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On imaging, how can we differentiate retroperitoneal fibrosis from lymphoma?

Retroperitoneal fibrosis pulls, tethers, and constricts structures inward/medially whereas lymphoma displaces and surrounds structures by pushing them outward/laterally without constriction. On imaging, for retroperitoneal fibrosis look for medial tethering ureters with ureteral strictures and hydronephrosis as well as abdominal aortic encasement without deviation. Lymphoma pushes things outwards so look for anterior displacement of abdominal aorta and lateral deviation of ureters which may be encased by soft tissue but not strictured. On MRI, retroperitoneal fibrosis would classically be T2 dark due to the fibrotic tissue. Lymphoma on MRI would typically be T2 isointense to spleen. Both can show delayed enhancement on MRI.

What is a classic appearance for renal lymphoma?

Renal lymphoma typically presents as bilateral homogeneous hypovascular round and oval circumscribed masses within the renal parenchyma. This has been described as a 'cannon ball appearance'. Other less common manifestations can include smooth renal enlargement and/or perinephric soft tissue infiltration. With more aggressive lymphomas you may see infiltrative renal lesions. Most cases of renal lymphoma occur with widespread systemic disease. Primary renal lymphoma is much more rare than secondary renal lymphoma from systemic disease, typically NHL. Renal lymphoma is often clinically asymptomatic.

Can you develop primary lymphoma of the urinary bladder?

No. There is no lymphoid tissue in the bladder so lymphoma of the bladder is always secondary.

What is a typical appearance for splenic lymphoma?

Most commonly, splenic lymphoma will manifest as diffuse enlargement of the spleen (splenomegaly) without a discrete lesion/mass. This is most common for a low-grade lymphoma. On FDG PET/CT you would expect splenomegaly with uptake of FDG above that of liver. Higher grade lymphomas involving the spleen may have discrete splenic nodules that would be focally FDG avid. On CT imaging these nodules are typically hypovascular compared to the normal spleen. Look for associated lymphadenopathy elsewhere as splenic lymphoma is typically a manifestation of systemic disease.

What is the most common primary tumor of the spleen that is not lymphoma?

Splenic angiosarcoma which shows infiltrative masses with internal necrosis and hemorrhage.

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What is the typical imaging appearance for testicular lymphoma?

Testicular lymphoma appearance as a homogeneous hypoechoic vascular testicular mass(es) that may be indistinguishable from a testicular seminoma. Both seminoma and testicular lymphoma appear as homogeneous testicular masses whereas other testicular tumors are classically heterogeneous. Testicular lymphoma is most commonly diffuse large B cell lymphoma and is most common in older males and is frequently bilateral and may involve the epididymis. Lymphoma is the most common testicular tumor in patients over 60 years of age. Seminomas are usually seen in younger men (around 30s).

What is the typical treatment of testicular lymphoma?

Surgery/orchiectomy.

Why?

The blood testes barrier prevents chemotherapy from reaching the testicles! So, you need to surgically remove the testicles. Beware of the follow-up FDG PET scan that shows that lymphoma throughout the torso is no longer seen but testicular activity above normal persists. Sometimes testicular lymphoma is not appreciated on a baseline FDG scan due to extensive hypermetabolic disease elsewhere, especially if both testicles are involved and appear symmetric. However, after systemic chemotherapy, all other sites resolve and you now see the testicles that are very hypermetabolic and easier to appreciate. This is the imaging manifestation of systemic chemotherapy eradicating disease elsewhere but not in the testicles due to the blood-testes barrier. Appropriate treatment is therefore typically orchiectomy.

How can colonic adenocarcinoma and lymphoma manifest differently on imaging?

If you see colonic bowel wall thickening with obstruction think adenocarcinoma. If you see bowel wall thickening without obstruction this could be colonic lymphoma or less likely something like fungal infection. Key is that lymphoma typically does not obstruct. For small or large bowel lymphoma can present with aneurysmal dilatation of a bowel loop without obstruction, whereas adenocarcinoma constricts and obstructs the bowel lumen. On MRI, bowel lymphoma shows T2 mass isointense to spleen with delayed enhancement.

What are the top malignant causes of intussusception?

1. Lymphoma. 2. Melanoma.

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What is the significance of the small bowel target sign?

This sign is the result of bowel wall edema with associated enhancement of the luminal mucosa and the external muscularis propria that give a target appearance. If you see multiple small bowel target signs, think lymphoma or metastatic melanoma. If you see a single small bowel target sign think GIST, primary adenocarcinoma, or an ectopic pancreatic rest.

What is the typical appearance of bowel lymphoma on fluoroscopy?

On fluoroscopy, bowel lymphoma may manifest as multiple thickened folds with nodularity in a segmental or diffuse pattern. A helpful mnemonic for the fluoro "thick folds with nodularity" pattern is MAIL COW. Metastasis, Abscess, Infection, Lymphoma, Crohn's, Other (such as lymphangiectasis), Whipple's disease. Small bowel lymphoma is rare in the United States. Most common site for small bowel lymphoma is the ileum (most lymphoid tissue there) followed by jejunum and then duodenum. Additional signs of possible small bowel lymphoma as focal circumferential narrowing of the bowel. Note that Mantle cell lymphoma has a characteristic extremely polypoid appearance on fluoroscopy. IF you have an ileocecal mass causing intussusception lymphoma is high on the differential diagnosis.

What is benign nodular lymphoid hyperplasia in the bowel and how does this appear different than lymphoma?

Benign nodular lymphoid hyperplasia appears as scattered clusters of lymph node follicles that are all of the same size. This is a reactive process seen with entities like IgA deficiency, asthma, or infections. Lymphoma has larger and more variable nodules.

What are some common risk factors for small bowel lymphoma?

Celiac disease, Crohn's disease, AIDS, and lupus are common risk factors for small bowel lymphoma.

True or false: Hashimoto's thyroiditis has increased risk of developing thyroid lymphoma?

True. Patient's with Hashimoto thyroiditis have an approximately 75% increased risk of developing thyroid NHL in addition to increased risk of papillary and Hurthle cell neoplasms.

Is hepatic lymphoma typically primary or secondary?

Primary hepatic lymphoma is very rare. If present, hepatic lymphoma usually manifests with one or more hepatic masses that are hypoechoic on ultrasound and are hypovascular on CT/MRI. Prognosis for primary hepatic lymphoma is very poor. The imaging features of secondary hepatic lymphoma are variable and include a miliary disease pattern, infiltrative disease pattern, or mass-like presentations.

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For secondary hepatic disease, look for co-existing splenomegaly and lymphadenopathy. For hepatic lymphoma, Hodgkin's disease is slightly more common than non-Hodgkin's lymphoma.

Hepatic or splenic lymphoma can present with peliosis. What is peliosis?

Peliosis is a rare condition that manifests with multiple blood-filled cystic spaces in solid organs, most commonly the liver and spleen. Causes include lymphoma, oral contraceptive use, men on steroids, AIDS, renal transplantation.

The most common extranodal site for non-Hodgkin's lymphoma is what organ?

The stomach is the most common extranodal site of NHL.

What are typical imaging features of gastric lymphoma?

Gastric wall thickening without gastric outlet obstruction, even when extensive wall thickening is present. Note that primary gastric lymphoma is mucosa-associated lymphoma tissue (MALT) as stomach has no intrinsic lymphoid tissue. Both gastric lymphoma and gastric adenocarcinoma can cross the pylorus into the duodenum. Gastric lymphoma can also have a linitis plastica (leather bottle) appearance which can also be seen with infiltrative metastases from lung, breast, or other cancers. Compared to lymphoma, gastric carcinoma is more likely to present with a focal mass and gastric outlet obstruction. At a more detailed level, gastric lymphoma is typically either extranodal marginal zone lymphoma which has homogeneous wall thickening with perigastric lymphadenopathy or diffuse large B cell lymphoma which has wall thickening typically >4 cm with lymphadenopathy and possible cavitation.

What is most common—gastric adenocarcinoma or gastric lymphoma?

Gastric adenocarcinoma comprises about 95% of gastric cancers and lymphoma comprises the majority of the remaining 5%. GIST also occurs in the stomach and typically has characteristic smooth margins without lymphadenopathy.

Does H. pylori infection increase risk of gastric lymphoma?

Yes, H. pylori raises risk of both gastric adenocarcinoma and gastric lymphoma. Chronic H. pylori infection causes gastritis and over time this inflammation causes the mucosa to gradually acquire lymphoid tissue (MALT) that is at risk for monoclonal proliferation. Interestingly, low grade MALT lymphoma can sometimes be cured with H. pylori eradication. If H. pylori is untreated, you can progress from low-grade to aggressive gastric lymphomas such as diffuse large B cell lymphoma.

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What is a classic appearance for mesenteric lymphoma?

Confluent lobulated homogeneous soft tissue masses that encase mesenteric vessels. This has been termed the sandwich sign (soft tissue masses sandwiching the mesenteric vessels). With mesenteric lymphoma you can see fat between the mesenteric mass. Mesenteric mass(es) may distort surrounding structures but does not occlude. NHL most common.

What is misty mesentery and is this a sign of potential lymphoma?

Misty mesentery manifests as fat stranding in the central mesenteric fat. Misty mesentery is a sign of lymphatic insufficiency and is most commonly seen in middle aged males and is typically stable over time and idiopathic, inflammatory, or related to portal hypertension. However, if you see misty mesentery and abnormal lymph nodes, this is suspicious for lymphoma. Misty mesentery can also less commonly result from lymphatic infiltration from a GI malignancy.

What is the deal with Burkitt lymphoma?

Burkitt lymphoma is a very aggressive B cell lymphoma (can double in size in 24 hours) that has early metastases. Unfortunately, this is the most common type of NHL in kids but fortunately children have a good prognosis with appropriate chemotherapy. Adults, however, have a worse prognosis. Burkitt lymphoma is much more common in boys and in Africa so if you see an aggressive appearing lymphoma with widespread manifestation of disease in a young African boy on a board exam question you need to consider Burkitt lymphoma. Endemic Burkitt lymphoma in Africa is linked to Epstein-Barr virus infection and/or malaria infections. Can also happen with HIV or immunosuppression to include post-organ transplantation.

What are B symptoms?

B symptoms are fever, night sweats, and weight loss (unintentional loss of >10 % body weight in six months). Lymphoma commonly presents with B symptoms so look for these in a question stem on your board exams. This results from elevated inflammatory cytokines.

Do B symptoms have prognostic implications?

Yes, if B symptoms are present this generally predicts poorer prognosis for lymphoma patients. Under the Lugano classification system, lymphoma is staged higher if B symptoms are present.

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What is the Lugano classification system for staging of lymphoma?

Lugano stages lymphoma based on two main divisions: limited disease or advanced disease. You can look up the details elsewhere but limited disease is basically lymphoma only a few lymph nodes on the same side of the diaphragm and advanced disease has lymph nodes on both sides of the diaphragm. Limited disease is stage 1 and 2 and advanced disease is stage 3 and 4.

Can you have stage 4 lymphoma without having lymph node involvement?

Yes, stage 4 may or may not have lymph node involvement of disease but requires diffuse involvement of at least one extranodal organ or extranodal disease that can't be treated with radiation therapy.

What is the size cutoff in the Lugano classification for a lymph node to be considered as bulky disease?

10 cm. If a lymph node is >10 cm in diameter this is considered bulky disease.

What is more common, Hodgkin lymphoma or non-Hodgkin lymphoma?

Non-Hodgkin lymphoma is more common and comprises about 2/3 of lymphoma cases with Hodgkin lymphoma comprising 1/3 of lymphoma cases.

True or false: Hodgkin lymphoma is curable in most cases?

True. Hodgkin's lymphoma is curable in about 90% of cases.

What is the pathologic hallmark of Hodgkin's lymphoma?

Reed Sternberg cells are the histologic hallmark of Hodgkin's lymphoma.

What are classic imaging manifestations of Hodgkin's disease?

Hodgkin's lymphoma typically manifests as lymphadenopathy that starts in the chest, axilla, and/or neck. Extranodal disease is not common. However, in advanced cases, any organ/tissue may be involved. When extranodal disease is present, this may fairly often be seen in the bones (lytic early and blastic later) followed by the lungs (may see direct extension from hilar lymphadenopathy into the pulmonary parenchyma). Look for anterior vertebral body erosions from paravertebral lymphadenopathy and/or an ivory vertebra (single high-density vertebral body—differential considerations include other metastatic disease, TB, Paget disease).

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What entities are part of the non-Hodgkin lymphoma family

NHL is a catch-all for everything that is not Hodgkin's lymphoma. This includes Burkitt lymphoma, mantle cell lymphoma, follicular lymphoma, T- and Nk-cell lymphomas, and post-transplant lymphoproliferative disorders.

What is the most common subtype of non-Hodgkin lymphoma?

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of NHL. Less aggressive NHL subtypes such as follicular lymphoma can transform into the more aggressive DLBCL over time. If you see images of an indolent lymphoma that rapidly progresses on imaging, DLBCL is in the differential.

True or false: most cases of post-transplant lymphoproliferative disease occur greater than 1 year after organ transplantation?

False. Most cases of PTLD occur within 1 year of transplant.

Common treatment of PTLD includes what?

First, reduction of immunosuppression. Therefore, you have to strike a balance between risk of PTLD and risk of transplant allograft rejection. Other treatment options include surgery, radiation, and chemotherapy.

What is the hallmark genetic translocation in cases of follicular lymphoma?

A t(14:18) translocation is classic for follicular lymphoma.

What are some classic cytogenetic features of diffuse large b cell lymphoma?

c-MYC, BCL2 and/or BCL6 rearrangements.

What is the Deauville score?

The Deauville score is a 5-point score for use of staging lymphoma based on degree of uptake on FDG PET/CT. Key is to remember that a score of 4 or 5 shows uptake above that of liver and denotes active/progressive disease (if new disease this is a score of 5). A score of 1-3 denotes absent uptake (score of 1) or uptake below (2) or equal (3) to that of liver (score of 2 has uptake below liver and below or equal to mediastinal blood pool, score of 3 has uptake above mediastinal blood pool but below or equal to liver).

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Which Deauville scores can denote a complete response to therapy?

Deauville scores of 1, 2, or 3 can denote a complete metabolic response to therapy. On the other hand, Deauville scores of 4 or 5 can denote stable disease, progressive disease, or partial response depending on whether uptake is the same, better, or worse compared to prior and whether there is new disease (if new disease it is a Deauville score of 5).

Bonus tip: It is possible to be considered a CR when using Deauville score even if there is a large residual mass, as long as uptake is absent or very low.

Diffuse bone marrow uptake can be a sign of lymphoma bone marrow involvement but can also be seen in what other settings?

Diffuse bone marrow uptake can be seen with lymphoma but can also be seen other settings such as bone marrow stimulation from filgrastim or other colony stimulating factor agents, bone marrow rebound post-chemotherapy, or bone marrow rebound from anemia of other causes.

How can bone marrow involvement of lymphoma be confirmed?

Bone marrow biopsy is frequently performed as part of lymphoma evaluation and staging, most commonly in the iliac bone. On imaging, look for linear subcutaneous fat stranding in a linear manner in the posterior iliac subcutaneous tissues along with FDG uptake in the subcutaneous tissues and iliac bone as imaging manifestations of recent bone marrow biopsy.

How can you differentiate between brown fat uptake and lymph node uptake on FDG PET/CT?

Uptake of brown fat aka brown adipose tissue can look very similar to hypermetabolic lymphadenopathy on FDG PET only images. However, when you evaluate the associated CT images there will be no associated lymph nodes in the region(s) of uptake on PET imaging but only normal fat will be seen in the areas of uptake. The most common locations for brown fat uptake are the mediastinum, neck and supraclavicular regions, paravertebral regions, and upper para-aortic regions. You must carefully scrutinize areas of brown fat uptake to see if there are co-existent lymph nodes as you can have mixed lymphadenopathy and brown fat, with both showing uptake. If areas of uptake correspond with lymph nodes this is potentially pathologic, if areas of uptake show only fat on CT, and the pattern is analogous with brown fat, then brown fat uptake is confirmed. Note that brown fat uptake is a potential cause of diagnostic error for lymphoma staging so it is important to be aware of this entity. Brown fat uptake is also something that is easily testable on radiology and nuclear medicine board examinations.

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What can be done to minimize brown adipose FDG uptake?

Various strategies exist including warming the PET uptake rooms where the patient waits prior to PET imaging, administering benzodiazepines or beta blockers in patients who have had prior brown fat uptake, and encouraging patients to stay warm prior to arriving at the imaging suite for FDG PET imaging.