Abdominal sarcoidosis: cross-sectional imaging findings

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ABSTRACT

Sarcoidosis is a multisystem inflammatory disease of unknown etiology. The lungs and the lymphoid system are the most commonly involved organs. Extrapulmonary involvement is reported in 30% of patients, and the abdomen is the most common extrapulmonary site with a frequency of 50%-70%. Although intra-abdominal sarcoidosis is usually asymptomatic, its presence may affect the prognosis and treatment options. The lesions are less characteristic and may mimic neoplastic or infectious diseases such as lymphoma, diffuse metastasis, and granulomatous inflammation. The liver and spleen are the most common abdominal sites of involvement. Sarcoidosis of the gastrointestinal system, pancreas, and kidneys are extremely rare. Adenopathy which is most commonly found in the porta hepatis, exudative ascites, and multiple granulomatous nodules studding the peritoneum are the reported manifestations of abdominal sarcoidosis. Since abdominal sarcoidosis is less common and long-standing, unrecognized disease can result in significant morbidity and mortality. Imaging contributes to diagnosis and management of intra-abdominal sarcoidosis. In this report we reviewed the cross-sectional imaging findings of hepatobiliary, gastrointestinal, and genitourinary sarcoidosis.

Sarcoidosis is a multisystemic inflammatory disease of unknown etiology. It is characterized by noncaseating epithelioid cell granulomas in the absence of other granulomatous diseases such as tuberculosis, fungal infections, autoimmune processes, or delayed-type hypersensitivity reaction to foreign antigens (1). Epidemiology of the disease varies among racial groups. The global prevalence is reported to be 2–60 per 100,000 people (2). Higher rates are detected in people of Scandinavian and Irish descent (2).

Sarcoidosis is usually diagnosed between 20 and 40 years of age (3). Women are more frequently affected than men (3). The etiology of the disease is still not exactly clarified. The lungs and the lymphoid system are the most commonly involved sites with a frequency of 90% and 30%, respectively (4). Extrapulmonary involvement of sarcoidosis is reported in 30% of patients and the abdomen is the most common extra-thoracic site with a frequency of 50%-70%. Liver (50%-80%), spleen (40%-80%), lymph nodes (30%), and kidney are frequently involved abdominal sites, sometimes without symptoms. Cardiopulmonary involvement is the main cause of death.

Diagnosis of sarcoidosis is based upon clinical features and demonstration of noncaseating granulomas in at least two different organs. A negative staining and culture for acid fast bacilli, exclusion of drug-induced disease and exposure to toxins are also included in the diagnostic criteria. The overall prognosis is good, although most patients would have permanent organ impairment. Corticosteroids and steroid-sparing agents such as methotrexate, azathioprine, and anti-TNF-α are instituted for immunosuppressive treatment when major organs are involved or organ function is threatened.

Abdominal sarcoidosis can occur in the absence of lymphatic or pulmonary disease (4). Although usually asymptomatic, the presence of symptomatic abdominal involvement may affect the prognosis and treatment options. Symptomatic abdominal sarcoidosis requires treatment with immunosuppressant agents. Surgical interventions may be required in the presence of gastrointestinal complications such as massive hemorrhage, strictures, obstruction, or perforation. Splenectomy can be performed for symptomatic relief in splenic involvement or as prophylaxis for splenic rupture.

The lesions in abdominal sarcoidosis are less characteristic, mimicking more common neoplastic or infectious diseases such as lymphoma, diffuse metastasis, granulomatous or mycobacterial infections (5). Furthermore, it is reported that a significant fraction (26%) of subjects may have hepatic sarcoidosis without pulmonary involvement (6). In this article we aimed to review the imaging manifestations of abdominal sarcoidosis.
Liver and biliary tract

Hepatic involvement of sarcoidosis follows lymph nodes and lung in frequency. It has been reported in 50%–79% of patients by biopsy, and 67%–70% in autopsy series (7). Despite this common hepatic involvement, the frequency of liver function test abnormalities is about 35% (8). Liver biopsy is the only way to make a definitive diagnosis of hepatic involvement (4). Less than 5% of patients with sarcoidosis suffer from symptomatic liver disease.

Hepatomegaly is the most common imaging finding of hepatic sarcoidosis, detected on computed tomography (CT) of the abdomen in about more than half of the patients (9). It is often associated with splenomegaly. Other findings range from asymptomatic incidental granulomas becoming more confluent with increasing size, to portal hypertension and cirrhosis because of chronic inflammation, granuloma formation, and fibrosis in the portal triads. Focal nodules are seen in the range of 0%–19% (10–12). Another frequent complication of hepatic sarcoidosis is the portal vein thrombosis as a result of stasis from obliterated small portal veins (13). It has also been proposed that there is a correlation between chronic hepatic sarcoidosis and hepatocellular carcinoma (14).

Granulomatous inflammation of the gallbladder or extrinsic compression of the cystic duct by enlarged lymph nodes may lead to acute cholecystitis (15). Subacute or chronic cholecystitis due to granulomas in the gallbladder wall has also been reported as a complication of biliary sarcoidosis (16). Granulomatous involvement of the common hepatic duct and accompanying enlarged granulomatous lymph nodes are reported leading to obstructive jaundice (17). Sarcoidosis may cause strictures in extrahepatic bile ducts mimicking cholangiocarcinoma. Several case series have implied that, there is an association between sarcoidosis and sclerosing cholangitis (18).

Ultrasonography (US) findings of hepatic sarcoidosis include increased parenchymal echogenicity and coarsening of the parenchymal appearance with or without discrete nodules (Fig. 1) (19). Calcification can rarely be seen if the disease is long-standing (19). The nodules which represent the coalescence of small granulomas are typically innumerable, diffusely distributed, and range from 1–2 mm to several centimeters in size. They have been reported to be hypoechoic on US and hypodense on CT scans, relative to the liver parenchyma (Fig. 2) (19). However, they may also be hyperechoic depending on background liver echogenicity and the degree of fibrosis present in the granuloma. Because of these nonspecific imaging findings, tissue biopsy may be necessary to differentiate hepatic sarcoidosis from metastases and lymphoma (20). Focal nodules are identified in 5% of patients at imaging examinations (Fig. 3) (21). Contour irregularity of the shrinking liver became prominent within three years (Fig. 4) (19).

On MRI, nodular lesions of 5–20 mm are characteristically hypointense on all sequences which are most apparent on the T2-weighted fat-saturated images (Fig. 5a) (22). This finding helps excluding metastases and inflammatory diseases which are usually hyperintense on T2-weighted fat-saturated images. They enhance less than the background liver on gadolinium-enhanced T1-weighted images (Fig. 5b) (22). Contour irregularity of the liver...
and high periportal signal intensity are
the other reported MRI findings of he-
patic sarcoidosis (19).

Spleen
Splenic involvement has been re-
ported in 24%–53% of cases (23). Splen-
omegaly due to sarcoidosis is com-
monly associated with involvement of
the lungs and the liver. Splenic in-
filtration can be homogeneous or in
the form of multiple discrete nodules
(24, 25). Splenic nodules can be seen in
15% of the abdominal CT scans and are
more common than the hepatic
nodules (21). The differential diagno-
sis of hypodense nodules in both liver
and spleen includes tuberculosis, lym-
phoma, metastasis, and abscess. Infec-
tions such as candidiasis should also be
considered if the patient is immu-
nocompromised.

Similar to hepatic nodules, the
splenic nodules are seen as multiple,
hypoechoic, hypodense, hypointense,
and nonenhancing lesions, scattered
in the spleen (Figs. 6, 7a). They tend to
be discrete, but may coalesce as they
increase in size (22). Contour irregu-
larity is another abnormal finding of
splenic sarcoidosis (Fig. 7b) (19).

Gastrointestinal tract
Gastrointestinal (GI) tract involve-
ment in sarcoidosis is extremely rare
and the majority of the cases are as-
ymptomatic. On autopsy series, about
10% of patients with systemic sarcoid-
osis were found to have gastric gran-
ulomatous mucosal infiltration, most
commonly in the antrum (26). Dif-
ferential diagnosis of gastrointestinal
sarcoidosis includes Crohn’s disease, carcinoma,
foreign body reactions, intestinal tu-
berculosis, Whipple’s disease, and
celiac disease. Elevated angiotensin
converting enzyme levels, superficial
mucosal involvement instead of trans-
mural inflammation, absence of peri-
anal disease, fistulas, or strictures may
favor the diagnosis of sarcoidosis (32).
Sigmoid colon is the most frequently
involved site of large bowel (27). Col-
orectal sarcoidosis can occur despite
the presence of a grossly normal appear-
ing mucosa. Multiple nodules, polyps,
aphthous erosions, ulcers, obstructive
lesions, or stenosis are the imaging
findings of manifest colonic sarcoidosis
(Fig. 8) (33–36). External compression by
fibrosis due to granulomatous infiltra-
tion, widespread mucosal thickening,
rigidity, and reduction in lumen size
have been reported (26–28). Antral nar-
rowing and deformity owing to gastric
mucosal fold enlargement may lead to
gastric outlet obstruction mimicking
Menetrier’s disease (29, 30). The most
common imaging finding of upper GI
involvement is a segmental linitis plastica-
type appearance which should be dif-
ferentiated from gastric carcinoma (29).
Extrinsic compression from extensively
enlarged retroperitoneal lymph nodes
may also occur throughout the GI tract.
Small bowel is the least common site
of involvement in GI sarcoidosis (27).
Reported manifestations of intestinal
sarcoidosis include intestinal obstruc-
tion due to extrinsic compression by
enlarged mesenteric and abdominal
lymph nodes or reduction of the lu-
men size secondary to cicatrizing con-
striction of mucosal granulomatous
lesions (Fig. 8) (4, 31). Differential
diagnosis of small bowel sarcoidosis
includes Crohn’s disease, carcinoma,
Whipple’s disease, and celiac disease.
enlarged lymph nodes is the most common reason of intestinal obstruction.

Sarcoidosis has been reported to be one of the causes of noninfectious granulomatous appendicitis, along with foreign body reaction and Crohn’s disease. A markedly enlarged, unopacified appendix of soft tissue density, larger than that is seen in “simple acute appendicitis” and indistinguishable walls may be the findings on CT (Fig. 9). The absence of fat stranding or periappendiceal fluid and the presence of enlarged lymph nodes in a subject with distended appendix should alert radiologists for the possibility of a granulomatous appendicitis, carcinoma, or lymphoma (37).

Peritoneum and lymph nodes
Peritoneal involvement is extremely rare in sarcoidosis (38, 39). The most frequent clinical presentations of peritoneal sarcoidosis are exudative ascites, multiple granulomatous nodules studying the peritoneum, or a single peritoneal lesion (Fig. 8). Peritoneal biopsy is required to rule out carcinomatosis, tuberculosis, and fungal infections (4, 31). Symptoms usually regress without any treatment or with short-term treatment of corticosteroids (39).

Enlarged lymph nodes are detected in approximately 30% of patients particularly in the porta hepatitis, para-aortic region, and the celiac axis (9, 21). Unlike lymphoma, the lymph nodes are typically smaller than 2 cm in diameter and more discrete rather than confluent. Compared to lymphoma, involvement of the retrocral area is less common (9). Affected lymph nodes show soft tissue attenuation on CT.
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(Fig. 10). They appear homogenously hyperintense or may resemble central hypointensity surrounded by peripheral high signal intensity on T2-weighted fat-saturated images. They are mildly enhanced on gadolinium-enhanced T1-weighted images (40).

Pancreas
Pancreatic sarcoidosis has been detected in 1%–3% of cases with systemic disease on autopsy series. It may lead to symptoms such as abdominal pain, nausea and vomiting, weight loss, and obstructive jaundice; however, it is rarely symptomatic during life (41). Sarcoidosis of pancreas may be in the form of direct tissue infiltration, duct obstruction, or constrictive peripancreatic lymphadenopathy. Tissue infiltration has been reported to be diffusely nodular in about half of the cases (42). In the other half, a focal pancreatic mass is seen usually in the head of the pancreas; this mass mimics pancreatic cancer and requires surgical resection for differential diagnosis (Fig. 12) (42). However, cholangiograms typically show a long, smoothly tapered narrowing rather than the more abrupt termination associated with tumor (43).

On CT scans, pancreatic sarcoidosis manifests as solitary ill-defined pancreatic masses, dilatation of the common bile duct and pancreatic duct, or peripancreatic lymphadenopathy. On MRI, T1-weighted images show multiple hypointense masses, T2-weighted images show mildly elevated signal intensity, and gadolinium-based intravenous contrast administration shows reduced enhancement compared to normal pancreas (44).

Kidney
Nephrocalcinosis, nephrolithiasis, and interstitial calcium deposition which may lead to renal failure have been reported in sarcoidosis. Interstitial nephritis is a possible manifestation, and may demonstrate a striated nephrogram on contrast-enhanced CT (45). The most frequently detected effect of sarcoidosis on the kidney is nephrocalcinosis. It results from hypercalcemia and hypercalciuria secondary to production of calcitriol typically by the extrarenal granulomata (20, 46). In the presence of nephrocalcinosis, corticosteroids are used in addition to management of hypercalcemia and hypercalciuria.

Direct granulomatous involvement of the kidneys is rarely observed; however, it is indistinguishable from lymphoma or metastasis (47). Glomerular nephritis from direct infiltration may also occur, although it usually does not impair renal function (46).
Granulomatous pseudotumors are exceedingly rare presentations of renal sarcoidosis with only a few pathologically-proven case reports (48, 49). These pseudotumors are focal, exophytic nodules which may be singular or multiple, unilateral or bilateral and echogenic on US (42). They may be hypo-, iso-, or hyperdense on unenhanced CT relative to the normal renal parenchyma, and but are hypo-enhancing on contrast-enhanced CT (Fig. 13) (48–50). On MRI, poor circumscivation of the mass or masses from the renal parenchyma is demonstrated, indicating interstitial infiltration. On unenhanced T1- and T2-weighted imaging, the pseudotumor may be homogenous or slightly heterogenous, predominantly remaining isointense to the surrounding renal parenchyma (48–50). There is less early and delayed enhancement relative to the normal renal cortex following gadolinium-based intravenous contrast administration (46). Although renal carcinoma, metastasis, lymphoma, xantogranulomatous pyelonephritis, angiomyolipoma, and oncocytoma are included in the differential diagnosis of such focal renal lesions, the clinical history of sarcoidosis and involvement of other organs would prevent unnecessary surgical interventions for the diagnosis.

Genital tract

The diagnosis of genital tract sarcoidosis was made on surgical specimens in previously reported cases. Uterus is the most commonly involved site of the female genital system (51). It is usually detected while investigating the cause of abnormal uterine bleeding in patients with a previous history of sarcoidosis at other anatomic sites (52). Ovarian sarcoidosis is extremely rare and known to mimic ovarian malignancy with soft tissue nodules (51). There is no specific radiological finding in the literature to describe ovarian sarcoidosis (51).

Sarcoidosis involving the male reproductive tract has rarely been reported. Granulomas may be detected in the epididymis, testis, and prostate gland, in order of decreasing frequency. Spermatic cord, scrotum, and penis are rarely involved (53, 54). Testicular (Fig. 14) and extratesticular (Figs. 15, 16) involvement need to be differentiated from other granulomatous diseases such as tuberculosis, syphilis, Wegener’s granulomatosis, granuloma inguinale, lymphogranuloma venereum, filariasis, coccidioidomycosis, blastomycytosis, actinomycosis, and schistosomiasis (55). The lesions are hypoechoic on US and generally hypointense on T2-weighted images. They exhibit enhancement on gadolinium-enhanced T1-weighted images (56). Open testicular biopsy needs to be performed to exclude malignancy, on account of coexisting testicular tumors reported with sarcoidosis (57–59).

Conclusion

Sarcoidosis is a multisystemic inflammatory disease which has been reported in every system and organ of the human body. Abdominal sarcoidosis is less common and most often asymptomatic. It may mimic more common infectious diseases or neoplasms. Awareness of the imaging findings of intra-abdominal sarcoidosis would help to prevent long-standing unrecognized disease.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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