Localized Renal cell carcinoma s/p surgery with recurrence of solitary metastasis in appendicular skeleton after multiple years.

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History

- 69 years old male diagnosed with left sided renal cell carcinoma in 2006.

- It was localized to left kidney and did not have extra-capsular extension or angio-lymphatic invasion at that time.

- Patient underwent left nephrectomy without any chemo or radiotherapy and shortly after that he underwent left total knee arthroplasty.

- For four years patient did not have any problems with the prosthesis but then he started having left knee pain and difficulty ambulating.

- Labs were positive for inflammatory markers, elevated white cell count (11.8 X 10^3 microliter) and ESR (36 mm/hr – normal range 0-20 mm/hr)

- Subsequently patient underwent multiple imaging examination.
Plain film of the Left Knee – AP and Lateral view

- Large lytic lesion measuring 6m cranio-caudally with ill defined margins in the distal left femur in close proximity to the femoral component of the total knee arthroplasty.

- High risk of pathological fracture.

- Differential diagnosis
  1. Metastasis
  2. Myeloma
  3. Giant cell reaction (GCR) due to close proximity to prosthesis. GCR less likely since no evidence of failure of prosthesis itself and lesion is very large with ill defined margins which are not typical in giant cell reaction.
A large solid, contrast enhancing mass in the distal femoral metaphysis measuring 7cm X 5cm X 5.5cm.

The mass extends through posterior femoral cortex with associated soft tissue component posteriorly.

Lesion corresponds to lytic lesion seen on radiograph and is positioned immediately adjacent to the femoral component of patient’s total knee arthroplasty.

Since patient has known renal cell carcinoma metastasis is first consideration.

Other possibility could be myeloma given the lytic nature of lesion, a primary bone malignancy i.e. sarcoma is less likely.
Three Phase Whole Body Bone Scan

Increased radiotracer uptake in all three phases of bone scan in the distal left femur adjacent to prosthesis representing hyperemic lesion in the distal left femur and given the history of renal cell carcinoma would be most consistent with metastatic lesion but a primary malignant disease of bone and infection of the prosthesis would have similar appearance.

No evidence of other sites of metastases.

Subsequently **CT Chest, Abdomen and Pelvis** was done which did not show any other site of recurrence of malignant disease.
The low power view shows a collection of clear cells within the bone marrow space (big circle) which is the tumor.

The large dense pink fragments (small circle) is bone and the areas in between bone and tumor is the bone marrow space.

The high power view shows nests of cells with abundant clear cytoplasm (from glycogen/lipid), distinct but delicate cell boundaries & delicate (“chicken wire”) vasculature and sinusoids adjacent to the nests of cells.

This morphology is consistent with Renal cell carcinoma, clear cell type.

**Biopsy distal left femur**

*Clear cell carcinoma, morphologically consistent with Renal primary.*
Treatment Plan and Follow Up

- Treatment plan for this patient is curative resection of the distal third of left femur and revision of the left total knee arthroplasty.

- Most probably patient will also undergo chemotherapy.

- This patient did have standard follow up for RCC per recent guidelines but all imaging studies were negative and patient was asymptomatic until when he had left knee pain and then he had adequate work up to evaluate the cause of knee pain.

- Performance status is an important predictor of bone metastasis in patients presenting with presumed RCC lesions. Bone scan should be performed in patients with an ECOG score of greater than 0 regardless of T stage but is unnecessary in those presenting with an ECOG score of 0, particularly when lacking symptoms and extra-osseous metastasis (7).

- We do not know what was patient’s ECOG Score was at the time of diagnosis since work up and treatment was at outside institution but may be he was a candidate for pre–op bone scan which may have helped with earlier detection of this bone metastasis in distal left femur.
Solitary metastasis from Renal Cell Carcinoma

- Most common cancers which metastasize to bone: Breast, Prostate, Thyroid, Lung & Kidney.
- Cancers with lytic lesions in the bone: Thyroid, Lung and Kidney.
- Renal and lung cancers have metastases in distal skeleton.
- Renal cell carcinoma (RCC) is the most common primary renal malignant neoplasm in adults and accounts for approximately 90% of renal tumors and 2% of all adult malignancies.
- RCC is the 10th leading cause of cancer deaths in males in United States.
- Solitary metastasis develop in 1/3rd cases of RCC which is localized at the time of initial diagnosis.
- Different sites of solitary metastases from RCC reported in literature: Bone, Lung, Abdomen (pancreas, adrenal), Brain, Soft tissue.
- Resection of solitary metastases from RCC: associated with 5yr survival rate of 35% to 50%.
- Patients with recurrent RCC who can undergo a curative resection of their disease have a good opportunity for long-term survival, particularly those with a single site of recurrence and/or a long Disease Free Interval.
- Progression-free survival was longer and response rates were higher in patients with metastatic renal-cell cancer who received sunitinib than in those receiving interferon alfa (NEJM).

- **Follow Up of RCC:** For stage I and II disease, H & P, CXR, LFTs, BUN, Creatinine and Calcium are recommended every 6 months for 2 years, then annually for 5 years while for stage III same tests should be done every 4 months for 2 years, every 6 months for 3 years, and then annually for 5 years. Abdominal CT scan is recommended once at 4-6 months and then as indicated.
- Bone and brain surveillance studies should be prompted by site specific symptoms, elevated alkaline phosphatase levels or the diagnosis of metastasis at another site.
Currently, the Fuhrman grading system is most widely used by pathologists in Europe and the United States; this system categorizes renal cell carcinoma (RCC) with grades 1, 2, 3, and 4 based on nuclear characteristics and represents one of the most significant prognostic variables in patients with all stages of renal cell carcinoma (RCC). The conventional Fuhrman grading system is currently validated for grading clear cell renal cell carcinoma (CCRCC).

**Grade 1**
Using the 10× objective, the nuclei of the tumor cells are small (<10 µm), hyperchromatic, and round (resembling mature lymphocytes), with no visible nucleoli and little detail in the chromatin, as shown in the image below.

**Grade 2**
Using the 10× objective, the nuclei of the tumor cells are slightly larger (15 µm) with finely granular "open" chromatin but small, inconspicuous nucleoli (see the following image). The nucleoli are often present, and many appear as small chromocenters at 10× objective, with confirmation of their nature at higher power, but this does not count.

**Grade 3**
Using the 10× objective, the nuclei of the tumor cells are larger (20 µm in size) and may be oval in shape, with coarsely granular chromatin (see the image below). The nucleoli are easily unequivocally recognizable.

**Grade 4**
The nuclei are pleomorphic with open chromatin or hyperchromatic and single or multiple macronucleoli, as depicted in the following image.
Staging of RCC

- **Staging**
  - The Robson modification of the Flocks and Kadesky system is uncomplicated and is used commonly in clinical practice. This system was designed to correlate stage at presentation with prognosis. The Robson staging system is as follows:
    - 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
  - The tumor, nodes, and metastases (TNM) classification is endorsed by the American Joint Committee on Cancer (AJCC). The major advantage of the TNM system is that it clearly differentiates individuals with tumor thrombi from those with local nodal disease. In the Robson system, stage III disease includes both inferior vena caval involvement (stage IIIA) and local lymph node metastases (stage IIIB). Although patients with Robson stage IIIB renal carcinoma have greatly decreased survival rates, the prognosis for patients with stage Robson IIIA renal carcinoma is not markedly different from that for patients with Robson stage I or II renal carcinoma. The TNM classification system is as follows:
    - **Primary tumor (T)**
      - TX - Primary tumor cannot be assessed
      - T0 - No evidence of primary tumor
      - T1 - Tumor 7 cm or smaller in greatest dimension, limited to the kidney
      - T2 - Tumor larger than 7 cm in greatest dimension, limited to the kidney
      - T3 - Tumor extends into major veins or invades adrenal gland or perinephric tissues but not beyond the Gerota fascia
      - T3a - Tumor invades adrenal gland or perinephric tissues but not beyond the Gerota fascia
      - T3b - Tumor grossly extends into the renal vein(s) or vena cava below the diaphragm
      - T3c - Tumor grossly extends into the renal vein(s) or vena cava above the diaphragm
      - T4 - Tumor invading beyond the Gerota fascia
    - **Regional lymph nodes (N)** - Laterality does not affect the N classification
      - NX - Regional lymph nodes cannot be assessed
      - N0 - No regional lymph node metastasis
      - N1 - Metastasis in a single regional lymph node
      - N2 - Metastasis in more than 1 regional lymph node
    - **Distant metastasis (M)**
      - MX - Distant metastasis cannot be assessed
      - M0 - No distant metastasis
      - M1 - Distant metastasis
    - **AJCC stages**
      - AJCC stage I - T1, N0, M0
      - AJCC stage II - T2, N0, M0
      - AJCC stage III - T1-2, N1, M0 or T3a-c, N0-1, M0
      - AJCC stage IV - T4; or any T, N2, M0; or any T, any N, M1
  - The division of patients with renal cell carcinoma into low-, intermediate-, and high-risk groups with or without metastases may be useful in choosing appropriate therapy for them.\(^5\,^6\)
References

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