Here There Be Monsters:

Uncharted Waters in the Retroperitoneum

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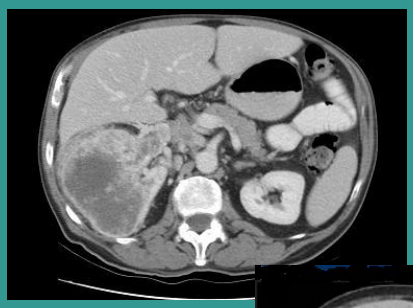
Urology Grand Rounds

June 8, 2011

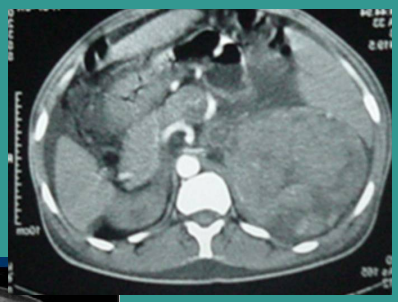
Disclosure

- Nothing to disclose (there is no money in sarcoma work!)

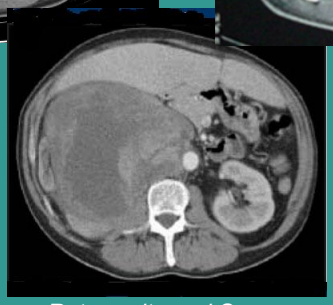
Rationale for Rounds



Renal cell cancer



Adrenocorticocarcinoma



Retroperitoneal Sarcoma

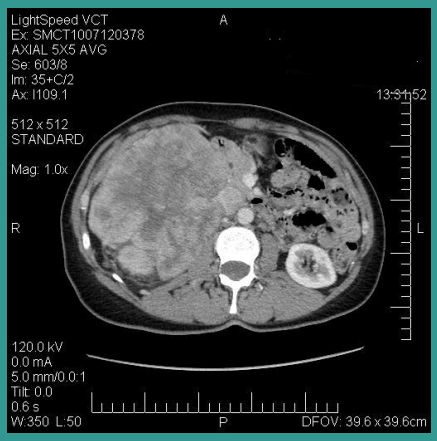
BC Statistics

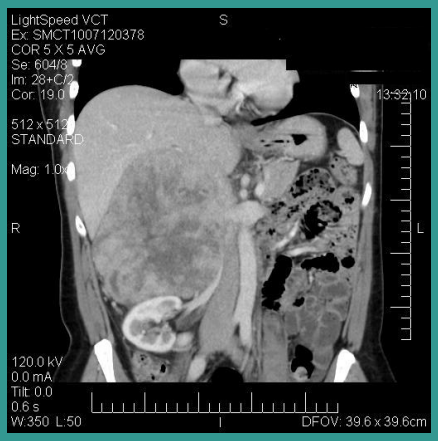
- Review 2000-2009 BCCA CAIS database
- Coding for RP tumour identified 228 patients diagnosed with retroperitoneal tumours
- 86 were retroperitoneal sarcoma for which outcome data was available
- 14 were operated on by urologists (of which only 2 were referred to BCCA prior to surgery)
- In half of these cases the preop diagnosis was thought to be renal cell cancer

Case Presentation 1

- 46 year old woman
- Presented with a palpable mass
- 15 cm on US, same on ct

CT image





Case 1 Cont'd

- Had metabolic w/u to exclude pheo
- Taken to OR by urologist for 'adrenal carcinoma invading kidney and vena cava'
- 25 cm tumour described at surgery

Pathology

- High grade leiomyosarcoma
- 18 cm
- Margins involved
- "multinodular mass with torn outer surface and exposed tumour"
- "some of the tumour was present as separate fragments"

Conference Review

- Referred to BCCA for consideration of further treatment
- Operative field too big for adjuvant XRT
- No role for adjuvant chemotherapy
- Extremely high risk for recurrence
- Currently on F/U (under 6 months post op)

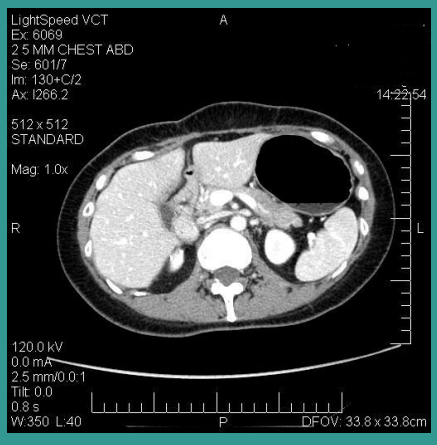
Case Presentation 2: What can be expected for Case 1

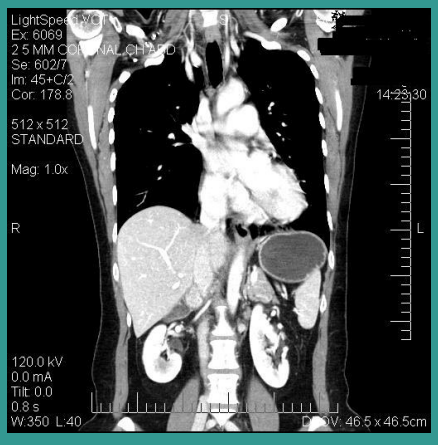
- Similar case from 2006
- Actually same age, sex, preop diagnosis
- Initial pathology: grade 2 leiomyosarcoma involving IVC with close (?positive margins)
- Again not amenable to postoperative adjuvant therapy
- Followed with CT imaging

Case 2 Cont' d

- Recurred with 2.3 cm mass on the IVC 3 years later
- No evidence of distant metastases

CT at recurrence





- Discussed at conference
- Since localized recurrence amenable to XRT
- Repeat surgery including gall bladder and renal artery and IVC
- 2.4 cm mass close margin (?retraction artefact)
- No recurrence (yet) now 2 years out

Retroperitoneal Sarcoma

- 1-2 % of all solid malignancies are sarcomas
- Of all sarcomas RPS are still uncommon constituting less than 10% of all soft tissue sarcomas
- Peak 5th decade; Equal M:F
- 1/3 of RP masses are sarcomas

  Windham, RPS. Cancer Control 2005 12(1):36-43
- Majority of retroperitoneal soft tissue tumours are malignant
- Best management is a function of the diagnosis

Differential Diagnosis

- Sarcoma
- Neural -schwannoma, ganglioneuroma, paraganglioma
- Lymphoma
- Adrenal (adenoma, carcinoma, myelolipoma)
- Renal (carcinoma, angiomyolipoma)
- Metastatic nodes- testicular, nongerm cell

Histology of Sarcomas

- Most common are liposarcomas
  - May not have substantial fatty component on imaging but often there is some asymmetry in the amount or character of the retroperitoneal fat on the involved side
- Leiomyosarc
  - Typically vascular origin- IVC, renal vessels
- MFH

Tumour Staging

Table 1
Classifications

Histological grade (G)	
G1	Well differentiated
G2	Moderately well differentiated
G3	Poorly or very poorly differentiated
Primary site (T)	
T1	Tumor less than 5 cm in diameter
T1a	Superficial tumor
T1b	Deep tumor
T2	Tumor 5 cm or more in diameter
T2a	Superficial tumor
T2b	Deep tumor

N.B. Retroperitoneal and pelvic sarcomas are classified as deep tumors

Staging Sarcoma

Table 2
American Joint Committee staging of soft tissue sarcomas

Stage	Classification	Description
IA	GI, T1, N0, M0	Grade 1 tumor, <5 cm in diameter no regional lymph nodes and/or distant metastases
IB	GI, T2, N0, M0	Grade 1 tumor, 5 cm or more in diameter, no nodes and/or metastases
IIA	G2, T1, N0, M0	Grade 2 tumor, <5 cm in diameter, no nodes and/or metastases
IIB	G2, T2, N0, M0	Grade 2 tumor, 5 cm or more in diameter, no nodes and/or metastases
IIIA	G3, T1, N0, M0	Grade 3 tumor, <5 cm in diameter, no nodes and/or metastases
IIIB	G3, T2, N0, M0	Grade 3 tumor, 5 cm or more in diameter, no nodes and/or metastases
IIIC	G1–3, T1, 2, N1, M0	Tumor of any grade and/or size, with regional involved nodes, but no metastases
	G1–3, T3, N0,	Tumor of any grade invading bone vessels/nerves,

Usual Stage at Diagnosis

- Nearly all retroperitoneal sarcomas are large and >5 cm and are deep to the superficial fascia.
- Nearly all are therefore Stage IIB (large, low-grade, and deep) or stage III (large, high-grade and deep)
- Distinction between these two made only on the basis of histologic grade.

Presentation

- Usually huge at diagnosis unless found on imaging done for something else
- Symptoms: vague abdominal pain or protrusion or intestinal complaints due to mass effect.
- Median 4 months of symptoms before diagnosis
- May present with neurologic/MSK symptoms in the lower extremity
  - » Cancer 2005, 104, 669-75)
- Occasionally unexpected finding at laparotomy for other disease

Management of the Retroperitoneal Mass

- Core biopsy should be used for tissue diagnosis after all functional investigations are completed.
- Biopsy via the retroperitoneal approach
- Because of the location of these lesions, it is usually not possible to excise the biopsy tract.
- Early referral for consultation is extremely important

Staging

- Chest CT to r/o mets
- Usually CT abdomen /pelvis is adequate for local imaging
- occasionally MRI if there is a question about vascular involvement
- PET not generally helpful
- Differential renal scan if concern re adequacy of residual renal function

Determinants of Prognosis

- The major factors that affect survival are the tumor grade and resectability
- Patients who have had a successful complete resection and also have low-grade tumors have the best survival rates.

BC Outcome Data

- Review of 2000-2009 (preliminary data)
- 86 patients with RPS identified in CAIS with outcome data available
- 43 referred prior to resection, 43 after
- 42/43 vs 27/43 had complete resection
- 34/43 vs 18/43 alive on follow-up
- $p<0.05$ for both

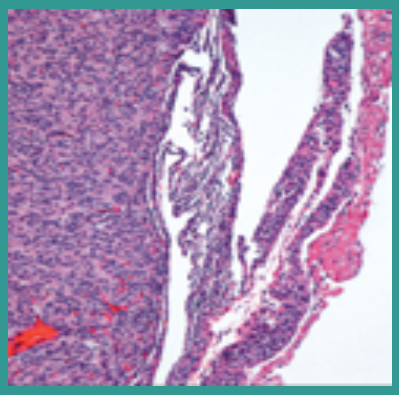
Surgeon Beware

- A large mass is not an indication for an emergency operation, no matter how anxious the patient (family, referring MD, radiologist, neighbours… may be)
- Ask yourself, are there any contraindications to getting a tissue diagnosis first? What are the cons?
- A thoughtful approach is more likely to result in the best possible outcome

Surgical Management

- 75% of resections involve resection of at least one adjacent organ (usually kidney, colon or adrenal)
- Need to be prepared
- Tend to invade contiguous organs
- Even if invasion is not apparent on imaging resection is required of contigous organs
- Malignant pseodocapsule gives false impression of a margin
- Resection at the level of pseudocapsule is assoc'd with up to 80% LR

Sarcoma Pseudocapsule



Successful Surgery

- Complete resection rate between 65–99%
- Highest in centres with high volume
- Complete resection has been shown to improve survival
- Incomplete resection is ineffective with no benefit except in very low grade tumours
- More likely to achieve complete resection at first surgery

Unexpected RP Masses

- Do not perform an undergo incisional biopsy.
- This contaminates the peritoneal cavity and substantially decreases the cure rate
- Core biopsy may be acceptable if hemostasis can be assured and contamination of the peritoneal cavity avoided.
- Tissues should not be mobilized to expose the tumour for biopsy purposes.

Adjuvant Treatment in RPS

- Preoperative multidisciplinary conference preoperative should be the goal for all RPS patients
- In BC, preoperative radiation for high grade tumours or low grade tumours where wide excision is not feasible or for locally recurrent tumours
- Radiation has not been studied in RCT, so practice varies in different centres

Why not just give XRT postoperatively?

- Radiation can't be given after the mass is out due to toxicity to fixed bowel in the operative field (due to adhesions)
- The postop radiation field is much larger with dose limiting toxicity to adjacent organs

Evidence for XRT

- One randomized trial using IORT showed improved local control
- Several retrospective and prospective studies suggest improved local control
- Some evidence that XRT delays, although does not prevent, local recurrence
- Decreased LRR and time to LR with no change is OS
  - » Stoeke, Cancer 2001:(92), 359

What about chemotherapy?

- In high-grade disease, administration of adriamycin and ifosfamide may yield partial responses in up to 50% of patients with increased overall survival
- Complete responses are seen in less than 10% of patients.
  - » Raut CP, Pisters PW. *J Surg Oncol.* 2006;94(1):81–7.

Chemotherapy and RPS in BC

- Reserved primarily for metastatic setting
- Selected use in very fit patients ‘neoadjuvantly’ as sequential therapy followed by XRT for large, high grade tumours

Metastatectomy in Sarcoma

- Most common site of distant metastases is lung
- 25% prolonged relapse free survival even with resection of multiple pulmonary metastases

Prognosis

- Despite ‘complete’ resections, 5- and 10-year survival rates are only 51% (11-63%) and 36% (10-50%) respectively
- Higher survival rates with increased magnitude of resection (43% at 10yrs)
- Most frequent site of recurrence is local in the surgical bed.
- Most recurrences occur within 2 years but can be very delayed with low grade disease

Outcome

- Local recurrences may be suitable for re-excision.
- Median survival following resection of local recurrence is 60 months vs 20 months without surgery
  - » Windham, Cancer Control 2005, 12(1) 36-43)
- Re-operative surgery is generally palliative and should be offered for symptom control

Outcomes after Local Recurrence

- Cures following re-excision of lesions that were not treated with primary wide local excision have been reported (case 2?)
- Prolonged palliation can be achieved for low grade tumours.
- Generally no value in high grade tumours with equivalent median survival to non-operative patients

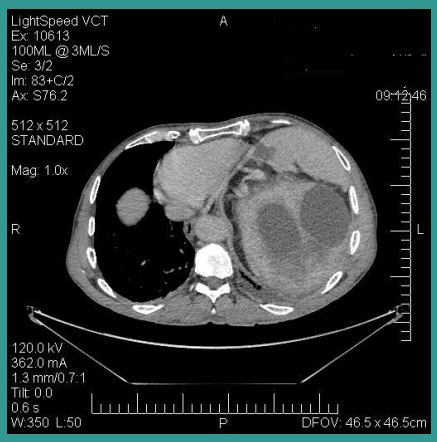
Follow-up Recommendations

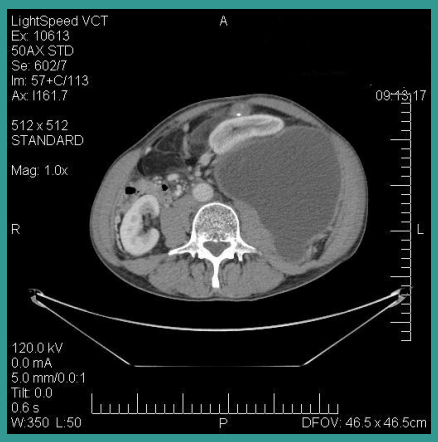
- CT or MRI
- Frequency of follow-up dictated by the completeness of resection and tumour stage.
- CT or MRI every 3–4 months for 2 years, then every 4–6 months for 3–5 years, and every 12 months thereafter
- Follow up for greater than 5 years is recommended as marked delay in appearance of recurrent disease can occur

Are we getting better? Case 3

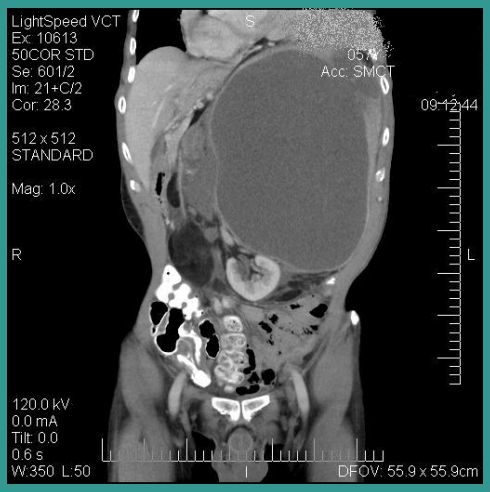
- 57 yo man felt mass in LUQ
- Imaging 23 cm adrenal carcinoma? Diff sarcoma
- Referred to community urologist
- Referred on to urologic oncologist because of potential technical challenge of surgery
- Pheo w/u (negative)
- CT guide biopsy arranged

CT images



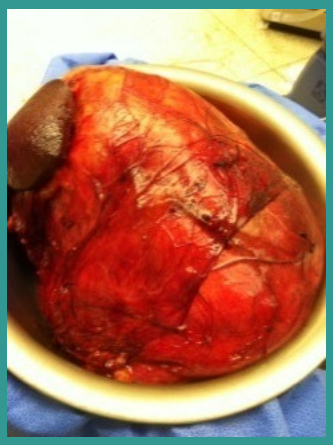


CT Images



- Core biopsy = liposarcoma
- Referred for surgical oncology opinion
- CT chest- no metastases
- Discussed at sarcoma conference
- High grade features on imaging tho' path did not show high grade
- Technically feasible for preop XRT
- Planned surgical resection including left nephrectomy, distal pancreatectomy and splenectomy

Final Pathology



Surgical specimen including left nephrectomy, distal pancreatectomy and splenectomy

47 x 25x 15cm high grade dedifferentiated liposarcoma

Margins clear!

Thank you

- To Drs. Alan So and Peter Black for the invitation to speak to this group