When Good Things (or at least not-so-bad things) Look Bad...

An Overview of Selected Mimics of Metastatic Disease in Abdominal Imaging

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Objectives

• Review intra-abdominal masses which mimic metastatic disease
• Review other intra-abdominal lesions which mimic metastatic disease
• Discuss imaging features which allow correct diagnosis
• Review current diagnosis and treatment for selected lesions

Leiomyomas

• Leiomyomas of the uterus are exceedingly common (40% of women > 35 yrs)
• Uterine leiomyomas may be symptomatic - pelvic pain, menorrhagia, urinary frequency/ urgency
• Current research suggests that leiomyomas do not undergo malignant degeneration; leiomyosarcomas arise independently

Masses Mimicking Metastases

Leiomyomas

• Leiomyomas may be found outside the uterus
  • Typically post-myomectomy or hysterectomy for leiomyomas
  • Extrauterine leiomyomas are rare but increasingly reported – related to gynecologic surgical technique?

Leiomyomas

• Imaging of extra-uterine leiomyomas:
  • All modalities – same appearance as intra-uterine leiomyoma but extra-uterine (and very importantly, extra-ovarian) location
  • US = typically hypoechoic mass, often heterogeneous
  • MR = T1 iso-hypo, T2 hypointense mass
• Treatment:
  • Masses generally enlarge with estrogen (i.e. OCP) but may regress with progesterone
  • Or just wait for post-menopausal regression
  • Spontaneous regression has been reported
**Parasitic Leiomyoma**

- Exophytic leiomyomas may eventually adhere to other structures and develop an alternate blood supply, later detaching from the uterus

**Benign Metastasizing Leiomyoma**

- Multiple leiomyomas outside the uterus
  - 120 cases reported (2006)
  - Usual site = lung
  - Also reported = heart, brain, nodes, bone, skin
  - Often indolent, rarely respiratory symptoms
  - Variable imaging manifestations
    - Common = enhancing pulmonary nodules
    - Less common = small nodules, miliary nodules
    - Adenopathy is rare

**Benign Metastasizing Leiomyoma**

**Disseminated Peritoneal Leiomyomatosis**

- Intra-peritoneal extra-uterine leiomyomas
  - DDx:
    - #1 to exclude = peritoneal carcinomatosis
    - Others to consider – desmoids, lymphoma, peritoneal TB, peritoneal mesothelioma

**Disseminated Peritoneal Leiomyomatosis**
Disseminated Peritoneal Leiomyomatosis

• Leiomyomas in uterine and systemic veins
  • 80% have myometrial/parametrial venous involvement,
  • ~20% extend up to the right atrium
• Rare (150 reported cases)
• Variable clinical course depending on pelvic vs IVC vs intracardiac involvement

Intravenous Leiomyomatosis
Intravenous Leiomyomatosis

- Imaging:
  - US = venous filling defect with flow on Doppler
  - CT = enhancing intravenous filling defect
  - MR = T1 iso-hypo-, T2 hypointense enhancing intravenous mass
- DDx:
  - Intravenous leiomyosarcoma
  - Bland vs malignant thrombus
- Treatment = surgical resection +/- anti-estrogen
Granulomatous Disease

- Granulomata may present as small solid nodules
- May have regions of central necrosis (necrotizing granuloma)
- May seed solid organs or serosal surfaces
- Often associated with adenopathy

Sarcoidosis

- 90% of patients have thoracic involvement (lymphadenopathy > pulmonary parenchymal)
- Approximately 30% of patients have abdominal involvement
  - Mesenteric and retroperitoneal adenopathy is most common
  - Hepatosplenomegaly in 60%
  - Liver/spleen granulomas
Epithelioid Haemangioendothelioma

- "Low-intermediate grade vascular neoplasms"
- But in practice, appear malignant
  - Multiple pulmonary nodules
  - Often additional hepatic (15-20%) or osseous lesions
  - Frequently with pleural masses

Epithelioid Haemangioendothelioma

- Imaging:
  - Hepatic – peripheral-enhancing hypodense round nodules which coalesce over time
  - DDx = metastases (but show minimal growth)

Epithelioid Haemangioendothelioma

Castleman Disease

- Castleman disease = angiofollicular lymph node hyperplasia
- Subdivided into 2 histologic types and 2 clinical presentations
  - Hyaline vascular vs plasma cell type
  - Localized vs disseminated presentation
  - Localized form usually with hyaline vascular type, more common and with better prognosis
Castleman Disease

- Presentation is variable
  - Single hyperenhancing nodal mass
  - Infiltrative solitary mass
  - Extensive adenopathy but no discrete mass

- Imaging features:
  - Smaller lesions are usually hyperenhancing
  - Larger lesions are more heterogeneous
  - Calcifications in 10-15%

Sclerosing Conditions

- IgG4-related disorders have 3 key pathologic features:
  - Lymphoplasmocyte infiltrate of IgG4-positive cells
  - Storiform fibrosis
  - Obliterative phlebitis

- Fibromatoses of the aggressive type are infiltrative collagenous tumours
  - Associated with mutations of the β-catenin gene
Retroperitoneal Fibrosis

- Progressive infiltration of the retroperitoneum by fibrotic tissue
- Most "idiopathic" cases of retroperitoneal fibrosis are actually associated with IgG4 related disease
  - A small percentage of patients have true idiopathic RPF
  - RPF may also rarely be secondary to malignancy or medications

Retroperitoneal Fibrosis

- On CT/MRI:
  - Initially, small fibrotic (CT hypodense, T2 hypointense) plaque near the aortic bifurcation
  - Progressive enlargement
  - Usually centred along the midline
  - Rarely extends lateral to psoas muscles
  - Does not displace aorta/IVC from the anterior spine
Inflammatory Pseudotumour

• Many alternate names have been proposed!
  • Inflammatory myofibroblastic tumour
  • Plasma cell granuloma
  • Fibrous xanthoma, Pseudolymphoma, Inflammatory fibrosarcoma... and others...

• Terminology is confusing
  • Inflammatory pseudotumour = fibrous process, no metastatic potential
  • Inflammatory myofibroblastic tumour = low-grade malignancy with rare (~5%) metastases

Inflammatory Pseudotumour

• On CT/MRI:
  • Variable appearance – ill-defined and infiltrative or more mass-like
  • Classically, hypodense on CT and T2 hypointense on MRI but attenuation/intensity may vary also
  • May demonstrate enhancement

Autoimmune Pancreatitis

• One of the IgG4-related sclerosing conditions
  • Parenchymal infiltration by IgG-4 positive plasma cells with additional fibrosis

• Clinical features:
  • More common in males
  • Average age 60-65 years old
  • Presentation with abdominal pain and jaundice
  • 1/3 reported to present with acute pancreatitis

Autoimmune Pancreatitis

• On CT/MRI,
  • Most common = diffuse pancreatic involvement
    • "sausage-shaped" pancreas (enlarged with loss of normal lobulations)
    • +/- surrounding thin capsule, hypodense on CT or T2 hypointense on MRI
  • May also have focal involvement
    • Usually at the pancreatic head, often with upstream duct dilatation
    • Also hypodense on CT, T2 hypointense on MRI
Autoimmune Pancreatitis

• Differential diagnosis for the diffuse form = acute pancreatitis
  • Clinical correlation required
• Differential diagnosis for the focal form = pancreatic adenocarcinoma
  • Autoimmune pancreatitis may resolve on imaging after corticosteroid therapy
  • Both may be FDG-avid on FDG-PET
  • May require biopsy for definitive diagnosis

Desmoid Tumours

• A classic fibromatosis
• Benign (won’t metastasize) but locally aggressive and often recurs
• Solitary or multiple, children or adults, may arise at any site
  • Most common age = 10-40 yr
  • Characterized as abdominal wall, intra-abdominal, or extra-abdominal (then most common in the shoulder/upper extremity)
  • Increased incidence at surgical or previous trauma sites

Desmoid Tumours

• Associated with mutations of beta-catenin (sporadic types) and adenomatosis polyposis coli (APC) gene (FAP, Gardner syndrome)
  • Current belief is that beta-catenin mutation and the sporadic type are mutually exclusive from APC mutation and FAP
  • Multifocal tumours \( \rightarrow \) consider diagnosis of FAP and recommend colonoscopy for poly screen

Desmoid Tumours

• Imaging Findings:
  • Infiltrative mass / masses
    • Non-specific soft tissue masses on CT; MRI suggested for work-up
  • “Classic” = T2 hypointense, no enhancement
  • BUT morphology is variable, with varying degrees of T2 hyperintense signal and enhancement
  • When multiple, internal attenuation/signal and enhancement may vary between lesions

Desmoid Tumours

• Biopsy is required to confirm diagnosis
  • Main DDx = scar tissue, nodular fasciitis, fibrosarcoma
• Treatment depends on location and aggression
  • Prior standard of care = surgical resection
  • Now, first line = “Watchful waiting”; 5-10% will at least partially spontaneously regress
  • Symptomatic \( \rightarrow \) surgery, radiation or chemotherapy
  • Chemotherapy - anthracyclines, imatinib, tamoxifen
Desmoid Tumours

Metastatic Mimics with Malignant Association

Hepatic Adenomatosis

- Classically, a condition of multiple hepatic adenomas
  - Idiopathic; no glycogen storage disease or steroids
  - Over 10 lesions required
- Adenomatosis is a historical diagnosis; histologically, lesions are identical to solitary hepatic adenomas
  - Current thought is to diagnose multiple hepatic adenomas rather than a separate entity of adenomatosis

Hepatic Adenomatosis

- Risk factors for hepatic adenomas:
  - Female
  - Oral contraceptive use
  - Hepatic steatosis
  - Obesity/metabolic syndrome
  - Anabolic steroids
  - Glycogen storage diseases

Hepatic Adenomatosis

- Subtypes have recently been defined based on molecular characteristics; clinical correlations have also been outlined
  - HNF1A mutation (with contraceptive use)
  - β-catenin activated mutation (with obesity)
  - Inflammatory (with androgen use)
  - Undetermined
  - β-catenin activated type are at higher risk of malignant transformation to HCC
Hepatic Adenomatosis

- Variable imaging appearance on MRI
  - Often T1 hyperintense or with signal loss on T1 out-of-phase series (fat content)
  - Variable enhancement
  - No hepatobiliary phase uptake on Primovist MR

Treatment:
- If on oral contraceptives, stop
- If mass > 5 cm, resect
  - Other indications for resection = symptomatic, enlarging, β-catenin activated subtype, indeterminate
- Other treatment options = trans-arterial embolization, radiofrequency ablation
- If mass < 5 cm and of low-risk HNF1A-mutation subtype, consider conservative management with serial imaging follow-up

Oncocytosis

“Bilateral, multifocal, and synchronous renal oncocyтомas”
- MSKCC 2011 review (Journal of Urology):
  - 85% are asymptomatic (incidental imaging diagnosis)
  - 50% have chronic renal disease at diagnosis
  - 100% undergo nephrectomy (partial or total);
    - >1/2 of resected tumours = oncocytoma/chromophobe RCC hybrids
    - ½ = chromophobe RCC

Oncocytomas are benign without malignant potential
- But in patients with oncocytosis, hybrid (oncocytoma and chromophobe RCC) tumours and chromophobe RCC comprise ~85% of the dominant masses
- In the largest series, 70% of patients had chromophobe RCC among their renal masses
- Pathologically, oncocyтомas resemble chromophobe RCC, so biopsy is considered unreliable and complete lesion resection is recommended
  - However, new genetic markers (ie microRNA 15a) may help to differentiate oncocytoma from RCC

Imaging features:
- All modalities – solid renal vascular/enhancing mass lesion
- May have a stellate central scar on CT/MRI; this is not a distinguishing feature, as RCC may also demonstrate a central scar
Oncocytosis

Mimics of Paediatric Metastatic Disease

Nephroblastomatosis

- Paediatric condition – persistence of multiple nephrogenic rests
  - Kidneys develop from the ureteric bud and metanephric blastema
  - Immature metanephric blastema will persist as nephrogenic rests
  - Genetic associations – often abnormal Wilms’ tumour suppressor genes

Nephroblastomatosis

- Intralobar (within parenchyma) vs perilobar (diffuse perinephric)
  - Very rare, only reported in infants < 4mo = panlobar nephroblastomatosis

Nephroblastomatosis

- US = well-defined ovoid homogeneous hypoechoic mass, <2cm
- CT = soft tissue mass hypoenhancing compared to normal kidney
- MRI = T1 iso-, T2 iso-hyper intense soft tissue mass
- Concerning = spherical, >3cm, heterogeneous, invasive

Nephroblastomatosis

- Malignant association:
  - Incidental nephroblastomatosis in ~1% of infants
  - Nephroblastomatosis transformation rate to Wilms’ tumour reported at 1-3%
  - Nephroblastomatosis accounts for ~35% of Wilms’
  - Frequent screening therefore recommended – q3-4 months until 5-7 yrs with US
  - Enlarging lesions are usually treated as early-stage Wilms’ tumour with chemotherapy or surgical resection
  - Other lesions involute over time
Paediatric Focal Nodular Hyperplasia

- Focal nodular hyperplasia (FNH) is a rare tumour in children (incidence 0.02%)
- Relatively recently, high rates of FNH were identified developing among children who suffered from childhood cancers

Paediatric Focal Nodular Hyperplasia

- An association has been proposed between FNH and childhood stem cell transplant
  - Rates have been reported up to 5.2% of this population (260x higher than the general rate)
  - Lesions are usually first found on surveillance US as non-specific masses; MRI then recommended for characterization
Paediatric Focal Nodular Hyperplasia

• FNH in this population are generally atypical
  • Smaller and more numerous (usually >1 FNH / patient)
  • Less likely to have a central scar
  • Less likely to be occult on T1- and T2-weighted sequences
  • As per usual, avid arterial enhancement, but often maintain enhancement through all phases
  • Often enlarge (slightly) over time

Paediatric Focal Nodular Hyperplasia

• Atypical appearance of FNH in the post-treatment paediatric oncology patient can create a diagnostic dilemma
  • Underlying concern = metastases
  • Although FNH in this population are often atypical, the key feature is arterial hyperenhancement
  • Biopsy may still be required if lesions are deemed indeterminate

Summary

• Radiology is a challenging specialty!
  • Multiple solid lesions are not necessarily malignant
  • However, benign lesions often have associated morbidity or malignant associations, and aggressive management may be indicated
  • Differential diagnosis and clinicopathological correlation are, as always, very important

References