

# Sarcoidosis Masquerading as Pancreatic Cancer

by Ngozi Okoro, Christina Moldovanyi, Mohammed Wehbi and Kimil Obideen

**Sarcoidosis of the pancreas is a rare disease. Its clinical presentation is often similar to pancreatic cancer. We present a case of pancreatic sarcoidosis feared to be pancreatic cancer along with a discussion of the gastrointestinal manifestations of sarcoidosis. The patient presented with a pancreatic head mass encasing the celiac artery that was discovered incidentally on CT scan. She had elevated total bilirubin and positive tumor markers and her PET scan was consistent with metastatic pancreatic cancer. The patient had an exploratory laparotomy with multiple biopsies from the liver, pancreas and lymph nodes, which were all consistent with sarcoidosis. She was treated with steroids with good response.**

## CASE REPORT

**A** 49-year-old African American woman with no past medical history was referred to the surgery clinic for a pancreatic head mass. This lesion was discovered incidentally on a computed tomography (CT) scan of the abdomen which was done as part of her evaluation in the emergency room of an outside hospital following a motor vehicle collision. Prior to presentation in the clinic she complained of mild intermittent pruritis and abdominal discomfort. She was otherwise healthy. At the outside hospital, she had a CT guided biopsy of the mass which was negative for malignant cells. She was referred to our institution for further evaluation and possible pancreatoduodenectomy (Whipple procedure). Physical examination was unremarkable. Her laboratory studies were significant for alkaline phosphatase of 1040 U per liter, total

bilirubin of 1.5 mg per deciliter, alanine aminotransferase of 237 U per liter, aspartate aminotransferase of 206 U per liter, CA 19-9 of 130 U per milliliter, calcium of 9.7 mg per deciliter, and albumin of 3.4 g per deciliter. Antinuclear antibodies, anti-smooth muscle antibodies, and antimitochondrial antibodies were negative. The remainder of her laboratory analysis was within normal limits.

Abdominal CT scan (Figure 1) revealed intrahepatic ductal dilatation and a soft tissue density within the gallbladder fossa extending along the head of the pancreas and the celiac axis. An irregular low density area was noted at the head of the pancreas and calcified gallstones were visualized as well. Endoscopic retrograde cholangiopancreatography (ERCP) was performed and revealed dilated intrahepatic ducts with a stricture in the hilum (Figure 2). A stent was placed to relieve the obstruction. Brushings were sent for cytology and ultimately were negative. A surgical consultation advised that the patient was not a surgical candidate for excision, as the CT showed that the mass was encasing the celiac artery. A repeat abdominal CT scan with biopsy was performed and the biopsy was

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### A CASE TO REMEMBER



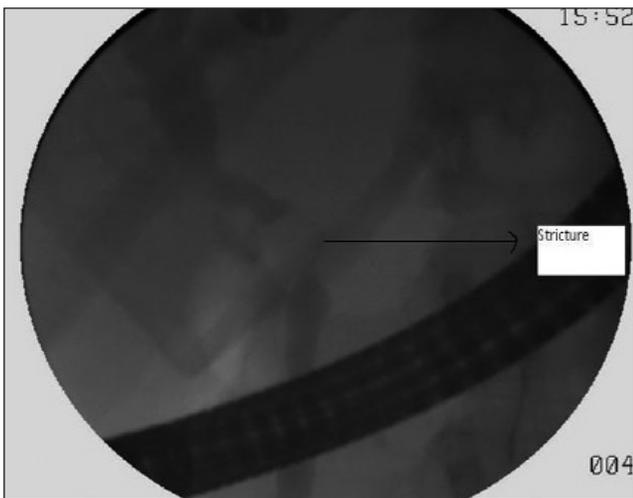
Sarcoidosis presenting as pancreatic head mass.



The mass encasing celiac artery.

**Figure 1.** Abdominal CT.

again negative for malignant cells. A positron emission tomography (PET) scan was obtained and it revealed hypermetabolic Fluro-deoxy-glucose (FDG) uptake in the pancreatic head mass, in the left lobe of the liver and in the medial gastric wall (Figure 3). These findings, along with the positive CA 19-9, were



**Figure 2.** ERCP showing stricture in the hilum with dilated intrahepatic ducts.

consistent with metastatic pancreatic cancer. The oncology service was consulted and they requested tissue diagnosis before initiating chemotherapy.

The patient underwent an exploratory laparoscopy which revealed two small lesions in the left lateral sector of the liver and a very hard head of the pancreas. The procedure was complicated with bleeding from the pancreas after biopsy. A decision was made to convert to an open laparotomy with abdominal exploration and biopsy of the hepatic hilum lymph nodes, wedge biopsy of the liver, and multiple biopsies of the pancreas with hemostatic suture of the pancreas. All pathologic specimens revealed chronic granulomatous inflammation with non-caseating granulomas (Figure 4).

These findings were consistent with sarcoidosis versus a granulomatous infection such as tuberculosis. All tissue cultures (bacterial, mycobacterial, and fungal) and AFB stains were negative.

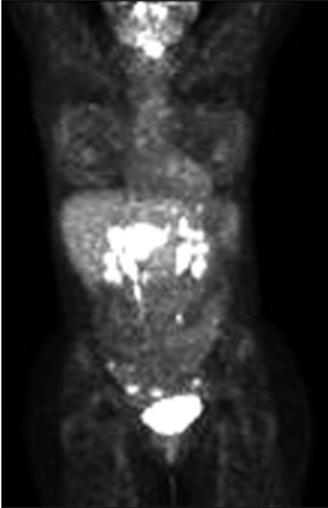
The patient had a normal chest CT scan, negative purified protein derivative (PPD), and a normal bronchoscopy with unremarkable transbronchial biopsies. The patient was commenced on prednisone 40 mg daily. A repeat ERCP revealed mild irregularities in intrahepatic ducts after five months and the stent was removed. Clinically she is asymptomatic and still doing well six months after the diagnosis. The latest follow up laboratory values are alkaline phosphatase 293 U per liter, total bilirubin 0.8 mg per deciliter, alanine aminotransferase 27 U per liter, and aspartate aminotransferase 32 U per liter.

### DISCUSSION

Sarcoidosis is a chronic multisystem disorder of unknown etiology characterized by the accumulation of T lymphocytes, mononuclear phagocytes and non-  
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**Figure 3.** Positive PET scan in the pancreas head, liver, and left gastric wall.

caseating granulomas in involved tissues which cause derangements of the normal tissue architecture (1). All parts of the body can be affected, but the organ most frequently affected is the lungs. Involvement of the skin (mostly at trauma sites) (2), eyes, liver, and lymph nodes are common (1). Hilar adenopathy and pulmonary infiltrates are often suggestive of the diagnosis. As there is no specific test to diagnose sarcoid,

the best way to diagnose it is to consider it as a potential diagnosis in the appropriate clinical setting

The disease has an estimated prevalence of 10 to 40 per 100,000 and affects women more often than men. African-Americans in particular are at risk, as the ratio of blacks to whites is at least 10:1. The lifetime risk of sarcoidosis in blacks in the United States is 2.4 percent, compared with 0.85 percent in whites (3). Seventy to 90 percent of cases occur between 10 to 40 years of age

(1). The disease is detected incidentally by radiographic abnormalities in approximately one-half of cases (1).

### PATHOGENESIS OF SARCOIDOSIS

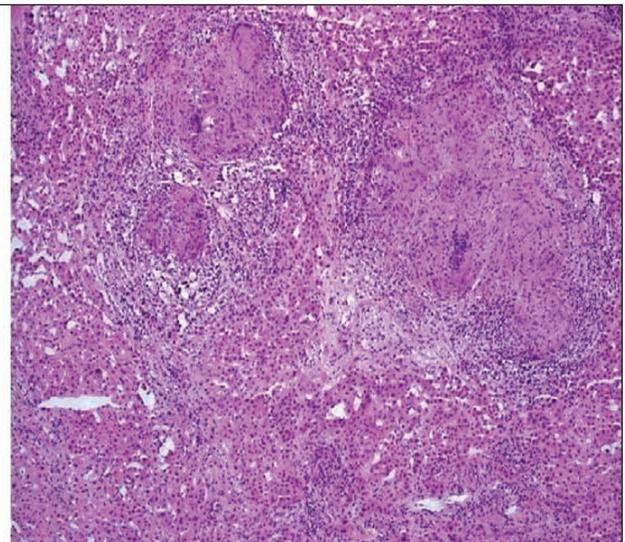
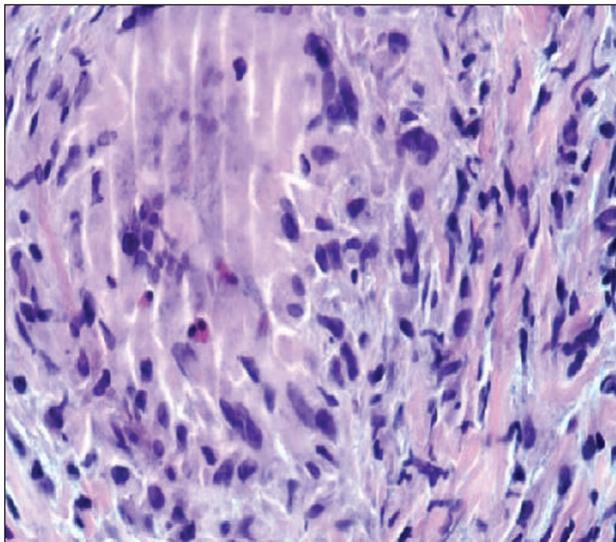
Sarcoidosis results from an exaggerated cellular immune response (acquired, inherited, or both) to a variety of antigens or self-antigens with accumulation of mononuclear inflammatory cells, mostly CD4+ TH1 lymphocytes and mononuclear phagocytes, in affected organs. If persistent, this inflammatory process is followed by the formation of granulomas. The accumulated inflammatory cells and granulomas result in distortion of the architecture of the affected tissue and, ultimately, organ dysfunction (1,4,5).

### ETIOLOGY

The antigenic stimulus which initiates the disease process remains unknown (6). However, infectious agents, genetic factors and immunologic disorders have all been implicated as potential causes (6).

### CLINICAL MANIFESTATIONS

As mentioned previously, sarcoidosis is a systemic disease that can affect any organ in the body. Pulmonary sarcoidosis occurs in over 90 percent of patients. The



**Figure 4.** Pancreatic (left) and hepatic (right) granulomas.

most common presenting symptoms are cough, dyspnea, chest pain and, less commonly, fever, weakness, and weight loss. Reticuloendothelial system involvement is common and involves lymphadenopathy in 40% of patients and hepatomegaly in 20% of patients. Other commonly involved organs in sarcoidosis are the skin (20%) and the eyes (20%) (7).

Gastrointestinal manifestations occur in 0.1% to 0.9% of patients with sarcoidosis; however, the incidence of subclinical involvement may be greater. The stomach is the most common portion of the gastrointestinal tract affected, but involvement of the esophagus, small intestine, large intestine, appendix, rectum, and pancreas have also been described (8–10).

There have been 60 cases of gastric sarcoidosis described in the literature (8,9). These patients typically present with epigastric pain, nausea, and emesis. Weight loss is common, as is heartburn and diarrhea. Symptoms are due to peptic ulceration, narrowing of the gastric lumen, and diminished peristalsis (9). Upper gastrointestinal bleeding secondary to sarcoid has been reported (11). Upper endoscopy may reveal nodular mucosal changes, gastritis, thickened mucosa, ulceration, or mucosal polyps (9,12). The diagnosis of gastric sarcoidosis is made when sarcoid affecting other organ systems is present and with histological evidence of noncaseating granulomas on biopsy. In the absence of multi-organ system involvement, the diagnosis is difficult to establish (9).

Sarcoidosis has been known to affect the small intestine as well, but very few cases have been reported. Of those described, intestinal sarcoid most often occurs in the fifth or sixth decades of life and approximately one-half of these patients have multi-organ system involvement. Most commonly, the patients present with non-bloody diarrhea or abdominal pain. Weight loss, anorexia, fever, and weakness may be seen (9,14). The differential diagnosis includes Crohn's disease, tuberculous enteritis, histoplasma enteritis, and Whipple's disease. The diagnosis should be considered in any patient with a history of sarcoid and persistent diarrhea. Small bowel enteroscopy with mucosal biopsy is the diagnostic procedure of choice.

Rarely, sarcoidosis involves the large intestine or rectum. Six definite cases have been reported in the literature (9,14). Abdominal pain was the most common

presenting symptom in all reported patients. Endoscopic examination with biopsy of the colon is essential to confirm the diagnosis (13).

Appendiceal sarcoidosis has been reported as well, with 10 cases currently in the literature. A pathologic series involving 71,000 surgically removed appendices noted only one specimen with findings consistent with sarcoid (9,14,15).

The liver may show signs of involvement in 21%–95% of patients with sarcoidosis (16), but clinically significant disease is uncommon. Presentation may involve biochemical abnormalities such as elevated alkaline phosphate and transaminases, cholestatic liver disease, hepatic vein thrombosis, or even cirrhosis. The diagnosis is suggested by liver biopsy, but the biopsy result itself is not sufficient to establish the diagnosis, as granulomas can be detected in many other diseases (1). In our case we describe another presentation of sarcoidosis with intrahepatic stricture and cholestatic liver disease. Alam, et al reported a case of sarcoidosis which presented similar to sclerosing cholangitis (18) and there are multiple case reports of sarcoidosis presenting similar to primary biliary cirrhosis (17,19,25,26). Treatment with corticosteroids showed improvement if started early in the active inflammatory process, before permanent damage was caused by fibrosis (18). In our case, the hepatic involvement of sarcoidosis resembled sclerosing cholangitis (with signs of intrahepatic stricture) and primary biliary cirrhosis (elevated alkaline phosphatase), with dramatic improvement after steroid treatment.

Pancreatic sarcoidosis is a rare entity more common in women (20). Its clinical presentation is similar to pancreatic cancer. As in our case, it can be detected as an incidental finding. In the first study of pancreatic sarcoid, an autopsy series of 92 patients with sarcoidosis conducted by Longcope and Freiman in 1952, five patients with incidental pancreatic sarcoidosis were identified (9,21). Another report reviewed nine major series and noted pancreatic granulomas in 3 of 287 autopsies of patients with sarcoidosis (10). In Germany, Hohmann, et al reviewed 486 pancreatic operations for suspected neoplasm. They found one case which was due to pancreatic sarcoid (22). In 1996, Garcia, et al reviewed the literature and

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found only thirteen patients with sarcoidosis of the pancreas. He added six cases, one which involved the body of the pancreas and five which involved the peripancreatic lymph nodes. These eighteen cases represent the largest review available for pancreatic sarcoidosis (20).

Symptoms of pancreatic sarcoidosis include weight loss, jaundice, anorexia, and abdominal pain. In the majority of reported cases, no previous history of sarcoid was reported (9). CT scan, ultrasonography, and nuclear imaging of the abdomen have been used to demonstrate the pancreatic mass. Unfortunately, these radiographic examinations have been unable to distinguish between granuloma, focal pancreatic inflammation, or malignancy, and for every patient the diagnosis was made at laparotomy (9, 20). Only one case reported pancreatic sarcoidosis diagnosed by endoscopic ultrasonography (28).

### TREATMENT

The management of pancreatic sarcoidosis involves careful observation or treatment with steroids for symptomatic patients. Prognosis of pancreatic sarcoidosis generally is good, with 80% of patients improving spontaneously or with steroid therapy (9,20,24). Trabelsi, et al reported regression of the pancreatic lesions after steroid treatment (29). Patients who had pancreatoduodenectomy (Whipple) for suspected malignancy have a good prognosis if they survive surgery (23,27). Our patient did very well with steroid therapy. In retrospect, we think the positive PET scan and elevated CA19-9 were due to the inflammatory process associated with sarcoidosis.

The preceding case highlights the rare clinical entity of pancreatic sarcoidosis presenting as suspected pancreatic cancer. The prognosis for the former is very good, while the prognosis for the latter is poor. Hence, accurate diagnosis is crucial. With increasing availability of imaging tests, sarcoidosis can be detected as an incidental finding. Because there is no one pathognomonic finding for sarcoidosis, recognizing characteristic clinical findings and radiographic abnormalities, ruling out infection, particularly tuberculosis; and obtaining histologic evidence of non-caseating granulomas are essential. ■

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