

# Isolated Pancreatic Histoplasmosis: An Unusual Suspect of Pancreatic Head Mass in an Immunocompetent Host

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Perm J 2015 Fall;19(4):e145-e147

<http://dx.doi.org/10.7812/TPP/14-238>

## ABSTRACT

Histoplasmosis is endemic to the Mississippi and Ohio River valley regions in the US. It usually affects patients with underlying immunodeficiency but can also be seen in immunocompetent hosts. Although gastrointestinal involvement is common in the setting of disseminated histoplasmosis, isolated gastrointestinal involvement is uncommon. We report a case of isolated pancreatic histoplasmosis in an immunocompetent patient, presenting as painless jaundice and pancreatic head mass.

## INTRODUCTION

*Histoplasma* infection is endemic to the Mississippi and Ohio River valley regions in the US. Although it can involve the gastrointestinal system primarily or as part of disseminated disease, most of such cases are asymptomatic and found on autopsy.<sup>1</sup> Only 3% to 12% of these cases manifest clinically, mostly involving the small intestine or colon.<sup>2</sup> We present a case of isolated pancreatic histoplasmosis presenting as painless jaundice and pancreatic head mass in an immunocompetent host.

## CASE REPORT

A 37-year-old woman was referred to the gastroenterology clinic for incidentally noticed conjunctival icterus of unknown duration and abnormal liver function tests by her primary care physician. She did not report any constitutional or systemic symptoms. Her medical history was significant for Roux-en-Y gastric bypass for obesity and cholecystectomy 4 years earlier. She had been born and brought up in Minnesota and previously worked at a fast food restaurant. She also had a 14-pack-year history of smoking. Family history was unremarkable for malignancy, and social history was unremarkable for recent travel, sick contacts, or any domesticated pets.

At the time of presentation, her vital signs and physical examination were unremarkable except for scleral icterus. Laboratory evaluation revealed elevated liver enzymes (alkaline phosphatase [1137 U/L], alanine aminotransferase [422 U/L], aspartate aminotransferase [223 U/L]), total bilirubin (5.3 mg/dL), and direct bilirubin (4.3 mg/dL). Complete blood count, electrolytes, renal function, serum albumin, lipase, international normalized ratio, and cancer antigen 19-9 were within normal limits. Abdominal ultrasound showed a 5 cm × 4 cm mass in the head of the pancreas with intra- and extrahepatic biliary dilatation. A follow-up computed tomography



Figure 1. Abdominal computed tomography scan axial view with intravenous contrast: pancreatic head mass with amorphous internal calcifications (long arrow) abutting the portal vein (short arrow) and intrahepatic biliary dilatation (double arrow).



Figure 2. Abdominal computed tomography scan coronal view with intravenous contrast: Pancreatic head mass (long arrow) with portal vein compression (short arrow) and extra- and intrahepatic biliary dilatation (black arrow).

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(CT) scan of the abdomen and pelvis with intravenous contrast confirmed a 5 cm × 4.2 cm × 3.7 cm pancreatic head mass with coarse internal calcifications, portal vein compression, and possible local invasion posteriorly into the inferior vena cava and left renal vein (Figure 1). No abdominal lymphadenopathy was noted on CT scan. Magnetic resonance imaging of the abdomen with and without intravenous contrast was performed to assess the vascular invasion seen on the CT scan. It showed a large (4.3 cm × 4.2 cm × 4 cm) mass in the head of the pancreas with numerous foci of amorphous calcification (Figure 2). The mass had numerous large cystic components measuring up to 2.3 cm in size, separated by thick enhancing septae (Figure 3). Common bile duct occlusion and portal vein narrowing from extrinsic compression by the mass were also noted. However, no vascular invasion was seen. Radiologic

features were highly suggestive for a mucinous neoplasm, particularly mucinous cystadenocarcinoma. Endoscopic ultrasound was not feasible because of the Roux-en-Y anatomy. Given the high likelihood of malignancy and absence of any metastasis, the pancreatobiliary surgeon decided to proceed with surgical resection.

Intraoperative pathologic examination of frozen section revealed benign necrotizing granulomatous tissue of pancreatic origin, and a Whipple pancreatectomy was performed. Pathologic examination of the resected specimen revealed caseating granulomas and chronic follicular pancreatitis with no dysplastic or neoplastic changes (Figure 4). Fungal yeast forms were seen in the pancreatic and portal lymph node tissue with Gomori methenamine silver stain (Figure 5). However, fungal culture from the resected specimen did not grow any organism. Fungal antibody screen postoperatively was positive for anti-*Histoplasma* immunoglobulin G antibody (titer 1:16, normal < 1:8). A diagnosis of pancreatic histoplasmosis was made on the basis of pathologic and serologic findings.

Postoperatively, the only recognizable risk factor for histoplasmosis was a history of growing up at a chicken farm. However, there was no history of frequent infections during childhood or presence of immunodeficiency disorders in the family. The patient tested negative for common immunocompromised states including human immunodeficiency virus, tuberculosis, syphilis, hepatitis B, and hepatitis C. She was subsequently started on itraconazole suspension but could not tolerate it. Itraconazole was replaced with voriconazole 200 mg twice a day, but she had an adverse event with this dose of voriconazole (vision change: white color appearing yellow). The adverse effect resolved after the voriconazole dose was reduced to 100 mg twice a day. Her voriconazole level 1 week after initiating the treatment was within normal limits. She was prescribed a 3-month course of voriconazole.

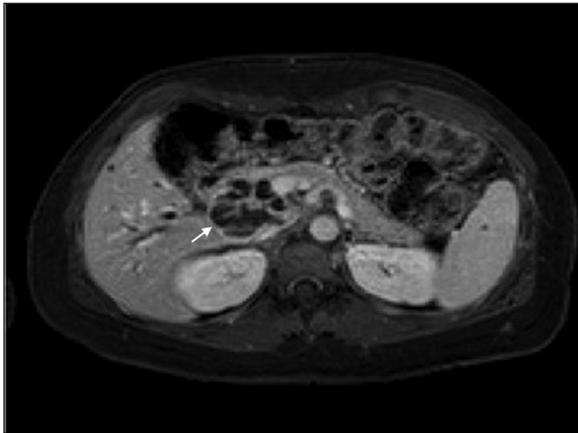


Figure 3. Abdominal magnetic resonance imaging (T1 weighted) with and without intravenous contrast: cavitory mass in the head of the pancreas with thick septations and peripheral enhancement (arrow).



Figure 4. Classic granulomas (arrow) in associated portal nodes with visible normal duodenal mucosa (arrowheads) on hematoxylin and eosin stain.

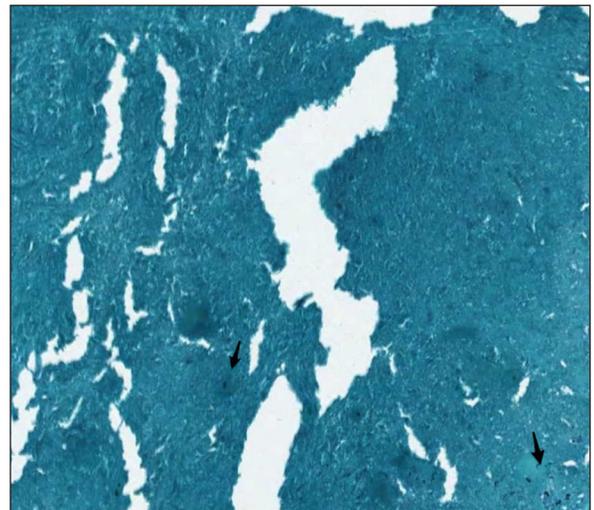


Figure 5. Magnified granuloma wall with rare dark-stained yeast forms (black arrows) with Gomori methenamine silver stain.

## DISCUSSION

To our knowledge, this is the first reported case of symptomatic histoplasmosis localized to the head of the pancreas in an immunocompetent host. Gastrointestinal histoplasmosis has been reported in the literature in immunocompetent hosts. Cappell et al<sup>3</sup> and Lamps et al<sup>4</sup> reported 77 and 52 cases of gastrointestinal histoplasmosis, respectively. The disease affected immunocompetent patients in 48% to 75% of cases.<sup>3,4</sup> The most common sites involved were the small intestine (56% to 79%) and colon (55% to 62%). Pancreatic involvement was reported by Lamps et al<sup>4</sup> in 3 patients (6%). However, it is not entirely clear whether the pancreatic involvement was associated with disseminated histoplasmosis or immunosuppression. Similarly, Suh et al<sup>5</sup> reported asymptomatic pancreatic enlargement on imaging in 2 cases with acquired immune deficiency syndrome. However, isolated symptomatic pancreatic involvement has not been described before in either immunocompetent or immunocompromised hosts.

There are several unique features in this case. The patient did not have any predisposing factors for histoplasmosis except the history of potential exposure in childhood. Her postoperative evaluation was negative for common immunodeficiency disorders or extrapancreatic disease. It may be prudent to rule out underlying immunodeficiency states and disease dissemination in patients diagnosed with isolated gastrointestinal histoplasmosis.<sup>6</sup>

Pancreatic involvement by *Histoplasma* on gastrointestinal imaging bore a remarkable resemblance to pancreatic malignancy. Lee et al<sup>7</sup> described a case of disseminated histoplasmosis presenting as a fungating mass in the transverse colon resembling a colon cancer for which the patient underwent a colectomy. Tuberculosis is another granulomatous disease that can mimic malignancy in the head of the pancreas including vascular invasion.<sup>8</sup> Endoscopic ultrasound was technically not feasible in our case owing to prior Roux-en-Y gastric bypass. A CT-guided biopsy could have helped in differentiating malignancy from *Histoplasma* infection. However, the patient did not have any symptoms, signs, or apparent risk factors for *Histoplasma* or tuberculosis to warrant such testing. *Histoplasma* has been reported to form caseating or noncaseating granulomas, cystic lesions, and tissue microcalcifications in the gastrointestinal tract.<sup>4</sup> All of these pathologic changes were seen in the pancreatic tissue on imaging or pathologic examination of resected specimen.

The diagnosis in this case was based on recognition of the yeast form of *Histoplasma* in the pancreatic tissue with Gomori methenamine silver stain and subsequent confirmation with positive antibody titer. The urine and serum antigen and the tissue fungal cultures were negative, indicating low fungal burden. This pattern of negative antigen testing and tissue cultures along with a positive serology is more likely to be seen in an immunocompetent state where the immune system will result in a low fungal burden.<sup>9,10</sup> Immunocompromised hosts, on the other hand, are more likely to have higher fungal burden with positive antigen tests and culture results and a negative serology.<sup>6,11</sup>

Itraconazole is considered the treatment of choice in noncritically ill patients with histoplasmosis.<sup>12</sup> However, gastric acid is required for adequate absorption of itraconazole pills and hence could not be used in this case owing to prior Roux-en-Y gastric bypass.<sup>13</sup> Itraconazole suspension can be used in this situation, but the patient could not tolerate it.<sup>14</sup> Voriconazole was chosen as an alternate, and the patient tolerated it well after the initial dose adjustment with therapeutic drug levels.

## CONCLUSION

Histoplasmosis can present with isolated symptomatic pancreatic involvement in immunocompetent hosts. Tissue sampling should be considered to make a definite diagnosis of malignancy of the head of the pancreas in areas endemic for histoplasmosis or other granulomatous disease, before undertaking surgical resection. ❖

## Disclosure Statement

The author(s) have no conflicts of interest to disclose.

## Acknowledgment

Mary Corrado, ELS, provided editorial assistance.

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