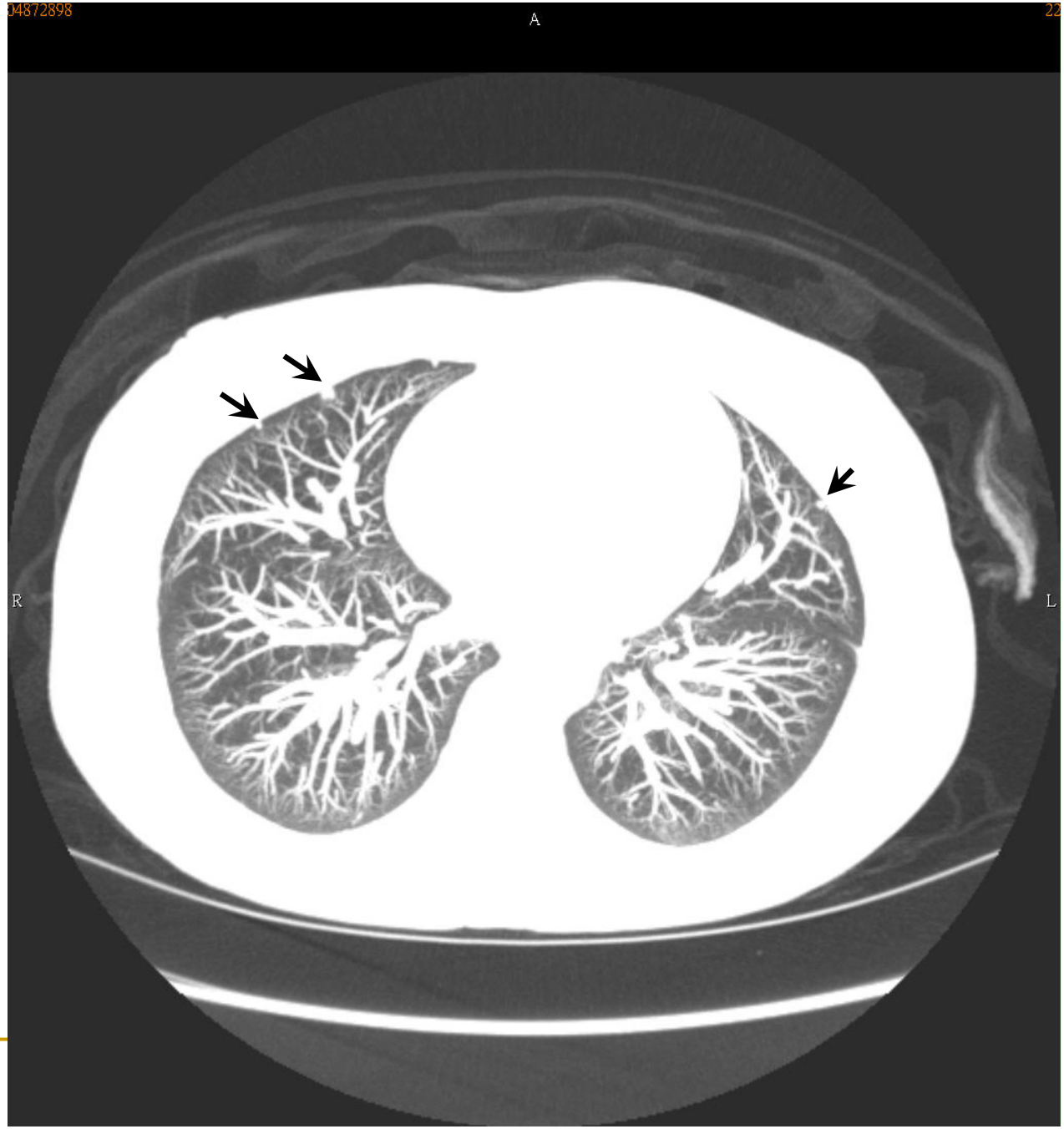
CT – delay phase



Low density lesion noted in left renal vein and IVC

Chest CT

Chest CT showed multiple nodules.



PET, bone scan

There are no hot spot or cold spot noted. No evidence of bone metastasis noted.

Differential diagnosis

- Renal cell carcinoma
- Oncocytoma
- Metastatic disease
- Transitional cell carcinoma

Renal cell carcinoma

- Primary malignant neoplasm of the kidney（85%）
- Solid and calcified lesion should be suggested RCC.
- Enhanced CT：renal cell carcinomas are often heterogeneous, with one or more low-density central areas.
- Larger tumours（>3cm） have ill-defined borders and may have cystic or necrotic areas with calcification.

Oncocytoma

- They can vary in size from 1 to 20 cm in diameter, but tend to be large.
- Ultrasound ：solid mass with internal echoes, which occasionally has a stellate hypoechoic centre.
- Contrast-enhanced CT ：well-defined solid mass which, when large, can contain a low attenuation central scar.

Metastatic disease

- The commonest primary tumours are bronchial, colorectal, breast, testicular, and gynaecological malignancies and malignant melanoma.
- Haematogenous metastases are usually small (<3 cm), multiple, and confined to the cortex.
- They are usually hypovascular on CT and do not tend to demonstrate calcification or renal vein invasion

Transitional cell carcinoma

- Most urothelial tumours present as filling defects within the renal pelvis or ureter.
- The commonest CT manifestation is an intraluminal soft-tissue mass in the renal pelvis, calices, or ureter.
- The tumours may be highly invasive and infiltrate the renal parenchyma.
- *Renal vein and inferior vena cava invasion is rarely seen in transitional cell carcinoma*

Key image finding

- Calcification seen in pre-contrast and pos-contrast enhancement.
- Heterogenous enhancement noted in post-contrast images.
- Low density lesion within the left renal vein and the IVC is noted, suggestive of tumor thrombus.
- Lung CT showed nodules suspected lung metastasis.

Final diagnosis

Renal cell carcinoma with lung metastasis

Discussions

Renal cell carcinoma

Renal cell carcinoma

- RCC represent about 1% to 3% of visceral cancer.
- RCC accounts for 90-95%of malignant neoplasm arising from the kidney.
- Often occurred among *older individuals* especially the sixth and seventh decades.
- Male preponderances 3：1（M：F）
- Tumor arises from proximal tubular epithelium.

Epidemiology of RCC

- Sporadic
  - Tobacco
  - Obesity
  - Hypertension
  - Unopposed estrogen therapy
  - Exposure to asbestos
  - Petroleum products
  - Heavy metals
  - Chronic renal failure
  - Acquired cystic disease
  - Tuberous sclerosis

Epidemiology of RCC（con.）

- Familial variants especially among young individuals
- Von-Hippel-Lindau syndrome：
  1. VHL gene
  2. Hemangioblastoma of the cerebellum and retina
  3. Bilateral renal cyst
  4. Multiple renal cell carcinoma
- Hereditary clear cell carcinoma
- Hereditary papillary carcinoma
  1. Multiple bilateral renal tumor with papillary histology
  2. MET protooncogen mutation

Classification of RCC

- Clear cell carcinoma（70-80%）
  1. Sporadic or familial or VHL gene mutation
  2. The most common type
- Papillary carcinoma（10-15%）
  1. Papillary pattern
  2. MET gene mutation
- Chromophobe renal carcinoma（5%）
  1. benign oncocytoma may be similar to this kind
  2. Better prognosis than clear cell carcinoma and papillary carcinoma

Clinical presentation

- The classic triad
  1. flank pain（40%）
  2. Hematuria（40%）
  3. flank mass is uncommon (10%)
- *25 to 30% of patients are asymptomatic.*
- Usually found on incidental radiologic study.
- One of the great 『mimics』 in the medicine

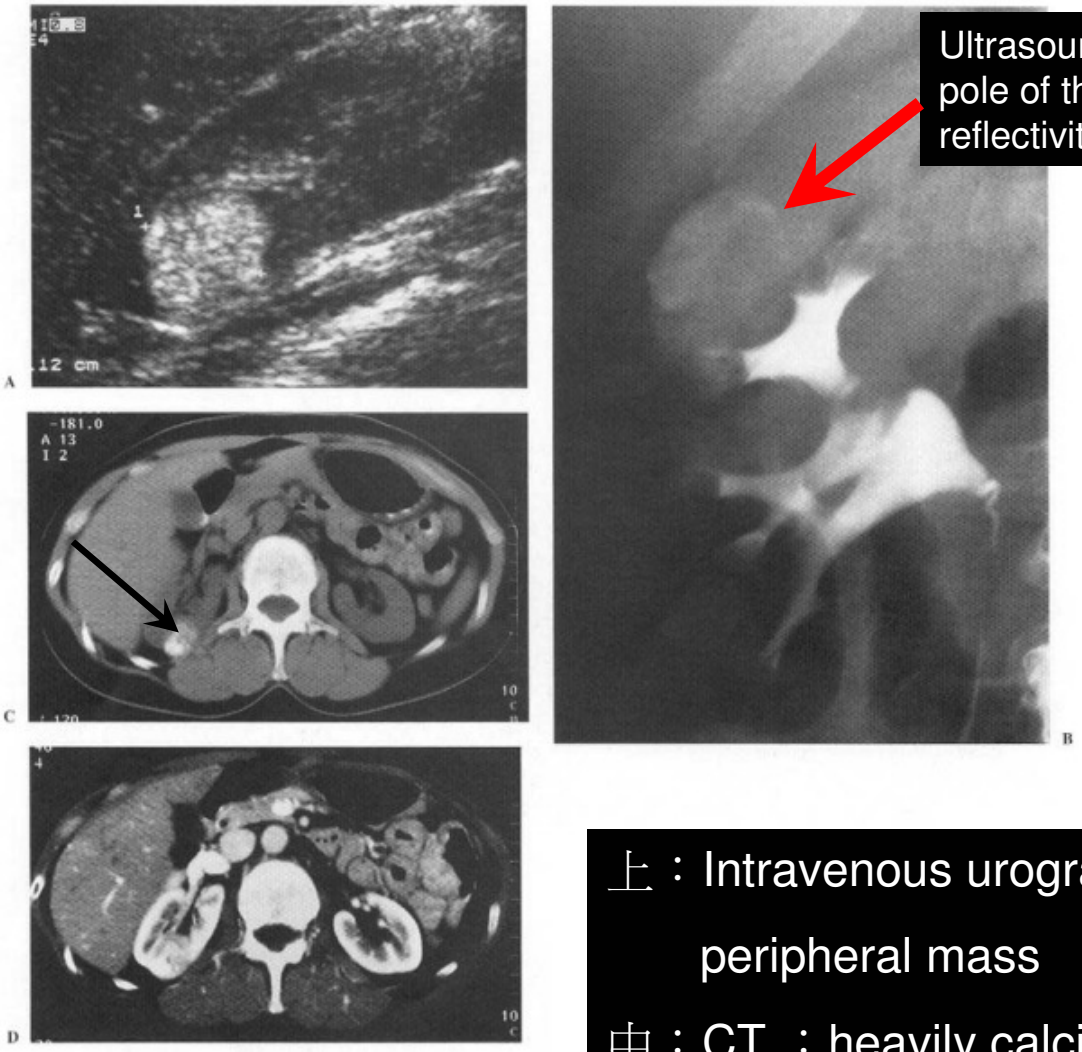
Clinical presentation（con.）

- Paraneoplastic syndrome
  1. Polycythemia
  2. Hypercalcemia
  3. Hypertension
  4. Hepatic dysfunction
  5. Feminization
  6. Masculinization
  7. Cushing syndrome
  8. Eosinophilia
  9. Leukemoid reaction
  10. Amyloidosis

- **Other signs and symptoms**
  - **Weight loss (33%)**
  - **Fever (20%)**
  - **Night sweats**
  - **Malaise**
  - **Varicocele, usually left sided, due to obstruction of the testicular vein (2% of males)**

Metastasis

- The tendency of metastasize widely before giving rise to any local symptoms and signs.
- 25% of RCC had metastasis
- *Most common location*：
  1. lung（more than 50%）
  2. bone（33%）
  3. Regional lymph nodes
  4. Liver, adrenal, and brain

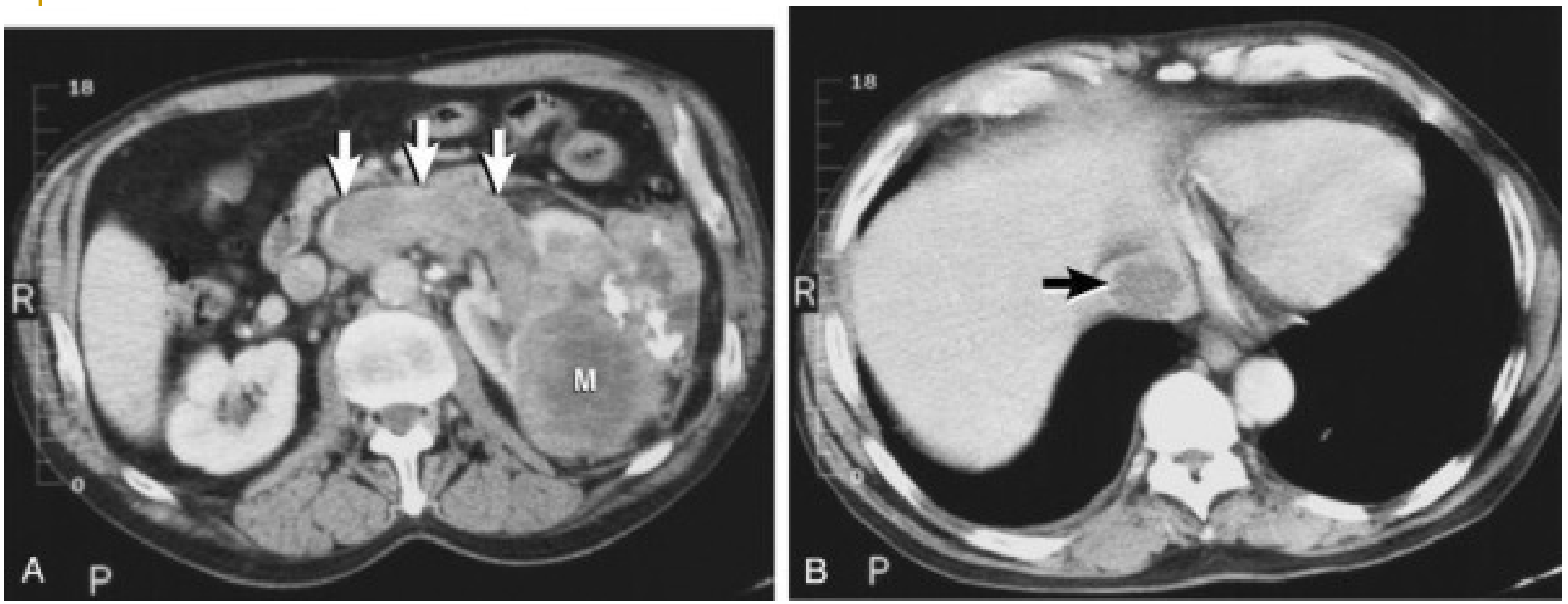


Ultrasound well-defined lesion in the upper pole of the right kidney with increased reflectivity.

上：Intravenous urogram ：calcified peripheral mass

中：CT ：heavily calcified.

下：corticomedullary phase CT images



CT scan at the mid portion of the kidneys (A) demonstrates a large left renal mass that **extends into the renal vein and into the inferior vena cava** (arrows). An image at the level of the base of the heart shows that the **tumor thrombus** (arrow) extends into the right atrium.

The Roboson staging of RCC

- Stage I - Tumor confined within capsule of kidney
- Stage II - Tumor invading perinephric fat but still contained within the Gerota fascia
- Stage III - Tumor invading the renal vein or inferior vena cava (A), or regional lymph-node involvement (B), or both (C)
- Stage IV - Tumor invading adjacent viscera (excluding ipsilateral adrenal) or distant metastases

Table -- Staging of renal cell carcinoma: Robson versus TNM system

Robson	Disease extent	TNM
I	Tumour confined to kidney	
	Small <2.5 cm	T1
	Large >2.5 cm	T2
II	Tumour spread to perinephric fat	T3a
IIIA	Tumour spread to renal vein or cava	T3b
IIIB	Tumour spread to local lymph nodes	N1–2
IIIC	Tumour spread to local vessels and nodes	T3b, N1–2
IVA	Tumour spread to adjacent organs, outside Gerota's fascia	T4
IVB	Distant metastases	M1

Treatment

- The treatment options
  1. **Surgery**：Nephrectomy
  2. **radiation therapy**：may be considered as the primary therapy for palliation in patients，4500 cGy
  3. **Chemotherapy**：5-FU, and vinblastine, paclitaxel (Taxol), carboplatin, ifosfamide, gemcitabine, and anthracycline (doxorubicin)
  4. **hormonal therapy**
  5. **Immunotherapy**
  6. **combinations of above**

Immunotherapy

- RCC revokes immune response which occasionally results in spontaneous remission.
- In an attempt to reproduce this response, various strategies have been used to include as follows：

1. Nonspecific stimulators of the immune system.
2. Specific antitumor immunotherapy
3. Adoptive immunotherapy
4. Administration of partial purified or recombinant cytokines.

Interferon alpha

- Effectiveness of INFa in *metastatic RCC* has been evaluated.
- One recent trial randomized 350 patients to subcutaneous INFa or oral medroxyprogesterone. INFa resulted in improved one year survival, 43% v.s 31 %（Renal cancer collaborators, Lancet 1999）
- Combination of INFa and INFg has shown some promising result.

Interlukine 2

- In 1995, FDA approved high bolus dose IL2 for treatment of metastatic RCC.
- Although the response rate was only 14% and there was high level of toxicity involved, the individuals response were impressive.
- *60% of responders have over 90 % regression of disease.*
- Trials of combination INFa and IL2 had been currently under investigation.

Treatment （con.）

- **Multi-kinase inhibitors（target therapy）**
  1. *Sorafenib*：
     1. a small molecule Raf kinase and VEGF multi-receptor kinase inhibitor
     2. Sorafenib targets serine/threonine and receptor tyrosine kinases, including those of RAF, VEGFR-2,3, PDGFR-b, KIT, FLT-3, and RET.
  2. *Sunitinib (Sutent)*：
     1. treatment of metastatic kidney cancer,
     2. The receptor tyrosine kinases inhibited by sunitinib include VEGFR 1-3 and PDGFR a and b.
  3. *Lapatinib*：
     1. EGFR and ErbB-2 dual tyrosine kinase inhibitor

Prognosis

- Renal cell carcinoma is *the sixth* leading cause of cancer death.
- The 5-year survival rates initially reported by Robson in 1969
  1. ***66% for stage I***
  2. ***64% for stage II***
  3. ***42% for stage III***
  4. ***11% for stage IV***

Reference

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