Abdominal Radiology (2019) 44:2988–3005
https://doi.org/10.1007/s00261-019-02100-5

REVIEW

Primary lymphomas of the intraabdominal solid organs and the gastrointestinal tract: spectrum of imaging findings with histopathological confirmation

Ali Devrim Karaosmanoglu[1] · Aycan Uysal[2] · Mehmet Ruhi Onur[1] · Peter F. Hahn[3] · Arzu Saglam Ayhan[4] · Mustafa Nasuh Ozmen[1] · Deniz Akata[1] · Musturay Karcaaltincaba[1]

Published online: 17 June 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Unlike nodal lymphoma, primary lymphomas of the intraabdominal organs are uncommon neoplasms whose diagnosis may be challenging in certain clinical circumstances. Despite this difficulty for imaging diagnosis, there are several imaging features on ultrasonography, computed tomography, magnetic resonance imaging, and positron emission tomography that may suggest the correct diagnosis. The scope of this review is to describe and illustrate the imaging features of primary lymphoma of intraabdominal organs providing clues to the diagnosis, together with their pathological correlations.

Keywords Primary lymphoma · Abdomen · Radiology

Abbreviations

NHL	Non-Hodgkin lymphoma
US	Ultrasonography
CT	Computed tomography
MRI	Magnetic resonance imaging
PET	Positron emission tomography
FDG	2-[Fluorine-18] fluoro-2-deoxy-D-glucose
PHL	Primary hepatic lymphoma
HCC	Hepatocellular cancer
DLBCL	Diffuse large B-cell lymphoma
PGL	Primary gallbladder lymphoma
MALT	Mucosa-associated lymphoid tissue
PSL	Primary splenic lymphoma
HIV	Human immunodeficiency virus
PPL	Primary pancreatic lymphoma
AIP	Autoimmune pancreatitis
PAL	Primary adrenal lymphoma
PRL	Primary renal lymphoma
RCC	Renal cell carcinoma
PBL	Primary bladder lymphoma
POL	Primary ovarian lymphoma
PCeL	Primary cervical lymphoma
PUL	Primary uterine lymphoma
PTL	Primary testicular lymphoma
PLS	Primary lymphoma of the stomach
PLSB	Primary lymphoma of the small bowel
PLC	Primary lymphoma of the colon

✉ Ali Devrim Karaosmanoglu
alidevrim76@yahoo.com

[1] Department of Radiology, Hacettepe University School of Medicine, 06100 Ankara, Turkey

[2] Department of Radiology, Gulhane Training and Research Hospital, 06010 Ankara, Turkey

[3] Department of Radiology, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114, USA

[4] Department of Pathology, Hacettepe University School of Medicine, 06100 Ankara, Turkey

Introduction

Extranodal lymphoma is characterized by lymphoproliferative disease in sites outside the lymph nodes including thymus and Waldeyer's ring (tonsils and adenoids), skin, and visceral organs. The exception is the spleen, which is considered as extranodal involvement site in non-Hodgkin lymphoma (NHL) while nodal involvement site in Hodgkin lymphoma [1]. Lymphomas are classified as extranodal when there is no or limited lymph node involvement as long as the extranodal involvement is dominant [2, 3].

Extranodal lymphomas may arise almost everywhere in the body outside the lymph node regions. Even organs without lymphoid tissue (e.g., soft tissue and brain) may develop extranodal lymphoma. Primary extranodal lymphoma is

characterized by the involvement of a single organ and immediately adjacent lymph nodes. Secondary extranodal lymphoma refers to involvement of more than one extranodal organ or involvement of an extranodal organ and distant/non-adjacent lymph nodes [2].

The abdomen is commonly affected in the course of systemic lymphoma. Abdominal organs become involved secondarily, especially in the advanced stage of the disease [4, 5]. Primary lymphoma originating from intraabdominal organs is relatively rare when compared to secondary involvement in systemic lymphoma. Two main types, within the four subgroups of lymphoproliferative malignancy, namely NHL and Hodgkin's lymphoma typically have findings on abdominal imaging, whereas the other 2 subtypes, lymphocytic leukemia and multiple myeloma (a malignant plasma cell dyscrasia) typically do not (other than possible lymph node or bone involvement). Extralymphatic involvement is rare in Hodgkin's lymphoma, but NHL often invades extralymphatic organs [6].

Extranodal lymphomas originating from abdominal organs may closely mimic other non-lymphomatous primary tumors and secondary metastases to these organs and this confusion may lead to diagnostic delay and unnecessary interventions. The aim of this manuscript is to present and illustrate the imaging findings of primary lymphomas arising from intraabdominal organs. Since cross-sectional imaging with ultrasound (US), computed tomography (CT), or magnetic resonance imaging (MRI) is usually the modality used at presentation, we emphasize the appearance of extranodal lymphoma with those techniques. FDG-PET/CT has been shown to be a useful complimentary imaging technique in staging, response evaluation, and posttreatment surveillance in most histologic subtypes of lymphoma, due to their hypermetabolic nature [7]. Differentiation between the metabolically active residual tumor and the areas of necrosis and fibrosis can be accomplished with FDG-PET/CT [8]. Therefore, FDG-PET/CT images of selected cases will be reviewed that illustrate the organ-confining nature of these tumors.

Liver

Primary hepatic lymphomas (PHL) are very rare tumors consisting of 0.016% of all NHLs and 0.4% of all extranodal lymphomas [9–11]. PHL is more common in men than women, and the usual age at presentation is 50 years [12]. Majority of the PHL demonstrates diffuse large B-cell immunophenotype. By definition, PHL is a lymphoma that is limited to the liver or with major liver involvement with or without adjacent perihepatic lymph nodes without detectable involvement of other organs, bone marrow, and distant lymph nodes for at least 6 months after the onset of the hepatic disease [9, 11]. Differentiation of PHL from secondary involvement in systemic lymphoma is crucial as the management and prognoses may significantly differ. Although liver contains lymphoid tissue, host factors make liver a poor environment for development of malignant lymphoma [13]. The pathogenesis of PHL is not clear, but it has been reported that viruses such as viral hepatitis B and C and Epstein-Barr virus can be the causative agent [12].

The presentation of PHL varies from asymptomatic disease to the onset of fulminant hepatic failure with rapid progression of encephalopathy to coma and death. The symptoms are usually non-specific, most of the patients present with abdominal pain, fatigue, weight loss, fever, anorexia, and nausea. Hepatomegaly is a common finding in physical examination. Definitive diagnosis is made by liver biopsy [11, 12].

Several different forms of involvement have been reported in PHL. The disease may manifest as a solitary lesion or multiple nodules within the liver parenchyma in the setting of normal levels of alpha-fetoprotein and carcinoembryonic antigen. Diffuse parenchymal and periportal soft tissue infiltration have also been reported [14]. Solitary lesion is the most common manifestation of PHL and was observed in 60% of the cases [15, 16]. Perihepatic regional lymph node involvement is also common in the course of the disease. As lymphomatous tumor deposits typically have homogenous internal structure the tumors appear as homogenous internal texture with well- defined borders. The lesions appear as hypoechoic or anechoic on US exams and may therefore mimic cysts [14]. Associated enlarged lymph nodes may be seen in the liver hilum. Cases of hepatic lymphoma confused with liver abscesses have been reported in the literature [17–19]. Cross-sectional imaging with CT and MRI is a commonly used approach to characterize focal liver lesions. Lesions typically demonstrate mild to no enhancement after contrast injection. Internal areas of necrosis and hemorrhage may occasionally be seen. Calcification is rare in the absence of any prior treatment [14]. The detection of vessels traversing the mass without any luminal deformity and occlusion, also known as "vessel penetration sign", may be a helpful clue to correct diagnosis (Fig. 1). The absence of perilesional hyperemia and pylephlebitis of the portal vein can be useful for differentiating the mass from a liver abscess [14]. PHL has been seen in immunocompromised patients and systemic lupus erythematosus [9]. Potential association between PHL and viral hepatitis B and C has been proposed [9]. Because of this potential association, PHL should also be considered in the differential diagnosis of any focal liver lesion in background cirrhotic liver not demonstrating typical imaging and contrast enhancement characteristic of a hepatocellular carcinoma (HCC). The absence of significant arterial phase enhancement and absence of vascular involvement may also be mentioned among the other helpful

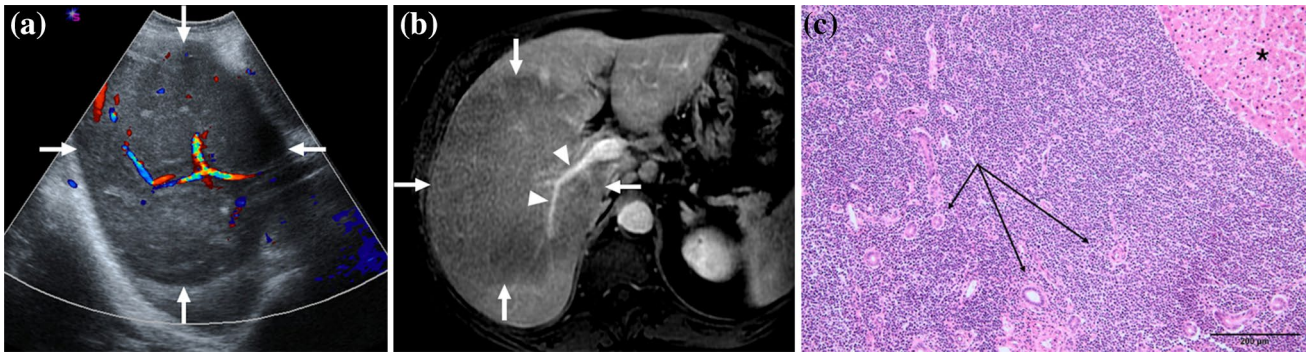

Fig. 1 75-year-old-male with previously treated inguinal liposarcoma and hypothyroidism now presenting with fatigue and abdominal pain. **a** Color Doppler US image demonstrates a well-defined, hypoechoic solid mass (arrows) encasing hepatic vessels without invading or occluding them. **b** Axial plane fat-suppressed T1-weighted image after gadolinium administration reveals mild enhancement within the mass. The right portal vein (arrowheads) traverses through the mass without any mass effect on the vessel wall (vessel penetration sign). The subsequent neck and chest CT scans were negative for any disease. **c** High power magnification hematoxylin and eosin (H&E) stained section demonstrates monocytoid nature of the infiltrate. Entrapped bile ducts can also be discerned (arrows). A patch of partially visualized residual liver parenchyma is denoted by (*). Findings are consistent with MALT lymphoma

imaging clues in favor of PHL over HCC. PHL typically appears as hypointense on pre-contrast T1-weighted images with associated hyperintensity on T2W images. Internal heterogeneity on T2W sequence may be detected due to intralesional hemorrhage and necrosis [15]. In these patients, differentiation from an intrahepatic cholangiocarcinoma or a liver metastasis may require histopathologic confirmation. FDG-PET/CT scan may demonstrate diffuse intense FDG uptake, which is sometimes referred to as hepatic superscan [20].

Treatment options mostly include chemotherapy sometimes with the combination of surgery and radiotherapy [11, 12]. The standard treatment of diffuse large B-cell lymphoma (DLBCL) is the CHOP regimen comprised of cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin), and prednisone. The incorporation of rituximab to the CHOP regimen improves complete response rate, prolongs survival, and remission in elderly patients with DLBCL [12].

Gallbladder

Primary lymphoma of the gallbladder (PLG) is an extremely rare clinical condition defined as primary extranodal lymphoma confined to gallbladder with or without involvement of adjacent lymph nodes [21]. Slightly more than 100 cases have been reported over 40 years (between 1973 and 2013) [22]. PLGs are often mucosa-associated lymphoid tissue (MALT) lymphoma or DLBCL type, similar to those in the gastrointestinal (GI) tract. The origin of this disease is unclear as lymphoid tissue is sparse in the gallbladder mucosa. In a small case series, a potentially strong association between cholelithiasis with chronic inflammation and PLG has been reported [23]. The chronic inflammatory process leads to a continuous antigenic stimulus causing chromosomal translocation which results in lymphoid proliferation as seen in stomach. PLG usually presents with long standing right upper quadrant pain or biliary colic or signs of cholecystitis. Cholecystectomy alone in localized MALT-PLG will be curative with an excellent prognosis. DLBCL is more aggressive and a high-grade tumor with a higher tendency of dissemination [21].

US is typically the initial imaging study for gallbladder imaging. CT and MRI are usually reserved for more complex gallbladder diseases but they are also commonly employed. Diffuse or focal wall thickening in the gallbladder is the most common imaging finding in all imaging modalities (Fig. 2). High-grade lymphomas, such as DLBCL, may form a large, solid mass or may present with marked, irregular gallbladder wall thickening. Low-grade lymphomas, such as MALT-PLG may show mild gallbladder wall thickening [21]. Among the non-neoplastic processes, acute and chronic cholecystitis as well as focal and diffuse adenomyomatosis may mimic PLG. Clinical history and detection of Rokitansky–Aschoff sinuses are helpful for differential diagnosis of the latter. Among neoplastic diseases, adenocarcinoma is the most common primary malignant neoplasm of the gallbladder comprising around 96% of the primary malignancies that affect this organ [24]. Surgery is typically the way to diagnose this rare primary lymphoma but fine needle aspiration has also been reported as an alternative to diagnose the disease [25].

Spleen

Spleen is a central organ of the lymphohematogenous system. Due to this central role, it is very commonly affected by lymphoma [26]. Splenic involvement is typically a

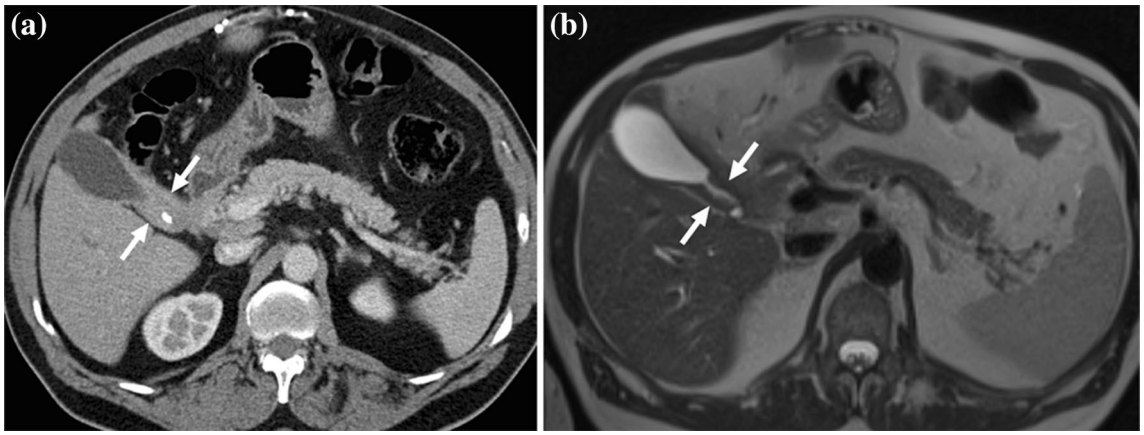

Fig. 2 50-year-old male presenting with recent onset right upper quadrant pain. **a** Axial contrast-enhanced CT image reveals concentric wall thickening in the gallbladder neck (arrows). The abdomen was otherwise unremarkable. **b** Axial T2W MR image of the same patient confirms the wall thickening (arrows). Chest CT was normal. The patient underwent surgery with a pre-operative diagnosis of gallbladder adenocarcinoma. Histopathologic examination of the cholecystectomy specimen instead showed gallbladder lymphoma

manifestation of advanced systemic disease. In contrast to its involvement in systemic lymphoma, primary splenic lymphoma (PSL) is a rare clinical entity with a reported incidence of less than 1% [27]. By definition PSL is diagnosed in patients whose disease is limited to spleen and hilar lymph nodes (without involvement of peripheral lymph nodes and bone marrow) with no recurrent disease for at least 6 months after splenectomy [28–30]. PSL is commonly seen in females and older males. It may be associated with human immunodeficiency virus (HIV) and hepatitis C infection [31]. Symptoms of PSL are usually non-specific with the most common presenting symptom is left upper quadrant pain, followed by weight loss and fever. Most of the PSLs are NHL and the most common histologic subtype is DLBCL [29, 30]. The diagnosis is classically made after splenectomy. However, more recent studies show efficacy of percutaneous biopsy in diagnosing splenic lesions [32].

Although diffuse infiltration is the most common pathological form, on imaging the typical presentation is that of a solitary solid lesion, which is at least three times more common than multifocal involvement [29, 30]. Adjacent organ invasion may be detected with enlarged lymph nodes in the splenic hilum [30]. Lesions may appear as hypodense or isodense lesions on pre-contrast CT scans. After contrast injection, lesions typically enhance less than the background splenic parenchyma. Central necrosis may also be detected in a subgroup of patients (Figs. 3 and 4). On pre-contrast T1W MR images, the lesions are typically hypointense with mild enhancement after gadolinium contrast injection, whereas they appear mostly hyperintense on T2W images [30]. Among other rare splenic tumors, littoral cell angioma and sclerosing adenomatoid nodular transformation should be considered. Presentations with non-focal splenomegaly or a miliary pattern of infiltration are extremely rare; granulomatous disease should be considered in the latter. Lymphomas present with marked FDG avidity on FDG-PET/CT [33]. Treatment options include splenectomy and immunochemotherapy [34].

Pancreas

Primary pancreatic lymphoma (PPL) is a very rare clinical entity which represents 1% of all extranodal lymphoma cases and 0.2% of primary pancreatic tumors [35]. It is seven times more common in men than women [6]. By definition, the term PPL applies when the primary bulk of the disease is located within the pancreas with lymph node involvement confined to the peri-pancreatic region without hepatic or splenic involvement [6]. In addition to this definition, diagnostic criteria defined by Behrns et al. [36] also include; normal white blood cell count, no palpable superficial lymphadenopathy, and no mediastinal nodal enlargement on chest radiography [36]. Perilesional lymph node involvement and distant disease spread may be seen but the main clinical presentation should involve the pancreatic tissue [37]. NHL is the most common type of PPL [6]. The most common presenting symptom is abdominal pain, followed by abdominal mass, weight loss, jaundice, small bowel obstruction, and diarrhea [6].

As stated above, PPL is extremely rare and most of the information providing imaging characteristics of this clinical entity is derived from anecdotal case reports. On imaging studies, pancreatic lymphoma may be localized as a well-circumscribed tumor or diffusely infiltrates the majority of the gland [6]. A unique intense FDG uptake may be encountered in PPL on FDG-PET/CT [38].

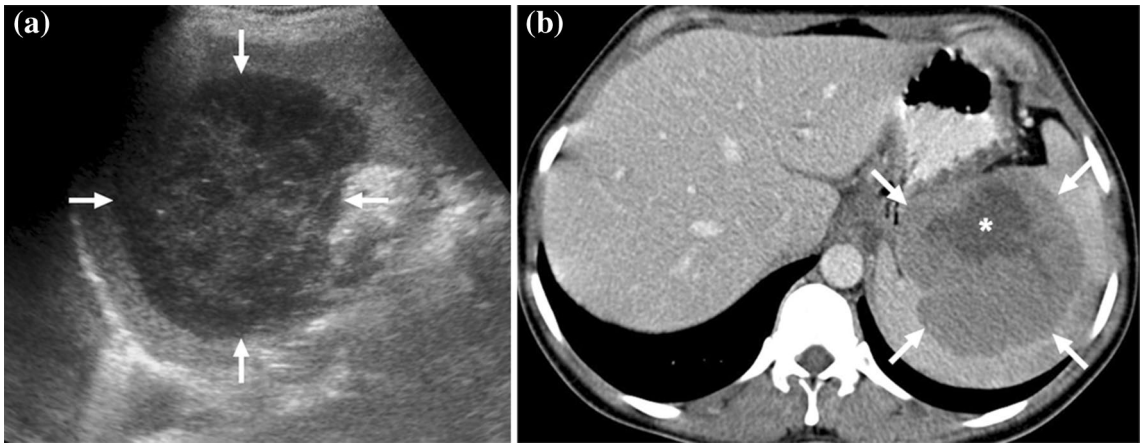

Fig. 3 35-year-old woman with no known previous medical history presented with fever, weight loss and left upper quadrant pain. **a** Abdominal US exam reveals a hypoechoic solid mass within the spleen (arrows). **b** Axial postcontrast abdominal CT image confirms the presence of the lesion (arrows). Also note the necrotic anterior portion of the mass (asterisk). Histopathologic exam confirmed diffuse large B-cell lymphoma. The subsequent PET-CT exam was negative for disease elsewhere

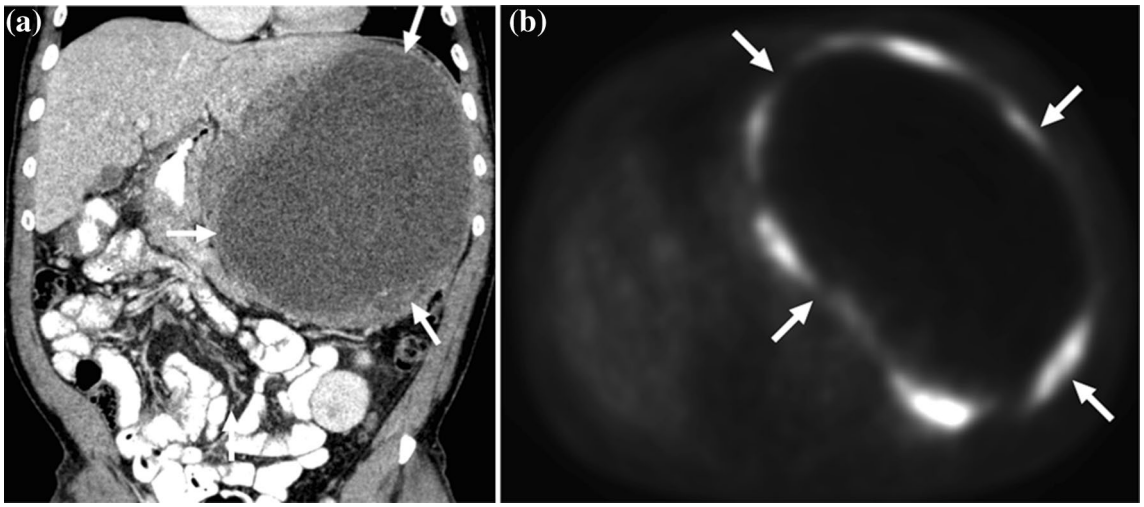

Fig. 4 54-year-old man with no significant past medical history presented with weight loss, fever and left upper quadrant pain. **a** Coronally reformatted postcontrast abdominal CT image demonstrates a large, predominantly cystic/necrotic splenic mass (arrows) almost replacing the entire splenic parenchyma. **b** Axial FDG-PET CT image demonstrates the intense FDG uptake of the peripheral part of the lesion (arrows). The other parts of the body were unremarkable. Pathologic and immunohistochemical examination of the splenectomy material confirmed primary diffuse large B-cell lymphoma

PPL is most likely to be misdiagnosed as pancreatic cancer [6]. Pancreatic adenocarcinoma is the most common primary malignant tumor of the pancreas and differentiating PPL from adenocarcinoma by imaging characteristics alone may sometimes be difficult. PPL has a higher cure rate than pancreatic adenocarcinoma [6]. In contrast to pancreatic adenocarcinomas, the majority of which tend to be located in the head, there is no specific predilection of PPL location in the pancreatic parenchyma. Vascular encasement may be seen in both clinical situations but it is usually less severe in patients with PPL as compared to adenocarcinomas. Necrotic areas or calcifications provide another diagnostic clue and exclude PPL [6, 39]. Simultaneous dilation of the pancreatic and common biliary ducts (aka, double duct sign), a very common and suggestive feature for adenocarcinoma, is relatively rare in PPL (Fig. 5) [40–43]. Consequently, imaging techniques alone cannot easily differentiate pancreatic adenocarcinoma and PPL. Therefore, the exact diagnosis of PPL is based on histopathological examination [6].

Autoimmune pancreatitis (AIP) is another important clinical entity that should be considered in differential diagnosis.

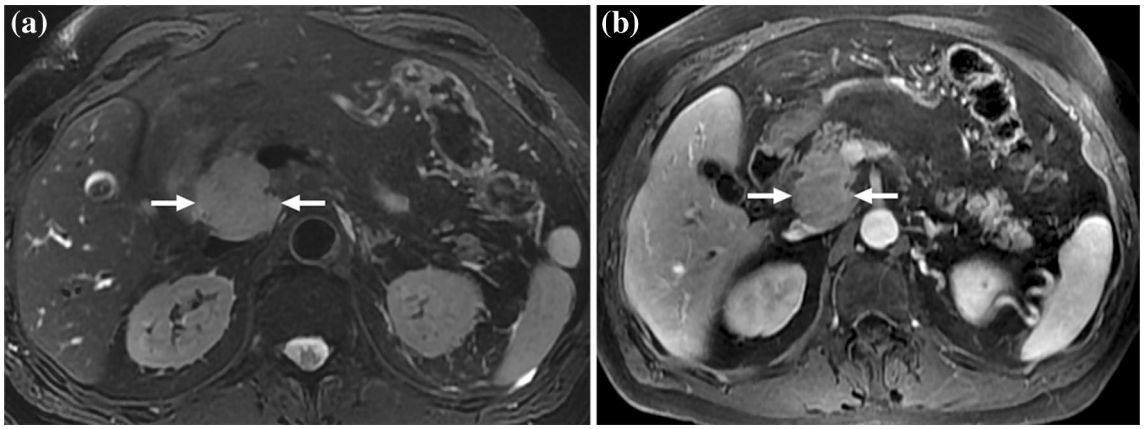

Fig. 5 75-year-old woman with recent complaints of jaundice, epigastric pain and weight loss. Preliminary US exam revealed cholelithiasis, biliary dilatation and a solid mass within the pancreatic head. **a** Axial T2W MR image demonstrates a solid, hyperintense mass with well-defined borders within the pancreatic head (arrows). **b** Postcontrast T1W MR image shows moderate enhancement of the mass. Also note the absence of pancreatic duct dilatation, which would be a characteristic finding for pancreatic adenocarcinoma. FDG-PET/CT scan demonstrated intense FDG uptake in the mass without any other site of involvement (not shown). Percutaneous image guided biopsy confirmed diffuse large B-cell lymphoma

As we mentioned before, PPL may be seen as diffuse pancreatic enlargement, infiltrating the majority of the gland with minimally dilated pancreatic duct and these imaging features may give an appearance like AIP [6]. It is important to differentiate these two entities because complete remission can be achieved with steroid treatment in AIP [44]. The parenchymal involvement is typically smaller in AIP patients but clinical symptoms are relatively less severe in contrast to PPL patients. Increased serum IgG4 level is also an important associated feature for diagnosing AIP over PPL [37, 45]. Clinical history should be considered in conjunction with imaging and serologic findings for correct diagnosis.

The treatment of PPL consists of chemotherapy or radiotherapy. Behrns et al. [36] reported the median survival of PPL patients treated by chemotherapy, radiotherapy, and combined chemoradiotherapy as 13, 22, and 26 months, respectively. Also, it has been shown that surgical resection alone is not effective in improving survival [46]. This is why definitive diagnosis with EUS-guided or percutaneous fine needle aspiration (FNA) is indicated over surgery. Therefore, the first choice for treatment of PPL should be combined chemoradiotherapy, rather than surgery [6].

Adrenal lymphoma

Adrenal glands may be involved in the course of systemic lymphoma but primary lymphoma of this gland is highly exceptional and accounts for less than 1% of all NHLs [47–50]. Primary adrenal lymphoma (PAL) is histologically proven lymphoma of one or both adrenal glands in patients with no prior history of lymphoma [49]. It is mostly a disease of elderly males, with a reported median age of 65 years [51]. Approximately 70% of the cases have bilateral involvement [49]. The most common subtype is DLBCL [52]. Epstein-Barr virus infection, genetic defects in p53 and c-kit, and immune dysregulation have been implicated in the pathogenesis of this disease [49, 53]. The diagnostic criteria for PAL is defined as histologically proven unilateral or bilateral adrenal lymphoma without involvement of other organs and lymph nodes with no signs of leukemic blood picture for at least 6 months after diagnosis [51]. Symptoms are mostly related to the mass effect of the tumor itself or due to gland dysfunction. Clinically, gland dysfunction is rare in patients with unilateral involvement as compared to bilateral involvement [47].

The disease usually manifests itself as large, bilateral solid adrenal masses that replace the adrenal glands completely (Fig. 6). The masses have typically well-defined contours even when they are large. Preservation of the typical triangular adrenal shape appears to be a common finding, an observation that can serve as a useful imaging clue [51]. Enhancement characteristics of these tumors may closely simulate other more common adrenal neoplasms and, therefore, differential diagnosis based on temporal contrast enhancement pattern on dynamic adrenal studies may not be very useful for diagnosis [51]. Bilaterality of the tumor may be helpful to differentiate primary adrenal lymphomas from primary adrenocortical cancers. Several endocrinopathies may also affect adrenal glands bilaterally. Associating clinical and serologic findings may be useful for differential diagnosis. Homogenous internal structure may be a helpful finding as both metastases and adrenocortical cancers typically have internal heterogeneity, however, primary adrenal

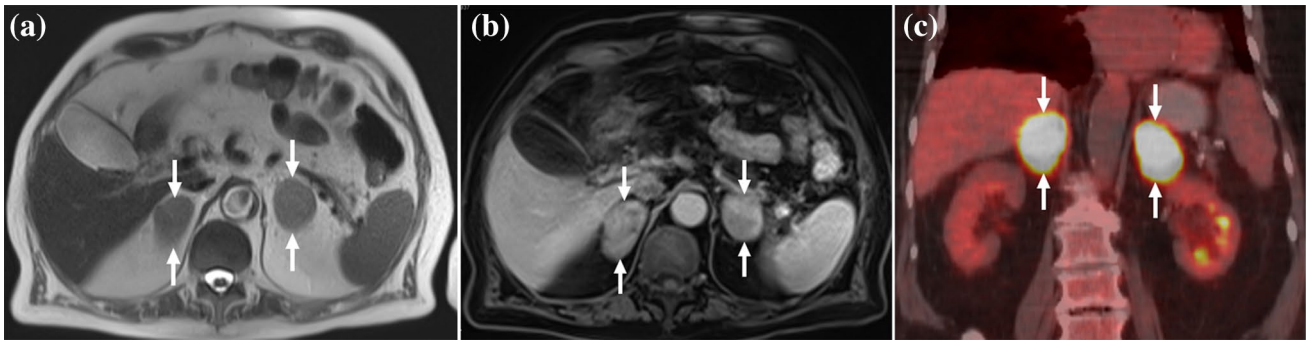

Fig. 6 81-year-old male with no significant medical history now presents with abdominal pain and fever. **a** Axial T2W MR image demonstrates solid masses within the suprarenal areas (arrows). Adrenal glands could not be visualized separately from these masses. **b** Post-contrast axial T1W MR image shows avid contrast enhancement within these solid masses (arrows). C) Coronal plane fused FDG-PET/CT image demonstrates intense FDG uptake in both masses (arrows) (SUVmax: 25.7 in left adrenal gland and SUVmax: 28.1 in right adrenal gland), highly suggestive for a malignant process. Diagnosis was confirmed as diffuse large B-cell lymphoma after percutaneous biopsy

lymphomas with internal cystic changes have also been reported [54, 55]. On MRI these tumors typically appear as hypointense/isointense on T1W images while hyperintense on T2W images [51]. FDG-PET/CT may have a decisive role with demonstration of intense FDG uptake especially in highly metabolic PALs. PET scan also has an important role in monitoring response to treatment and detecting recurrence [56]. Rituximab containing chemotherapy has been shown to increase overall survival of PAL [57].

Kidney

Renal involvement in systemic lymphoma is common but primary renal lymphoma (PRL) without evidence of disease elsewhere is rare, representing less than 1% of all extranodal lymphomas, and the first case was reported in 1980 [58, 59]. Bilateral presentation is seen in 10% to 20% of the cases [60]. PRL is most commonly seen in middle to advanced aged men [60]. As the kidneys lack a lymphoid system there is a debate that PRL whether truly exists [61]. Perirenal adipose tissue and renal capsule have been proposed as the source tissue (as they are rich in lymphatic structures) with subsequent renal extension. Chronic inflammatory and infectious processes like Sjogren's disease, systemic lupus erythematous, chronic pyelonephritis and EBV infection have been postulated to be the underlying etiology [58, 60, 62]. By definition, PRL refers to lymphomas localized to renal tissue without evidence of any other organ or lymph node involvement [62]. The most common presentation of PRL is acute renal failure, flank pain, and mass [60]. Fast recovery from renal failure after lymphoma treatment and biopsy confirmation are among the other situations that prompt diagnosis [63].

Due to rarity of PRL, imaging features could not be described thoroughly. On imaging, PRL may be seen unilaterally or in both kidneys (Fig. 7). Single or multiple masses may be seen in both kidneys and perirenal mass may also be seen. Diffuse renal enlargement without any discrete mass lesion is another presentation of the disease and renal sinus involvement is rare [58]. PRLs typically appear as large infiltrative renal masses that may extend into the retroperitoneum and the perinephric anatomic compartments. Despite their aggressive imaging appearance, extension into renal vein and inferior vena cava is rare, which may serve as a useful tip to differentiate PRL from a primary renal cell carcinoma (RCC) [64]. Urothelial cancers can also be highly aggressive tumors on imaging which may be a potential confounder. However, attentive evaluation showing the center of the mass is not within the collecting system may be useful for correct differentiation [65].

The correct differential diagnosis of PRL from RCC and transitional cell tumors is crucial as these solid tumors are mostly treated with surgery whereas PRLs may be treated by chemotherapy. Percutaneous biopsy would be crucial for differential diagnosis and patient triage. FDG-PET/CT has an important role in differentiation between PRL and RCC since renal lymphomas often exhibit avid enhancement on FDG-PET/CT in contrast to RCCs that have lower FDG uptake compared to adjacent renal parenchyma [66]. Despite the absence of a disseminated disease, the prognosis of PRL is poor [60].

Bladder

As there is no lymphoid tissue within the bladder, primary bladder lymphomas (PBL) are rare [67]. Slightly more than 100 cases have been reported in the literature [68, 69]. There

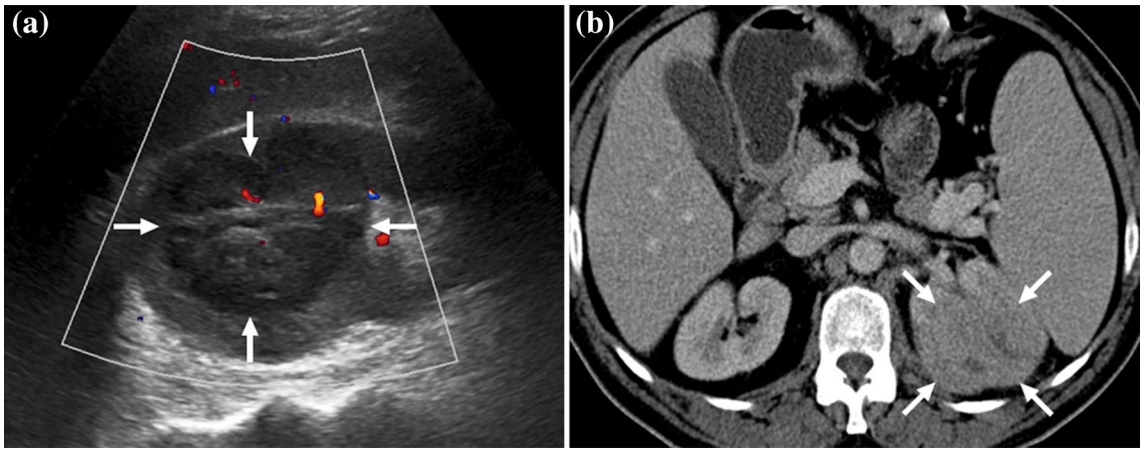

Fig. 7 63-year-old man with longstanding diabetes now presenting with gross hematuria. **a** Color flow Doppler US demonstrates well-defined, hypovascular, hypoechoic mass (arrows) with lobulated contours within the left kidney. **b** Axial postcontrast abdominal CT image of the same patient demonstrates heterogeneously enhancing mass with indistinct borders (arrows). Nephrectomy specimen revealed Epstein-Barr virus-related B-cell lymphoma

is a female predominance; and chronic cystitis has been suggested as a potential etiological factor with a documentation rate of over 20% [70–72]. PBL represents 0.2% of all extranodal NHL cases and < 1% of all bladder tumors [73]. The mean age at presentation is 64 years and the female/male ratio is 3:1, which is in contrast to male predominance of primary bladder cancer [74]. The most common presenting symptom is macroscopic hematuria [70]. Low-grade B-cell mucosa-associated lymphoid tissue (MALT) type or diffuse large B-cell type are the most common types in the PBL's reported [75]. PBL's typically appear as focal wall thickening and nodularity and diffuse infiltration of the bladder wall is unusual (Fig. 8) [76]. PBL is mostly centered in the dome or lateral walls of the urinary bladder and usually involves the submucosa without mucosal ulceration. The radiologic findings are non-specific and cannot be differentiated from other bladder neoplasms by imaging alone [74]. Definitive diagnosis is generally made by cystoscopic biopsy [73]. The prognosis is favorable as most of the tumors are of low grade and treatment can be accomplished with chemotherapy or local radiotherapy [76].

Ovary

The ovary is the most common gynecologic organ involved in both primary and secondary extranodal lymphoma [74]. Primary ovarian lymphomas (POL) represent 0.5% of all NHL and 1.5% of all ovarian neoplasms [77]. It has been proposed that the tumor originates from the lymphocytes in the vessels of the hilum or corpus luteum [78]. POL is most commonly seen in women more than 40 years of age with

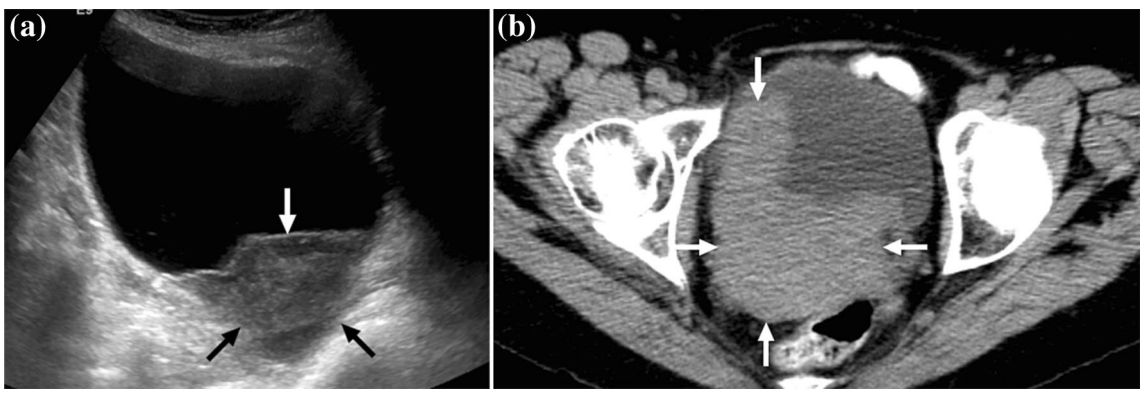

Fig. 8 81-year-old woman with hematuria and decreased urinary output. **a** Pelvic US shows a large solid mass filling the bladder base (arrows). **b** Axial postcontrast CT image demonstrates the same lesion as an avidly enhancing mass originating from the right lateral and posterior walls of the urinary bladder (arrows). Cystoscopic biopsy revealed primary Burkitt lymphoma of the urinary bladder

the mean age of 47. The most common subtype is DLBCL, followed by Burkitt lymphoma [74, 78]. Primary ovarian Burkitt lymphoma accounts for 50% of all pediatric age ovarian malignancies [79]. POL is defined as an extranodal lymphoma that is clinically confined to the ovary with no evidence of lymphoma elsewhere. There may be involvement of adjacent lymph nodes or direct infiltration to immediately adjacent structures without peripheral blood and bone marrow involvement and further extra-ovarian lesions should occur several months after the first diagnosis of POL [80]. Reactive lymphocytes may aggregate in ovary due to different ovarian disease such as endometriosis, pelvic inflammatory disease, benign and malignant lesions and follicular or surface inclusion cysts. Rarely, these reactive lymphocytes may give rise to POL. Sometimes, POL may be seen without any evidence of inflammation [78]. The histopathological features of ovarian lymphoma demonstrate diffuse malignant lymphoid cells infiltrating, but not destroying, the ovarian parenchyma and occasional areas of cystic degeneration and necrosis [74]. Although the most common presentation is abdominopelvic pain or mass, ascites and B symptoms may also be present [74, 78].

On US, typical POL's present as bilateral, hypovascular, homogenously hypoechoic, large ovarian masses always exceeding 5 cm in diameter and these findings may help to differentiate POL from primary epithelial ovarian cancers. Mild vascularity may be visualized on color Doppler US examination. CT typically shows solid, homogeneous, and hypovascular ovarian masses [74]. On MR imaging, lesions typically appear as hypovascular on pre-contrast T1W images with mild to moderate T2 hyperintensity. Postcontrast enhancement is not striking with mild to moderate contrast uptake (Fig. 9) [81]. Ascites is an inconsistent finding [74]. Implants may also be seen in POL, therefore, differential diagnosis from more common primary epithelial ovarian cancers may be difficult. Bowel segments may be encased by the primary mass [79]. The detection of enlarged pelvic lymph nodes, an unusual feature of epithelial ovarian neoplasms, is another helpful feature of POL's [82]. FDG-PET/CT shows strong uptake of FDG with high maximum standardized uptake values [83].

POL is less aggressive than secondary ovarian lymphoma [78]. The prognosis of POL is poor despite aggressive chemotherapy, with a 5-year survival rate of 57% [74]. The choice of treatment is most commonly with systemic chemotherapy [77]. Also, treatment of localized disease to one ovary may usually be achieved with unilateral surgical resection and subsequent systemic chemotherapy [78].

Uterine cervix

Primary cervical lymphomas (PCeL) represent less than 1% malignancies affecting this region [79]. The most common histologic subtype is DLBCL and the most common presenting symptom is abnormal vaginal bleeding at the age of 40 to 50 years. [74]. As initial epithelial involvement is infrequent Pap smears rarely detect this abnormality. The tumors are large at the time of diagnosis, mostly greater than 4 cm in diameter [84]. MRI is the main imaging modality for evaluating cervix with its unique soft tissue resolution. With MRI, the imaging patterns are not very different compared to much more common squamous cell carcinomas. Tumor may invade vagina, parametrium, or even the bladder [79]. On MRI, the mass appears as homogenous and relatively hypovascular after IV contrast injection. On

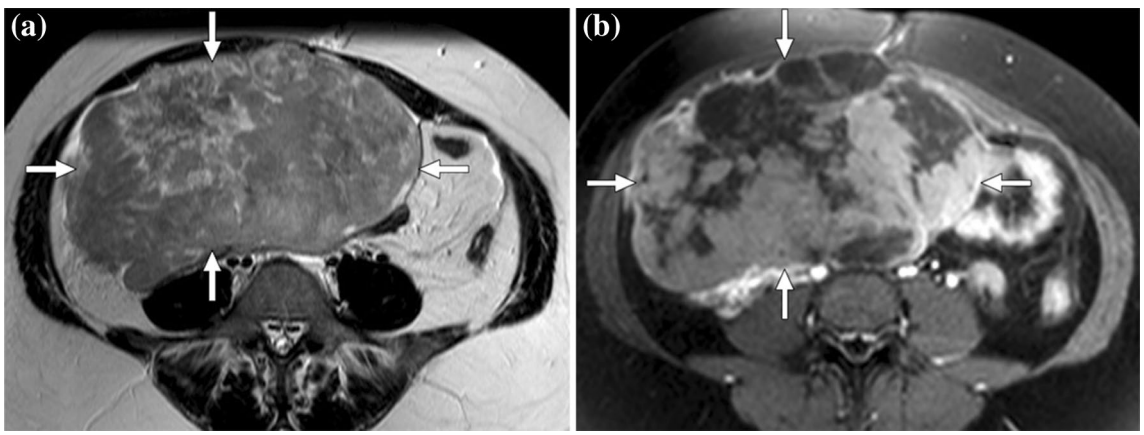

Fig. 9 34-year-old woman with no significant past medical history recently experiencing pelvic fullness and dull pain. Pelvic US exam showed a large mass with complex cystic and solid areas. **a** Axial T2W pelvic MR image reveals a large and predominantly solid pelvic mass (arrows). **b** Axial postcontrast T1W MR image demonstrates intense enhancement of the solid components of the mass (arrows). The presurgical diagnosis was malignant epithelial ovarian tumor. Surgical excision confirmed primary lymphoma of the right ovary. Postsurgical imaging studies did not reveal any involvement elsewhere in the body

pre-contrast T1W images, lesions are mostly homogenously hypointense whereas on T2W images the signal intensity of the mass is intermediately high (Fig. 10) [85, 86]. PCeLs present with increased FDG uptake on FDG-PET/CT [87]. Correct diagnosis is especially important in patients who desire to preserve fertility. For them, treatment is usually based on chemotherapy and careful observation rather than surgery [88]. The prognosis of PCeL is good, even in locally advanced disease at presentation [86].

Uterine body

Primary uterine lymphomas (PUL) are extremely rare. Less than 1% of all extranodal lymphomas arise from the uterus (both corpus and cervix). The cervix is around 10 times more commonly affected than the corpus [79]. The most common histologic subtype is DLBCL [74]. Presenting symptoms most commonly comprised of diffuse symmetric enlargement of uterus without mucosal abnormalities [79]. PULs may appear as a focal mass in the uterine corpus or as diffusely infiltrating both myometrium and endometrium (Fig. 11). As in cervix evaluation, MRI is the imaging modality of choice due its unmatched soft tissue resolution capabilities. Homogenous enlargement of the uterine body with preservation of the zonal architecture and homogenous contrast enhancement are among the key suggestive findings for correct diagnosis [79]. The absence of necrosis may be a helpful imaging feature for differentiating PULs from malignant mesenchymal tumors of the uterine body, as the latter tend to exhibit severe necrosis with marked internal heterogeneity and enhancement. However, tumoral necrosis with endometrial disruption has also been reported and this imaging finding should be regarded cautiously [89]. Preservation of endometrial-myometrial interface is a finding that may favor lymphoma over endometrial cancer. Treatment is typically based on systemic chemotherapy with or without radiation therapy [74]. The prognosis for PUL is good, with a 5-year survival rate of 67% to 100% [74].

Prostate lymphoma

Prostatic adenocarcinoma is among the most common cancers (around 90%) and other histological subtypes of prostatic cancers represent only 5 to 10%. Primary lymphoma of the prostate is even rarer, representing only 0.2 to 0.8% of extranodal lymphomas and 0.1% of all prostatic neoplasms combined. The majority of prostatic lymphomas reported in the literature are NHL. The most common histologic type is DLBCL [90]. Patients typically present with lower urinary tract symptoms, including increased frequency of urination, occasional hematuria, and acute retention. Prostate specific antigen elevation is seen in only 20% of the cases [91]. According to Bostwick et al. [92] diagnostic criteria of a primary prostate NHL were defined as first: absence of lymph node, liver, spleen, or bone marrow involvement; second: the major symptoms involve the prostate; and third: no progression of the disease in adjacent structures for at least one month from the diagnosis [92].

Due to the rarity of the disease, there is not much information in the literature on imaging characteristics. Diffusely

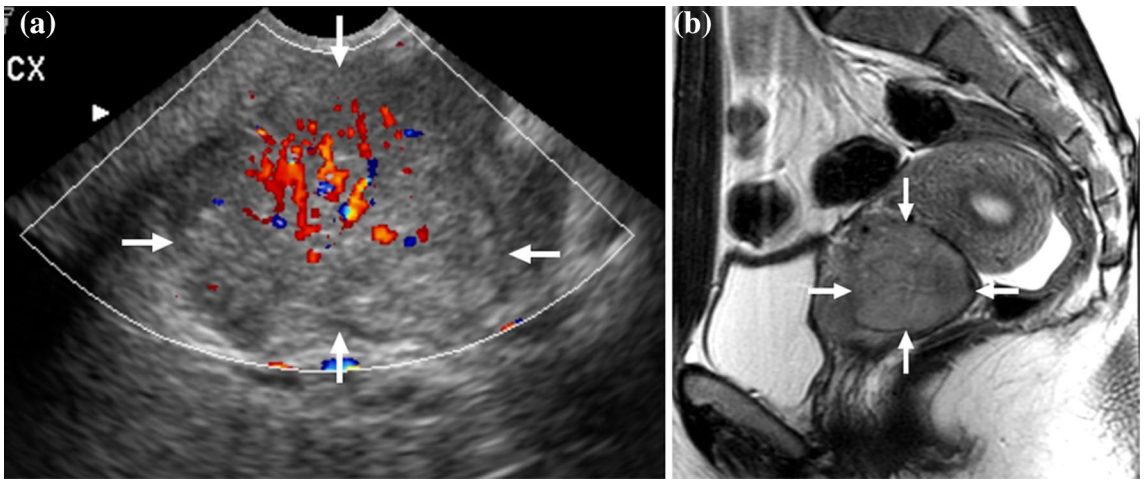

Fig. 10 34-year-old woman with no significant past medical history now complaining of pelvic fullness, postcoital bleeding and dull pain. **a** Transvaginal color Doppler US exam shows a large hypoechoic pelvic mass (arrows) with intense internal vascularity. **b** Sagittal T2W pelvic MR image shows the large, mildly hyperintense and predominantly solid cervical mass mostly located in the posterior aspect of the cervix (arrows). FDG-PET/CT scan demonstrated intense FDG uptake in the mass (not shown). Transvaginal biopsy confirmed diffuse large B-cell lymphoma. Bone marrow biopsy and PET-CT scan did not show any other site of involvement elsewhere. Two months after chemoradiotherapy follow-up MRI (not shown) confirmed total regression of the tumor

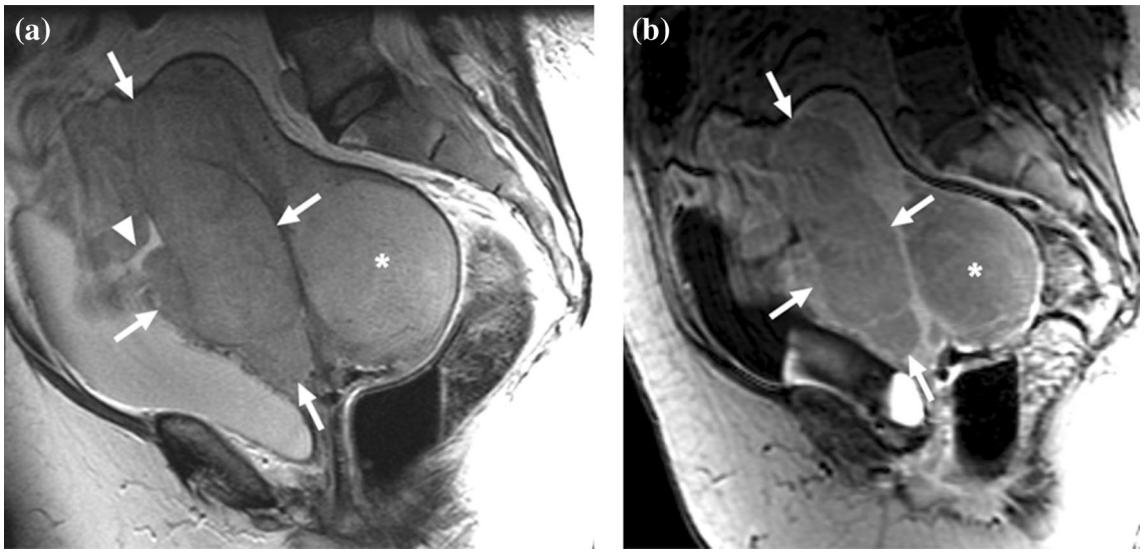

Fig. 11 67-year-old woman with no significant past medical history recently started to complain of pelvic fullness, pain and gross hematuria. **a** Sagittal T2W MR image reveals well-defined solid masses within the myometrium (arrows) and the cervix (asterisk). Both lesions are of intermediate signal intensity. Posterior wall of the urinary bladder appears to be invaded by the mass with a sinus tract forming between the mass and the bladder lumen (arrowhead). **b** Contrast-enhanced sagittal T1W image shows no significant enhancement within these masses (arrows). Cervical biopsy confirmed large B-cell lymphoma

enlarged prostate with a prostatic mass extending beyond the confines of the gland are typical findings (Fig. 12) [93]. However, it should be noted that several common and uncommon prostatic tumors present with the same imaging findings and histopathological diagnosis is almost always necessary for diagnosis. The first choice of treatment for primary prostatic lymphoma is chemotherapy [90]. The prognosis is poor, with a 5-year survival rate of 33% [74].

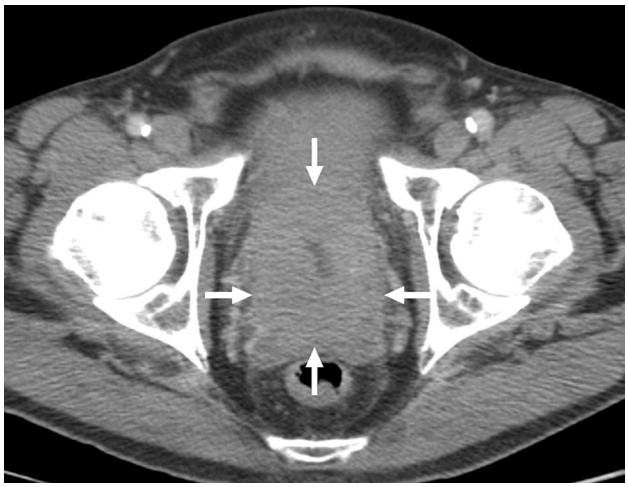

Fig. 12 73-year-old male with a primary complaint of acute onset urinary retention. Axial contrast-enhanced CT image reveals diffuse enlargement of the prostate (arrows) with homogeneous contrast enhancement. FDG-PET/CT scan demonstrated intense FDG uptake in the mass (not shown). Transrectal prostate biopsy revealed large B-cell lymphoma. Bone marrow biopsy and PET-CT scan did not show any other sites of involvement

Testis

Primary testicular lymphoma (PTL) is a rare but biologically aggressive disease. It represents less than 5% of all testicular malignancies and accounts for 1–2% of all NHL patients [94]. The median age at the time of diagnosis is 66–68 years and PTL is the most common testicular cancer in male patient population who are older than 60 years. PTL may be seen at an early age in HIV-positive patients. It is also the most common testicular tumor that simultaneously presents in both testes [74, 95, 96]. Painless testicular swelling/enlargement is the most common clinical symptom and the most common histologic type is DLBCL [74].

US is the primary and most commonly used imaging modality utilized for diagnosis. The tumor may present with either a diffusely infiltrative pattern or as focal regions of hypoechogenicity within the testicular parenchyma (Fig. 13). Differential diagnosis of PTL may be difficult as several more common benign and malignant lesions of the testes may mimic the disease.

As the PTL lesions are mostly hypervascular, color Doppler US is also commonly used for both assessing the lesion vascularity and depicting subtle lesions that may be missed on gray-scale US exam. The normal ovoid configuration of

the testis is preserved in the majority of patients [97, 98]. The testicular vessels traversing through the PTL lesions is also a very common imaging finding which may be helpful for differential diagnosis [97]. This finding is not specific for lymphoma. However, it suggests an infiltrative process and is infrequent in more common primary testicular neoplasms that present with focal parenchymal lesions. Benign infectious/inflammatory diseases may also present in an infiltrative way and in those cases histopathologic confirmation may be the only avenue for diagnosis [97]. Patient age, clinical symptomatology, diffusely infiltrative pattern on US scan in addition to bilaterality are crucial parameters that should be taken into account during the clinical decision-making process.

Inguinal orchiectomy is the first-line therapeutic approach for PTL. It provides definite diagnosis as well as removal of the primary tumor. Irradiation of the contralateral testicle, central nervous system prophylaxis, and systemic chemotherapy are also commonly added to the treatment plan. With this multimodal treatment plan the prognosis of PTL is good, with a 5-year overall survival of 87% [74].

Stomach

Primary lymphomas of the stomach (PLS) account for 1%–5% of all gastric malignancies [99]. It is the most common type of extranodal lymphoma and represents 50%–70%

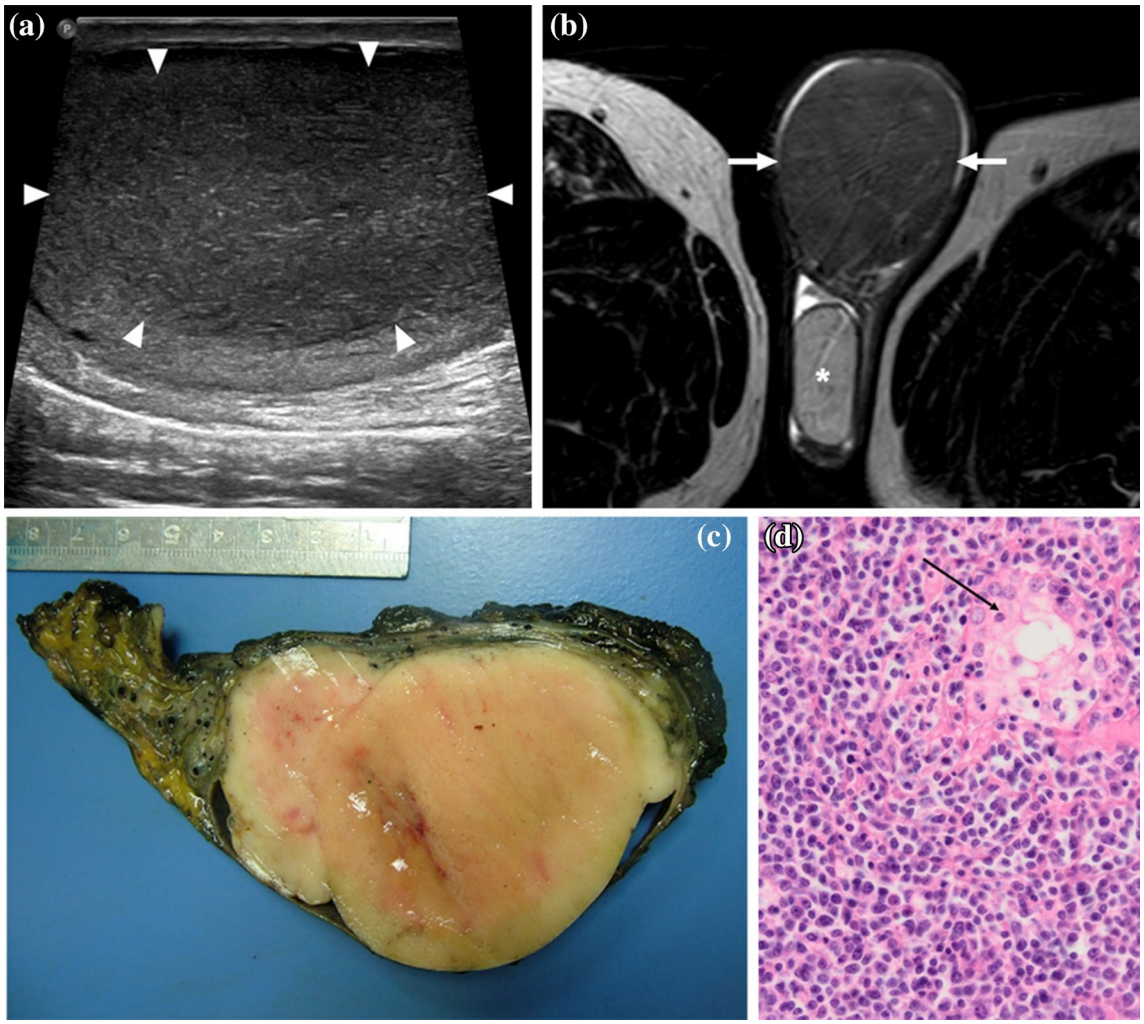

Fig. 13 72-year-old man with no significant medical history presenting with painless left sided testicular enlargement. **a** Testicular US demonstrates ill defined, hypoechoic, heterogenous mass lesion (arrowheads), almost completely replacing the right testicular parenchyma. **b** T2W MR image demonstrates diffuse low signal intensity of the testis secondary to tumor involvement (arrows). Note normal appearing left testis (asterisk). Pathologic examination of the orchiectomy material revealed diffuse large B-cell lymphoma of the testis. **c** Macroscopic image of the testis lymphoma. Note homogenous cream-colored nodular tumor with fish flesh appearance. **d** High power magnification demonstrates large atypical lymphoid cells with irregular nuclear borders and multiple nucleoli. There are entrapped seminiferous tubules (arrow)

of all primary gastrointestinal lymphomas [100]. The predominant histological subtypes of PLS are DLBCL and marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) [101, 102].

PLSs primarily originate as low-grade MALT lymphomas and subsequently degenerate into intermediate or high-grade large cell lymphoma, if diagnosis is delayed [103]. Early diagnosis and treatment allow a much better prognosis (between 75 and 91% 5-year survival) than high-grade MALT lymphomas (less than 50% 5-year survival) [103]. Chronic Helicobacter pylori gastritis is a well-known risk factor for low-grade MALT lymphomas. HIV infection, celiac disease, inflammatory bowel disease, and immunosuppression have also been associated with PLS [104]. The most common symptoms of PLS consist of epigastric pain, nausea, vomiting, weight loss, and GI bleeding [102].

On cross-sectional imaging, diffuse gastric wall thickening is the most common feature (Fig. 14). The magnitude of wall thickening correlates well with the increasing grade of lymphomas. The same direct correlation also holds true for the presence of abdominal lymphadenopathy [105, 106]. The absence of abnormality on CT examination was found to be highly predictive for a low-grade MALT lymphoma over its high-grade counterparts [105].

The differential diagnosis from more common gastric adenocarcinoma may be difficult. The preservation of perigastric fat planes even in the presence of extensive wall thickening is a common feature in PLSs. The luminal pliability is preserved even in the most advanced cases and gastric outlet obstruction is exceptional [107]. Linitis plastica type gastric adenocarcinoma may be extremely difficult to differentiate from PLSs. Transpyloric spread is not a commonly encountered imaging finding in gastric adenocarcinomas, as compared to PLSs, but this feature may be deceptive and should be considered only as suggestive of PLS [108]. Lymphadenopathy is common in both clinical conditions; however, the extension of enlarged lymph nodes below the renal hila and detection of confluent lymph nodes are more suggestive of lymphoma [100]. FDG-PET/CT is useful in both detecting PLS as well as differentiating PLS from non-lymphomatous gastric cancers [109]. Overall prognosis and treatment options of PLS depend on the histologic subtype and stage of the disease. There are many treatment options for PLS, including antibiotic therapy for H pylori eradication, immunotherapy, chemotherapy, and radiation therapy [104].

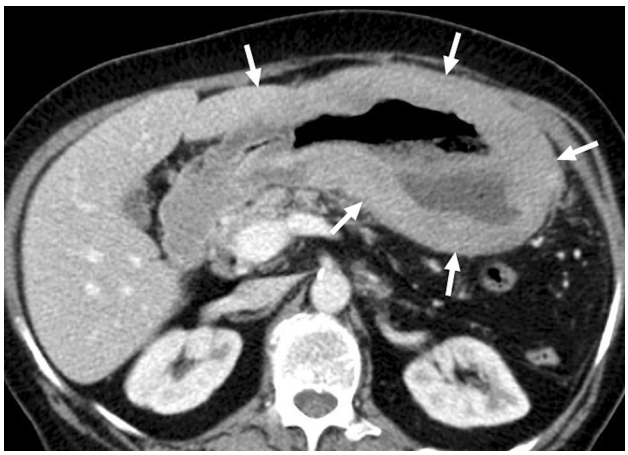

Fig. 14 80-year-old woman with weight loss, nausea, and epigastric pain. Axial postcontrast CT image demonstrates extensive, homogenous, diffuse wall thickening of the stomach (arrows) without any apparent perigastric lymph nodes or implants. Endoscopic biopsy revealed diffuse large B-cell lymphoma

Small bowel

As opposed to other intraabdominal solid organs and hollow viscus, primary lymphoma of the small bowel (PLSB) is the most common malignancy of small bowel segments [110]. Distal ileum is the most common site for PLSB, thought to be due to presence in this segment of relatively more extensive lymphoid tissue [111]. Most of the lymphomas involving the GI tract are NHL and they are usually of B-cell origin [111]. The diagnostic criteria of primary GI lymphoma defined by Dawson et al. [112], include absence of superficial palpable lymph nodes, normal chest x-ray and blood count, absence of hepatic and splenic involvement, and involvement of the GI tract and lymph nodes (if any) confined to the drainage area of the involved segment [112].

On cross-sectional imaging, the tumor most commonly appears as a circumferential mass in the bowel wall with pronounced local tumor extension into adjacent organs, bowel segments, and the mesentery (Fig. 15). Long segments of bowel may be involved and bowel perforation and ulceration may also be detected. Aneurysmal dilation of the involved small bowel segments is common and may be observed in 31% of small bowel lymphomas [113]. Bowel obstruction is rare, as compared to small bowel adenocarcinomas due to weak desmoplastic reaction within lymphomatous masses. In patients with T-cell lymphoma multifocal segmental involvement and perforation is more common [100]. With the developments in technique, CT and MR enterography are being more commonly used in diagnosis and staging [113].

Large bowel

Primary lymphoma of the colon (PLC) is rare, much less common than colonic adenocarcinomas. PLC represents 0.4% of all tumors involving colon; colorectal lymphomas account for 6–12% of GI lymphomas [114]. Most PLCs are

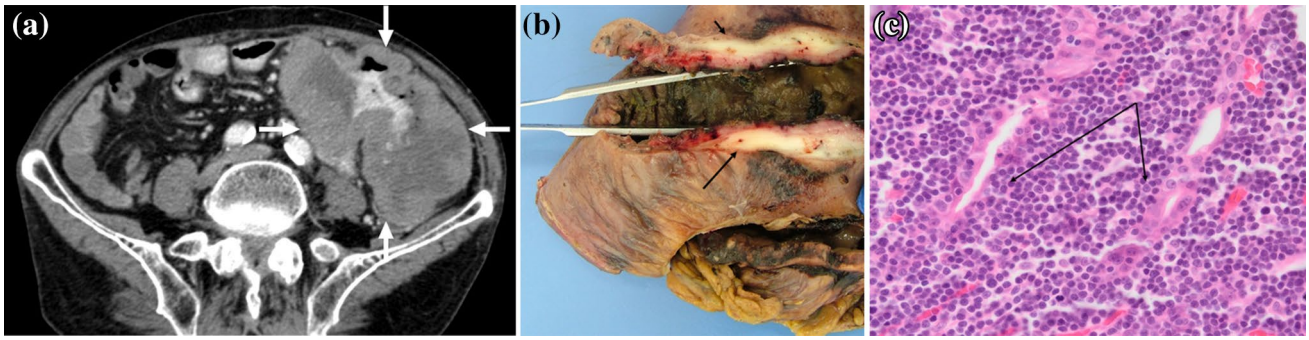

Fig. 15 59-year-old woman with diabetes and coronary heart disease now presenting with weight loss and diarrhea. The physical exam was positive for a palpable mass in left lower quadrant. **a** Postcontrast axial plane abdominal CT image demonstrates a large mass encircling a jejunal loop in the left lower quadrant (arrows). The chest and abdominal CT scans were otherwise negative for any associated disease. **b** Cut surface demonstrates diffuse thickening of the bowel wall with a cream-colored homogenous infiltrate (arrows). **c** High power magnification shows monotonous small-medium sized lymphoid cells which were found to be positive with CD2 and CD56 (arrows show residual intestinal glands). Findings were found to be consistent for monomorphic epitheliotropic intestinal T-cell lymphoma

non-Hodgkin lymphomas, usually of B-cell origin [100]. Cecum and rectum are more commonly affected than the other colonic segments [115]. In patients with cecal involvement intussusception may also occur (Fig. 16) [100]. Symptoms are generally non-specific, including change in bowel habit, abdominal pain, weight loss, rectal bleeding, and diarrhea. Diagnostic criteria include lymphoproliferative neoplasm confined to the colon and regional lymph nodes without distant lymph node involvement and the absence of involvement in abdominal organs and bone marrow [114]. Bowel obstruction is again uncommon when compared to patients with colonic adenocarcinoma due to relatively less severe desmoplastic reaction and weakening of the muscularis propria due to lymphoid infiltration.

PLCs typically appear as localized, large diameter masses with significant extraluminal extension. This imaging appearance may be seen in colonic adenocarcinomas as well but lymphomatous masses tend to be more voluminous and affect longer segments of the colon than do adenocarcinomas. Aneurysmal dilation of the affected bowel segment with ulcerative fistulas may also be detected [105]. Absence of extension into adjacent organs, relatively preserved pericolonic fat planes, and absence of bowel obstruction in the presence of disproportionately large colonic wall mass are other helpful imaging hints that favor PLC [100]. Extension into the terminal ileum without invasion of adjacent anatomic structures, in patients with cecal PLCs, is another sign that favors PLC over colonic adenocarcinoma [116].

Conclusion

Primary lymphomas of intraabdominal organs are very rare and initial consideration of this diagnosis, let alone confident diagnosis, may be extremely difficult. Clinical suspicion on the part of the radiologist is the most critical step to correct diagnosis. A timely alert to the clinical care team may prevent potentially unnecessary surgical interventions and organ loss. All cross-sectional imaging modalities, including US, CT, and MRI, often in conjunction with FDG-PET, may be liberally used, both separately or together, for diagnosis and staging.

Primary lymphomatous involvement in abdominal organs is usually detected on US. However, CT and/or MRI are usually required to depict primary abdominal visceral lymphomas by revealing absence of involvement in other organs, bone marrow and distant lymph nodes. FDG-PET/CT has an important role in the diagnosis and follow-up of primary lymphomas as well as posttreatment surveillance. FDG-PET/CT has shown to be more accurate in detecting extranodal sites of lymphoma involvement which were missed on CT study [8]. However, the FDG uptake intensity in primary lymphomas depends on many factors, including histologic type (Hodgkin disease versus NHL), grade (indolent versus aggressive NHL), tumor cell proliferation, viable tumor cell fraction, upregulation of glucose metabolism, local perfusion, and the presence of hypoxia [8].

Selection of the proper modality for relevant clinical indications is ultimately the responsibility of the imaging specialist. Despite the fact that non-invasive diagnosis without histopathologic confirmation appears to be a difficult, complex task, several imaging hints, provided in the above manuscript, may be helpful for imagers. Ultimately, consistent consideration of a differential diagnosis that includes lymphoma where appropriate will give the radiologist the best chance to contribute positively to the patient's care.

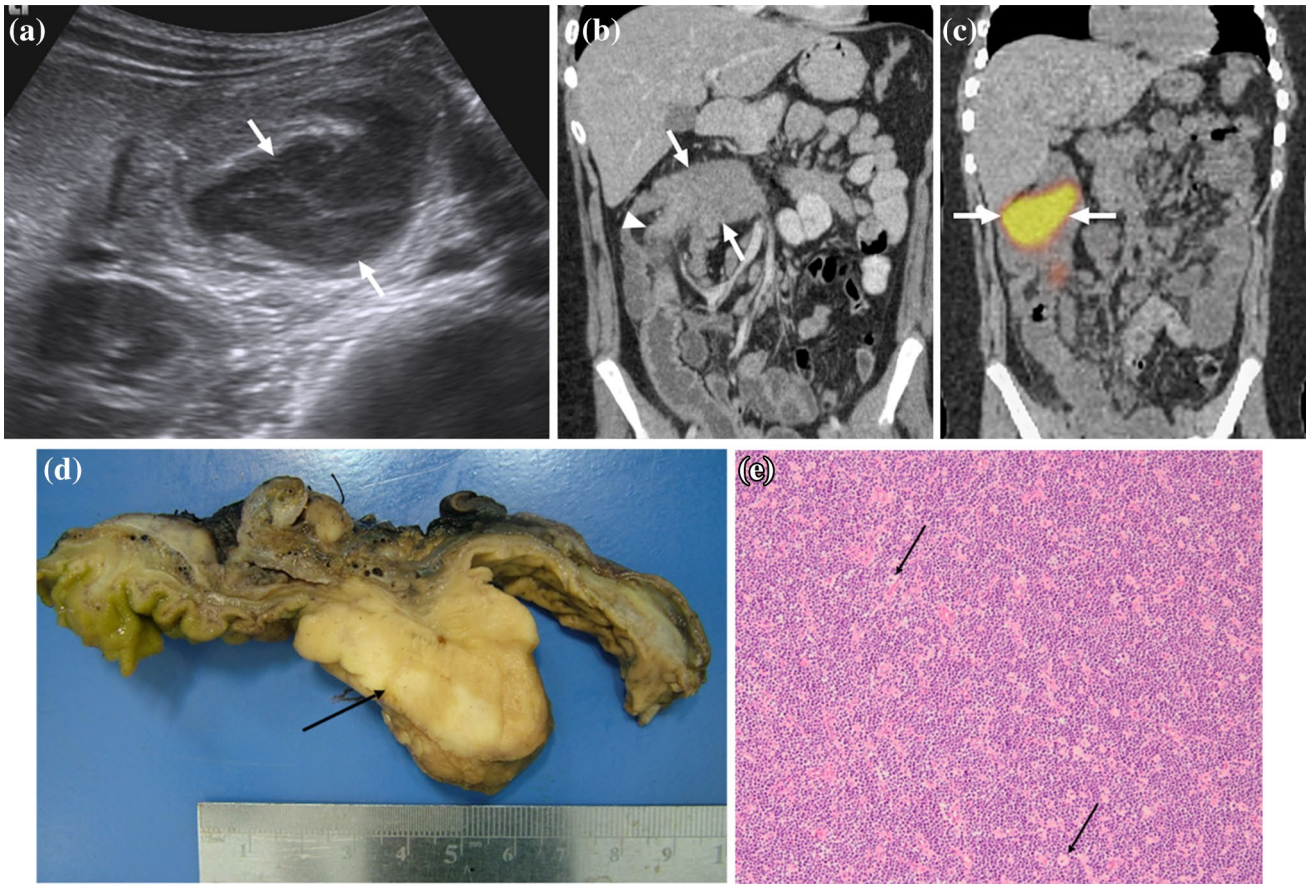

Fig. 16 15-year-old male with sudden onset abdominal pain and palpable mass in the right upper and lower quadrants. **a** Abdominal US exam shows a hypoechoic mass (arrows) in the right upper quadrant located medial to the liver. **b** Coronally reformatted CT image shows long segment ileocecal invagination (arrowhead) with significant colonic wall thickening (arrows). **c** Coronal fused FDG-PET/CT images shows hypermetabolic activity (arrows) with high FDG avidity (SUVmax: 25) in the thickened wall of the colon. **d** Macroscopic examination reveals a nodular cream-colored mass protruding into the lumen and infiltrating the colon wall (arrow). **e** Low power H&E histologic section reveals a lymphoid neoplasm diffusely infiltrating the colon wall. There is a "starry-sky" pattern due to abundance of "tingible-body" macrophages, two of which are marked by arrows, engulfing apoptotic debris. Immunohistochemistry demonstrated CD20 positivity. Findings were found to be consistent with Burkitt lymphoma. Postsurgical PET-CT study did not reveal any secondary foci of disease

References

1. Guermazi, A., et al., *Extranodal Hodgkin disease: spectrum of disease.* Radiographics, 2001. **21**(1): p. 161-79.
2. Leite, N.P., et al., *Cross-sectional imaging of extranodal involvement in abdominopelvic lymphoproliferative malignancies.* Radiographics, 2007. **27**(6): p. 1613-34.
3. Fajardo, L., et al., *Abdominal manifestations of extranodal lymphoma: pictorial essay.* Radiol Bras, 2016. **49**(6): p. 397-402.
4. Lee, W.K., et al., *Abdominal manifestations of extranodal lymphoma: spectrum of imaging findings.* AJR Am J Roentgenol, 2008. **191**(1): p. 198-206.
5. Kwee, T.C., R.A. Nievelstein, and D.A. Torigian, *Role of Structural Imaging in Lymphoma.* PET Clin, 2012. **7**(1): p. 1-19.
6. Baysal, B., et al., *Primary pancreatic lymphoma: A rare cause of pancreatic mass.* Oncol Lett, 2015. **10**(3): p. 1701-1703.
7. Ansell, S.M. and J.O. Armitage, *Positron emission tomographic scans in lymphoma: convention and controversy.* Mayo Clin Proc, 2012. **87**(6): p. 571-80.
8. Paes, F.M., et al., *FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease.* Radiographics, 2010. **30**(1): p. 269-91.
9. Lei, K.I., *Primary non-Hodgkin's lymphoma of the liver.* Leuk Lymphoma, 1998. **29**(3-4): p. 293-9.
10. Page, R.D., et al., *Primary hepatic lymphoma: favorable outcome after combination chemotherapy.* Cancer, 2001. **92**(8): p. 2023-9.
11. Ugurluer, G., et al., *Primary Hepatic Lymphoma: A Retrospective, Multicenter Rare Cancer Network Study.* Rare Tumors, 2016. **8**(3): p. 6502.
12. Masood, A., et al., *Primary non-Hodgkin lymphoma of liver.* Curr Oncol, 2009. **16**(4): p. 74-7.
13. Ryan, J., et al., *Primary lymphoma of the liver.* Cancer, 1988. **61**(2): p. 370-5.
14. Rajesh, S., et al., *The imaging conundrum of hepatic lymphoma revisited.* Insights Imaging, 2015. **6**(6): p. 679-92.
15. Maher, M.M., et al., *Imaging of primary non-Hodgkin's lymphoma of the liver.* Clin Radiol, 2001. **56**(4): p. 295-301.

16. Noronha, V., et al., *Primary non-Hodgkin's lymphoma of the liver.* Crit Rev Oncol Hematol, 2005. **53**(3): p. 199-207.
17. Chalamalasetty, S.B., et al., *Anaplastic large cell lymphoma presenting as liver abscess and portal vein thrombosis.* Indian J Cancer, 2009. **46**(3): p. 240-1.
18. Takeuchi, N. and K. Naba, *Primary hepatic lymphoma is difficult to discriminate from a liver abscess.* Case Rep Gastrointest Med, 2014. **2014**: p. 925307.
19. Tomasian, A., et al., *Hematologic malignancies of the liver: spectrum of disease.* Radiographics, 2015. **35**(1): p. 71-86.
20. Mahajan, S., et al., *Detection of Diffuse Infiltrative Primary Hepatic Lymphoma on FDG PET-CT: Hallmarks of Hepatic Superscan.* World J Nucl Med, 2016. **15**(2): p. 142-4.
21. Pezzuto, R., et al., *An Unusual Case of Primary Extranodal Lymphoma of the Gallbladder.* Hematol Rep, 2017. **9**(1): p. 6972.
22. Ayub, A., et al., *Primary Non-Hodgkin's Lymphoma of the Gallbladder: A Population-based Analysis.* Anticancer Res, 2017. **37**(5): p. 2581-2586.
23. Mani, H., et al., *Gall bladder and extrahepatic bile duct lymphomas: clinicopathological observations and biological implications.* Am J Surg Pathol, 2010. **34**(9): p. 1277-86.
24. Willen, R. and H. Willen, *Primary sarcoma of the gallbladder. A light and electronmicroscopical study.* Virchows Arch A Pathol Anat Histol, 1982. **396**(1): p. 91-102.
25. Yamamoto, T., et al., *Primary non-Hodgkin's lymphoma of the gallbladder.* AJR Am J Roentgenol, 2005. **184**(3 Suppl): p. S86-7.
26. Giovagnoni, A., C. Giorgi, and G. Goteri, *Tumours of the spleen.* Cancer Imaging, 2005. **5**: p. 73-7.
27. Ahmann, D.L., et al., *Malignant lymphoma of the spleen. A review of 49 cases in which the diagnosis was made at splenectomy.* Cancer, 1966. **19**(4): p. 461-9.
28. Dasgupta, T., B. Coombes, and R.D. Brasfield, *Primary Malignant Neoplasms of the Spleen.* Surg Gynecol Obstet, 1965. **120**: p. 947-60.
29. Dachman, A.H., et al., *Primary non-Hodgkin's splenic lymphoma.* Clin Radiol, 1998. **53**(2): p. 137-42.
30. Li, M., et al., *Imaging findings of primary splenic lymphoma: a review of 17 cases in which diagnosis was made at splenectomy.* PLoS One, 2013. **8**(11): p. e80264.
31. Khalid, S., et al., *Primary Splenic Diffuse Large B-Cell Lymphoma: A Rare Case of Massive Splenomegaly and Thrombocytopenia.* Cureus, 2018. **10**(7): p. e3026.
32. Tessier, D.J., et al., *Laparoscopic splenectomy for splenic masses.* Surg Endosc, 2008. **22**(9): p. 2062-6.
33. Thipphavong, S., et al., *Nonneoplastic, benign, and malignant splenic diseases: cross-sectional imaging findings and rare disease entities.* AJR Am J Roentgenol, 2014. **203**(2): p. 315-22.
34. Byrd, K.P., et al., *Multi-Database Description of Primary Splenic Diffuse Large B-Cell Lymphoma.* Anticancer Res, 2017. **37**(12): p. 6839-6843.
35. Yu, L., Y. Chen, and L. Xing, *Primary pancreatic lymphoma: two case reports and a literature review.* Onco Targets Ther, 2017. **10**: p. 1687-1694.
36. Behrns, K.E., M.G. Sarr, and J.G. Strickler, *Pancreatic lymphoma: is it a surgical disease?* Pancreas, 1994. **9**(5): p. 662-7.
37. Flejou, J.F., *[WHO Classification of digestive tumors: the fourth edition].* Ann Pathol, 2011. **31**(5 Suppl): p. S27-31.
38. Abe, Y., et al., *Unique intense uptake demonstrated by (18) F-FDG positron emission tomography/computed tomography in primary pancreatic lymphoma: A case report.* Oncol Lett, 2010. **1**(4): p. 605-607.
39. Boninsegna, E., et al., *CT imaging of primary pancreatic lymphoma: experience from three referral centres for pancreatic diseases.* Insights Imaging, 2018. **9**(1): p. 17-24.
40. Boninsegna, E., et al., *Pancreatic duct stenosis: Differential diagnosis between malignant and benign conditions at secretin-enhanced MRCP.* Clin Imaging, 2017. **41**: p. 137-143.
41. Fujinaga, Y., et al., *MR features of primary and secondary malignant lymphoma of the pancreas: a pictorial review.* Insights Imaging, 2013. **4**(3): p. 321-9.
42. Mortele, K.J., et al., *Multimodality imaging of pancreatic and biliary congenital anomalies.* Radiographics, 2006. **26**(3): p. 715-31.
43. Swerdlow, S.H., et al., *The 2016 revision of the World Health Organization classification of lymphoid neoplasms.* Blood, 2016. **127**(20): p. 2375-90.
44. Meng, Q., et al., *Diagnosis and Treatment of Autoimmune Pancreatitis in China: A Systematic Review.* PLoS One, 2015. **10**(6): p. e0130466.
45. Negrelli, R., et al., *Pancreatic duct abnormalities in focal autoimmune pancreatitis: MR/MRCP imaging findings.* Eur Radiol, 2015. **25**(2): p. 359-67.
46. Lin, H., et al., *Primary pancreatic lymphoma: report of six cases.* World J Gastroenterol, 2006. **12**(31): p. 5064-7.
47. Aziz, S.A., et al., *Primary adrenal lymphoma: Differential involvement with varying adrenal function.* Indian J Endocrinol Metab, 2011. **15**(3): p. 220-3.
48. Choi, C.H., et al., *Non-Hodgkin's lymphoma of the adrenal gland.* Arch Pathol Lab Med, 1990. **114**(8): p. 883-5.
49. Rashidi, A. and S.I. Fisher, *Primary adrenal lymphoma: a systematic review.* Ann Hematol, 2013. **92**(12): p. 1583-93.
50. Venizelos, I., D. Tamiolakis, and G. Petrakis, *High grade primary adrenal intravascular large B-cell lymphoma manifesting as Addison disease.* Rev Esp Enferm Dig, 2007. **99**(8): p. 471-4.
51. Zhou, L., et al., *Primary adrenal lymphoma: radiological; pathological, clinical correlation.* Eur J Radiol, 2012. **81**(3): p. 401-5.
52. Ichikawa, S., et al., *Clinicopathological analysis of primary adrenal diffuse large B-cell lymphoma: effectiveness of rituximab-containing chemotherapy including central nervous system prophylaxis.* Exp Hematol Oncol, 2013. **2**(1): p. 19.
53. Grigg, A.P. and J.M. Connors, *Primary adrenal lymphoma.* Clin Lymphoma, 2003. **4**(3): p. 154-60.
54. Kato, H., et al., *MR imaging of primary adrenal lymphoma.* Clin Imaging, 1996. **20**(2): p. 126-8.
55. Lee, F.T., Jr., et al., *MR imaging of adrenal lymphoma.* Abdom Imaging, 1993. **18**(1): p. 95-6.
56. Radhakrishnan, R.K., et al., *Unilateral Primary Adrenal Lymphoma: Uncommon Presentation of a Rare Disease Evaluated Using (18)F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography.* World J Nucl Med, 2018. **17**(1): p. 46-48.
57. Ram, N., et al., *Primary adrenal non-Hodgkin lymphoma: a case report and review of the literature.* J Med Case Rep, 2017. **11**(1): p. 108.
58. Ganeshan, D., et al., *Imaging of primary and secondary renal lymphoma.* AJR Am J Roentgenol, 2013. **201**(5): p. W712-9.
59. Coggins, C.H., *Renal failure in lymphoma.* Kidney Int, 1980. **17**(6): p. 847-55.
60. Bokhari, M.R. and S.R.A. Bokhari, *Cancer, Renal Lymphoma*, in *StatPearls*. 2019, StatPearls Publishing LLC.: Treasure Island (FL).
61. Kandel, L.B., et al., *Primary renal lymphoma. Does it exist?* Cancer, 1987. **60**(3): p. 386-91.
62. Shetty, S., A.C. Singh, and V. Babu, *Primary Renal Lymphoma - A Case Report and Review of Literature.* J Clin Diagn Res, 2016. **10**(9): p. Xd05-xd07.
63. Malbrain, M.L., et al., *Acute renal failure due to bilateral lymphomatous infiltrates. Primary extranodal non-Hodgkin's lymphoma (p-EN-NHL) of the kidneys: does it really exist?* Clin Nephrol, 1994. **42**(3): p. 163-9.

64. Wagner, J.R., S.C. Honig, and M.B. Siroky, *Non-Hodgkin's lymphoma can mimic renal adenocarcinoma with inferior vena caval involvement.* Urology, 1993. **42**(6): p. 720-3; discussion 723-4.
65. Sawa, N., et al., *Renal intravascular large B-cell lymphoma localized only within peritubular capillaries. Report of a case.* Intern Med, 2007. **46**(10): p. 657-62.
66. Karaosmanoglu, A.D., et al., *Role of multimodality imaging in the diagnosis of lymphoproliferative malignancies and hematologic disorders of the kidneys.* Abdom Radiol (NY), 2017. **42**(1): p. 242-253.
67. Wong-You-Cheong, J.J., et al., *From the Archives of the AFIP: neoplasms of the urinary bladder: radiologic-pathologic correlation.* Radiographics, 2006. **26**(2): p. 553-80.
68. Taheri, M.R., et al., *Multifaceted genitourinary lymphoma.* Curr Probl Diagn Radiol, 2008. **37**(2): p. 80-93.
69. Tasu, J.P., et al., *Primary malignant lymphoma of the urinary bladder: report of three cases and review of the literature.* Eur Radiol, 2000. **10**(8): p. 1261-4.
70. Hughes, M., A. Morrison, and R. Jackson, *Primary bladder lymphoma: management and outcome of 12 patients with a review of the literature.* Leuk Lymphoma, 2005. **46**(6): p. 873-7.
71. Ohsawa, M., et al., *Malignant lymphoma of bladder. Report of three cases and review of the literature.* Cancer, 1993. **72**(6): p. 1969-74.
72. Suzuki, T., T. Matsumura, and I. Ito, *Intravesical mass consisting of mucosa-associated lymphoid tissue.* Int J Urol, 2004. **11**(11): p. 1028-30.
73. Kuhn, N.C.a.A., *Case Report about a Primary Bladder Lymphoma.* International Archives of Urology and Complications, 2017. **3**(3).
74. Rohena-Quinquilla, I.R., G.E. Lattin, Jr., and D. Wolfman, *Imaging of Extranodal Genitourinary Lymphoma.* Radiol Clin North Am, 2016. **54**(4): p. 747-64.
75. Bates, A.W., A.J. Norton, and S.I. Baithun, *Malignant lymphoma of the urinary bladder: a clinicopathological study of 11 cases.* J Clin Pathol, 2000. **53**(6): p. 458-61.
76. Dahm, P. and J.E. Gschwend, *Malignant non-urothelial neoplasms of the urinary bladder: a review.* Eur Urol, 2003. **44**(6): p. 672-81.
77. Kumar, N., et al., *Primary ovarian lymphoma: a case report and review of literature.* J Obstet Gynaecol India, 2014. **64**(1): p. 65-7.
78. Bhartiya, R., et al., *Primary Non-Hodgkin's Lymphoma of the Ovary - A Case Report.* J Clin Diagn Res, 2016. **10**(5): p. Ed10-1.
79. Onyiuke, I., A.B. Kirby, and S. McCarthy, *Primary gynecologic lymphoma: imaging findings.* AJR Am J Roentgenol, 2013. **201**(4): p. W648-55.
80. Fox, H., et al., *Malignant lymphoma presenting as an ovarian tumour: a clinicopathological analysis of 34 cases.* Br J Obstet Gynaecol, 1988. **95**(4): p. 386-90.
81. Ferrozzi, F., et al., *Non-Hodgkin lymphomas of the ovaries: MR findings.* J Comput Assist Tomogr, 2000. **24**(3): p. 416-20.
82. Trenhaile, T.R. and M.A. Killackey, *Primary pelvic non-Hodgkin's lymphoma.* Obstet Gynecol, 2001. **97**(5 Pt 1): p. 717-20.
83. Komoto, D., et al., *A case of non-hodgkin's lymphoma of the ovary: usefulness of 18F-FDG PET for staging and assessment of the therapeutic response.* Ann Nucl Med, 2006. **20**(2): p. 157-60.
84. Muntz, H.G., et al., *Stage IE primary malignant lymphomas of the uterine cervix.* Cancer, 1991. **68**(9): p. 2023-32.
85. Dang, H.T., et al., *Primary lymphoma of the cervix: MRI findings with gadolinium.* Magn Reson Imaging, 1991. **9**(6): p. 941-4.
86. Thyagarajan, M.S., M.J. Dobson, and A. Biswas, *Case report: appearance of uterine cervical lymphoma on MRI: a case report and review of the literature.* Br J Radiol, 2004. **77**(918): p. 512-5.
87. Bural, G.G., et al., *FDG-PET is useful in staging and follow-up of primary uterine cervical lymphoma.* Clin Nucl Med, 2007. **32**(9): p. 748-50.
88. Johnston, C., et al., *Conservative management of primary cervical lymphoma using combination chemotherapy: a case report.* Gynecol Oncol, 1989. **35**(3): p. 391-4.
89. Cheong, I.J., S.H. Kim, and C.M. Park, *Primary uterine lymphoma: a case report.* Korean J Radiol, 2000. **1**(4): p. 223-5.
90. Petrakis, G., et al., *Primary prostatic lymphoma with components of both diffuse large B-cell lymphoma (DLBCL) and MALT lymphoma.* Hippokratia, 2012. **16**(1): p. 86-9.
91. Taleb, A., et al., *Primary lymphoma of the prostate treated with rituximab-based chemotherapy: a case report and review of the literature.* Cases J, 2009. **2**: p. 8875.
92. Bostwick, D.G., et al., *Malignant lymphoma involving the prostate: report of 62 cases.* Cancer, 1998. **83**(4): p. 732-8.
93. Chang, J.M., et al., *Pictorial review: Unusual tumours involving the prostate: radiological-pathological findings.* Br J Radiol, 2008. **81**(971): p. 907-15.
94. Moller, M.B., F. d'Amore, and B.E. Christensen, *Testicular lymphoma: a population-based study of incidence, clinicopathological correlations and prognosis. The Danish Lymphoma Study Group, LYFO.* Eur J Cancer, 1994. **30A**(12): p. 1760-4.
95. Cheah, C.Y., A. Wirth, and J.F. Seymour, *Primary testicular lymphoma.* Blood, 2014. **123**(4): p. 486-93.
96. Vitolo, U., A.J. Ferreri, and E. Zucca, *Primary testicular lymphoma.* Crit Rev Oncol Hematol, 2008. **65**(2): p. 183-9.
97. Bertolotto, M., et al., *Grayscale and color Doppler features of testicular lymphoma.* J Ultrasound Med, 2015. **34**(6): p. 1139-45.
98. Johnson, S., M. Feldman, and V. Krishnamurthi, *Primary testicular lymphoma.* J Urol, 2015. **193**(1): p. 315-6.
99. Gossios, K., P. Katsimbri, and E. Tsianos, *CT features of gastric lymphoma.* Eur Radiol, 2000. **10**(3): p. 425-30.
100. Ghai, S., et al., *Primary gastrointestinal lymphoma: spectrum of imaging findings with pathologic correlation.* Radiographics, 2007. **27**(5): p. 1371-88.
101. Koch, P., et al., *Treatment results in localized primary gastric lymphoma: data of patients registered within the German multicenter study (GIT NHL 02/96).* J Clin Oncol, 2005. **23**(28): p. 7050-9.
102. Wang, Y.G., et al., *Clinical characteristics and prognostic factors of primary gastric lymphoma: A retrospective study with 165 cases.* Medicine (Baltimore), 2016. **95**(31): p. e4250.
103. Yoo, C.C., et al., *Gastric mucosa-associated lymphoid tissue lymphoma: radiographic findings in six patients.* Radiology, 1998. **208**(1): p. 239-43.
104. Juárez-Salcedo, L.M., et al., *Primary Gastric Lymphoma, Epidemiology, Clinical Diagnosis, and Treatment.* Cancer Control, 2018. **25**(1): p. 1073274818778256.
105. Choi, D., et al., *Gastric mucosa-associated lymphoid tissue lymphoma: helical CT findings and pathologic correlation.* AJR Am J Roentgenol, 2002. **178**(5): p. 1117-22.
106. Park, M.S., et al., *Radiographic findings of primary B-cell lymphoma of the stomach: low-grade versus high-grade malignancy in relation to the mucosa-associated lymphoid tissue concept.* AJR Am J Roentgenol, 2002. **179**(5): p. 1297-304.
107. Ciftci, A.O., et al., *Gastric lymphoma causing gastric outlet obstruction.* J Pediatr Surg, 1996. **31**(10): p. 1424-6.
108. Cho, K.C., et al., *Transpyloric spread of gastric tumors: comparison of adenocarcinoma and lymphoma.* AJR Am J Roentgenol, 1996. **167**(2): p. 467-9.
109. Davis, B.S., T.A. Thompson, and E.A. Wolin, *18F-FDG PET/CT Imaging of Primary Gastric Lymphoma.* J Nucl Med Technol, 2016. **44**(4): p. 263-264.
110. Serour, F., et al., *Primary neoplasms of the small bowel.* J Surg Oncol, 1992. **49**(1): p. 29-34.

111. Levine, M.S., et al., *Non-Hodgkin's lymphoma of the gastrointestinal tract: radiographic findings.* AJR Am J Roentgenol, 1997. **168**(1): p. 165-72.
112. Dawson, I.M., J.S. Cornes, and B.C. Morson, *Primary malignant lymphoid tumours of the intestinal tract. Report of 37 cases with a study of factors influencing prognosis.* Br J Surg, 1961. **49**: p. 80-9.
113. Lo Re, G., et al., *Radiological Features of Gastrointestinal Lymphoma.* Gastroenterol Res Pract, 2016. **2016**: p. 2498143.
114. Lee, H.J., et al., *Primary colorectal lymphoma: spectrum of imaging findings with pathologic correlation.* Eur Radiol, 2002. **12**(9): p. 2242-9.
115. Dodd, G.D., *Lymphoma of the hollow abdominal viscera.* Radiol Clin North Am, 1990. **28**(4): p. 771-83.
116. Beaton, C., M. Davies, and J. Beynon, *The management of primary small bowel and colon lymphoma–a review.* Int J Colorectal Dis, 2012. **27**(5): p. 555-63.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.