INTEGRATIVE REVIEW
Turk J Surg 2024; 40 (2): 95-103

Hepato-pancreato-biliary tuberculosis: A review

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ABSTRACT

Hepato-pancreato-biliary (HPB) tuberculosis (TB) is a rare form of extra-pulmonary TB that poses a diagnostic dilemma and is a great masquerader of malignancy. It is almost always curable but requires a high degree of suspicion and corroboratory evidence to document its existence. Medline/PubMed was searched with keywords "hepatic", "liver", "biliary" and "pancreatic" with "tuberculosis". Data were gathered and analyzed. Common symptoms of HPB TB include jaundice, weight loss, abdominal pain and other constitutional symptoms that make it indistinguishable from malignancy. Imaging modalities such as ultrasonography, computed tomography, magnetic resonance imaging may reveal dilated intrahepatic biliary radicles, mass lesion, and biliary stricture or enlarged necrotic lymph nodes. Fine-needle aspiration cytology/biopsy, brush biopsy, acid-fast bacilli (AFB) staining and molecular testing may help clinch the diagnosis. Most cases require biliary drainage and initiation of anti-tubercular therapy (ATT) whereas surgery is reserved for medically refractory cases or fibrotic strictures. However, most cases are diagnosed post-operatively on histopathology where pre-operative diagnosis is malignancy. A high index of suspicion, coupled with streamlined investigations, may help identify patients pre-operatively to be managed with ATT as TB is completely curable with medical management in most of the cases.

Keywords: Hepato-pancreato-biliary, jaundice, neoplasms, tuberculosis

INTRODUCTION

Tuberculosis (TB) continues to be prevalent in African and Asian countries like India. The most common site of involvement in TB is the lung, i.e. pulmonary TB (PTB), and extra-pulmonary TB (EPTB) accounts for 15% of all cases of TB (1). Abdominal TB is one of the common types of EPTB. Co-existent active pulmonary TB is found in only around 6-30% of patients with abdominal TB. Abdominal TB is more commonly seen in young adults as compared to PTB which has no age predilection. Abdominal TB is primarily a gastro-intestinal disease and up to two-thirds of the patients with gastro-intestinal TB have co-existent abdominal lymphadenopathy and/or peritoneal involvement. Involvement of the hepato-pancreato-biliary (HPB) system is uncommon in abdominal TB. Hepato-pancreato-biliary TB can be classified into involvement of either a primary organ such as the liver, pancreas or the biliary tree or the adjacent lymph nodes (tubercular lymphadenitis). There are very few case series (largest consisting of 38 patients, from India) of HPB TB published in the literature (2). Isolated pancreatic tuberculosis is extremely rare owing to the resistance provided by the pancreatic enzymes (lipases and deoxyribonucleases) which have anti-mycobacterial properties that interfere with mycobacterial seeding in the pancreas, and consequently, only isolated case reports of pancreatic TB have been described in the literature (3).

Routes of Spread

Hepato-pancreato-biliary tuberculosis can be part of miliary (disseminated) TB or may be a localized involvement of the HPB system. Bacteria can reach the liver and the biliary tract via the hepatic artery from the lungs or via the portal vein from the gastro-intestinal tract. Mycobacteria swallowed with the sputum cause intestinal ulcers and can then gain access to the portal vein causing primary involvement of the liver (granulomatous hepatitis). Intestinal ulcers may heal with time and the patient may thus manifest as isolated HPB TB (4). Pancreas may be involved by contiguous retroperitoneal lymph nodes. Enlarged adjacent periportal, pericholedochal or peripancreatic tuberculous nodes may compress or caseating tuberculous

Cite this article as: Varshney P, Kapoor VK. Hepato-pancreato-biliary tuberculosis: A review. Turk J Surg 2024; 40 (2): 95-103.

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Received: 23.01.2024
Accepted: 14.03.2024
Available Online Date: 28.06.2024

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DOI: 10.47717/turkjsurg.2024.6338

lymph nodes may rupture into the cystic duct/common bile duct/pancreatic duct causing cholecystitis/cholangitis/pancreatitis. A stricture may form in these ducts as a result of healing by fibrosis after antitubercular therapy (ATT).

Clinical Presentation

Most common (80%) manifestation of HPB TB is pain while other symptoms like jaundice, pruritus, and gastric outlet obstruction (GOO) may be present depending upon the site of involvement. Constitutional symptoms of TB such as fever (typically low-grade with evening rise), night sweats, anorexia and weight loss may be present in one-third of the patients with HPB TB. Symptoms in most patients with HPB TB may closely resemble those of HPB malignancy further contributing to the diagnostic dilemma. Co-existent active PTB is seen in 6-38% of patients with HPB TB (5).

Liver is the most common site of involvement in HPB TB. Hepatic TB manifests most commonly as abdominal pain (40-83%), followed by fever (30-100%), hepatomegaly (10-100%) and less commonly as jaundice (0-60%), splenomegaly (0-40%) and ascites (5-25%) (6).

The order of involvement in the biliary system is as follows: Biliary tree, hilar lymph nodes followed by the gall bladder (GB).

Biliary tuberculosis may manifest as jaundice caused by the enlarged pericholedochal lymph nodes, pain and weight loss. Involvement of the intrahepatic biliary radicles (IHBR) by hepatic tubercular granulomas results in multiple and complex strictures which may resemble stone disease, cholangiocarcinoma or primary sclerosing cholangitis (PSC) (7). Isolated GB TB may present with features of acute cholecystitis or as a GB mass mimicking GB cancer (GBC). Rarely, it may even present as a cholecytoduodenal or cholecystocolic fistula (8,9).

Pancreatic TB may manifest as a mass resembling malignancy in 80% of the patients or as an abscess in around 10% (9). Concomitant peripancreatic lymph nodal involvement is seen in half of these patients. If the head of the pancreas is involved, pain (75%) and obstructive jaundice (20%) will be the predominant symptoms (10). Other presentations may include acute/chronic pancreatitis, gastro-intestinal hemorrhage secondary to splenic vein thrombosis (11-13). 50-70% of pancreatic TB is seen in patients less than 30 years of age (11).

Diagnosis

Most of the patients with HPB TB may have a history of TB or a co-existing immunocompromised state such as HIV/AIDS, long-term intake of steroids or use of biologicals. A thorough history with a high index of suspicion may help suspect HPB TB pre-operatively, especially in endemic areas. Basic investigations like Montoux test, inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may provide contributory evidence but are seldom sufficient to make the diagnosis. A positive Montoux test is very less reliable owing to the false-positive rates, especially in endemic areas and false-negative rates, especially in immunocompromised states (14). Chest X-ray evidence of healed or active pulmonary or pleural TB may support the diagnosis of HPB TB but a normal chest X-ray does not rule out the diagnosis of TB.

Imaging modalities such as contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP) may provide some clues in diagnosing HPB TB but are not specific. Hepatic TB may be either miliary or localized. Miliary hepatic TB, caused by hematogenous dissemination from an extrahepatic site via the hepatic artery, is the commoner variant and presents as diffused studding of the liver with tubercles up to 2 mm in size (6,15). Hepatic TB may manifest as multiple micro-abscesses or as micro-calcifications in the healing phase, dispersed in the liver. Localized hepatic TB, seen in one-fifth of the cases of hepatic TB, has an origin in the gastro-intestinal system and spreads via the portal vein with larger tubercles located near the portal triads. Imaging findings consistent with miliary TB include multiple dispersed low-density nodules while those with localized hepatic TB include larger nodules with enhancement at the periphery and calcifications (6). These nodules may mimic metastases or primary liver malignancy (4).

CT findings of pancreatic TB include a focal mass with mixed cystic attenuation with thin rim of peripancreatic enhancement and peripancreatic lymphadenopathy. Solitary parenchymal lesions are seen in two-thirds of the patients, whereas multifocal lesions may be seen in the remaining one-third (11,16). Calcification may be seen in 56-70% of cases and may range from punctuate to coarse (16). Even vascular invasion has been seen in up to one-third of patients with pancreatic TB, and it may appear as unresectable or borderline resectable pancreatic malignancy on imaging (17). Sometimes, the appearance may mimic that of a mucinous cystic neoplasm (MCN) (18). Pancreatic involvement may occur as part of disseminated (miliary) disease, involvement from retroperitoneal lymph nodes or as primary pancreatic TB (10). GB TB may present as a thick-walled GB on imaging (US, CT, MRI) leading to the diagnostic dilemma of GBC. Regional LNs may be enhanced in HPB TB. Ring enhancement or low-density areas within enlarged lymph nodes may indicate TB.

Sollano et al. have described the characteristic cholangiography features of biliary TB like pruning of the distal intrahepatic ducts, tight hilar strictures with dilated IHBR long smooth stricture of the distal bile duct (1-3). Biliary TB may mimic primary biliary malignancy or primary sclerosing cholangitis (PSC) on cholangiography (14).

Endoscopic ultrasound (EUS) may help to better characterize biliary involvement, especially of the lower CBD and enable a guided FNAC/biopsy from the thickened CBD or the enlarged

lymph nodes which may be crucial in clinching the diagnosis.

Magnetic resonance cholangiopancreatography (MRCP) can help delineate GB or pancreatic mass, the level and extent of biliary involvement and plan a subsequent biliary drainage procedure but is not of much diagnostic significance (8).

FDG PET has also been used but has not been found to be useful in differentiating TB from malignancies as both can be FDG-avid (19).

Laboratory parameters in HPB TB include elevated alkaline phosphatase (ALP), raised gamma-glutamyl transpeptidase (GGTP) and less commonly elevated liver enzymes [alanine transaminase (ALT) and aspartate transaminase (AST)]. Serum albumin levels may be low with reversal of the albumin: Globulin (A:G) ratio indicating a chronic debilitating illness (6). Serum amylase and lipase levels are not much useful owing to their positivity in only one-fourth of cases with pancreatic TB (9).

Image-guided fine needle aspiration cytology (FNAC) or biopsy may be done from highly suspicious areas. Endoscopic ultrasound-guided biopsy is superior to US or CT-guided biopsy (9). These biopsies should be subjected to both microbiological and histopathological examination. Microbiological methods include acid-fast bacilli (AFB) smear examination (sensitivity 0-60%) and AFB culture (sensitivity 0-10%) while histopathological examination shows caseating epithelioid granulomas with Langhan's giant cells (sensitivity 14-100%) (6,20). Caseation and multinucleated Langhan's giant cells differentiate TB from other granulomas, i.e. sarcoid. Latest molecular-based diagnostic modalities, i.e. nucleic acid amplification tests (NAAT) such as GeneXpert, interferon-gamma (IFN-γ) release assays (IGRA), polymerase chain reaction (PCR), multiplex-PCR, can also be performed on the biopsy specimens (21-23). Bile obtained during ERCP can be subjected to AFB staining as well as PCR for diagnosing TB. Brush cytology may be obtained during ERCP although the yield is low (24). Liver biopsy is sometimes required in cases of hepatic abscess not responding to conventional therapies. Tuberculosis DNA may be assessed in blood and bile samples in patients having a high index of suspicion. Even tumor markers like CA 19-9 may be elevated in HPB TB owing to biliary obstruction.

In these cases, the co-existent involvement of the pulmonary system should be actively looked for on chest X-ray, CT imaging, bronchoscopy and broncho-alveolar lavage (BAL). Even extra HPB sites in the abdomen such as peritoneum, omentum must be carefully screened for involvement in all these cases (15). Serum adenosine deaminase (ADA) levels of the ascitic fluid may be an indicator of TB as the etiology of the peritoneal disease.

The suggested sequence of investigations for the diagnosis of HPB TB is biochemical, imaging, molecular, histological, and microbiological. A definitive diagnosis of HPB TB may be very difficult in the absence of biopsy and only surgical intervention with a suspicion of malignancy may yield the final diagnosis in majority of these patients. In a series from a large center in India, none of the seven patients with HPB TB could be identified pre-operatively (5). In another series, only four (three cases of pancreatic TB, diagnosed on FNAC of presumed unresectable cancer and one case of hilar TB diagnosed on cytological evaluation of bile obtained during biliary drainage for cholangitis) out of 18 patients of HPB TB could be diagnosed pre-operatively (8). A large series of 38 patients of HPB TB included hepatic TB in 20 patients, biliary TB in 15 and mixed variant in three patients with the patients being diagnosed on the basis of microbiological and histopathological features and responding well to anti-tuberculous therapy (ATT) (2).

Therapeutic trial of ATT without a confirmed diagnosis has been given in a few cases but a fibrotic reaction following ATT has been seen in 6-25% of cases leading to worsening of the jaundice further re-iterating the diagnosis of malignancy and prompting endoscopic/surgical intervention (25,26).

Treatment

Tuberculosis is a benign infectious disease and is curable with medical management without resorting to surgical resections if the diagnosis can be made pre-operatively (5,8). Management is the prompt initiation of ATT drugs which may provide resolution of symptoms. The literature recommends the use of standard first-line anti-tuberculous drugs for 6-12 months. Multi-drug resistance (MDR) TB and drug-induced hepatoxicity mandate the use of alternative regimes. Worsening of jaundice in case of biliary strictures has been reported in 6-25% of patients due to fibrotic reaction that may develop after the initiation of ATT (25,26). Endoscopic intervention and stenting may be required in a few cases to decrease the serum bilirubin level before ATT is started. Some case series have described initiating treatment with full-course ATT despite initial abnormal LFTs unless evidence of chronic liver disease (CLD) is present (2).

Unfortunately, only a few patients can be diagnosed with investigations, and one may have to resort to surgical procedures for obtaining diagnosis and management. Surgery remains the mainstay of diagnosing HPB TB as pre-operative diagnosis is difficult. A large variety of surgical interventions varying from simple cholecystectomy to pancreatoduodenectomy and extended liver resections with a pre-operative suspicion of malignancy have been described in literature but with better outcomes in terms of morbidity and mortality when compared to malignant lesions.

Surgical options for HPB TB are varied and primarily depend on the site of involvement and the performance status of the patient (Table 1). Localized isolated hepatic TB may require surgical interventions varying from anatomical hepatectomies to just enucleation of the mass or drainage of abscesses in addition to the ATT (6). Anecdotal case reports of biliary TB symptoms

Table 1. Summary of cases of hepato-pancreato-biliary cases in literature

No	Study (Reference no.)	No of cases	Diagnosis	Pre-operative evidence for TB (FNAC/biops/brush cytology)	Management (all patients have received ATT as part of management)	Post-operative biopsy +ve for TB
1	Narayan et al. (29)	1	Cholestatic jaundice with disseminated tuberculosis	FNAC from cervical LN and liver lesions	ATT only	NA
2.	Eso et al. (30)	1	Granulomatous hepatitis with disseminated BCG injection	Liver biopsy	ATT only	NA
3.	Chong et al. (15)	1	Obstructive jaundice due to biliary TB and ampullary carcinoma	Bile aspirate and hilar stricture biopsy positive for AFB, Ampullary biopsy positive for malignancy	Whipple's surgery	Yes
4.	Jethwani et al. (31)	1	Obstructive jaundice with distal CBD stricture	PCR of bile aspirate, axillary LN biopsy +ve	ERCP stenting, ATT	NA
5.	Durairajan et al. (32)	3	1. Obstructive jaundice with mid CBD stricture	Brush cytology-non contributary	Open cholecystectomy with Roux-en-Y HJ	Yes
			2. Obstructive jaundice with mid CBD stricture	Brush cytology +ve for malignancy initially, TB after review	Radical extrahepatic bile duct excision with Roux-en-Y HJ	Yes, no malignancy
			3. Acute calculus cholecystitis	NA	Subtotal cholecystectomy	Persistent sinus
6.	Saluja et al. (8)	18	1. Hepatic TB	-ve	Segment VIII excision with CBD exploration and T-tube drainage	Yes
			2. Hepatic TB, splenic TB	-ve	Left lateral segmentectomy with splenectomy and chlecystojejunostomy	Yes
			3. GB TB	-ve	Enbloc resection of GB, segment IVB, V, with LN resection antrum and 1st part duodenum, GJ	Yes
			4. GB TB	-ve	Cholecsytectomy with omental biopsy	Yes
			5. GB TB	-ve	Cholecystectomy and lymph node biopsy	Yes
			6. Periportal LN TB, chronic cholecystitis	-ve	Cholecystectomy with CBD exploration with T tube drainage with LN biopsy	Yes
			7. Periportal LN TB, chronic cholecystitis	-ve	Cholecystectomy with CBD exploration with T tube drainage with frozen section	Yes (frozen biopsy)
			8. Periportal LN TB, chronic cholecystitis	-ve	Exploratory laparotomy + frozen section + cholecystectomy & Roux-en-Y choledochojejeunostomy	Yes (frozen biopsy)
			9. Bile duct TB	-ve	Palliative hepaticojejunostomy, LN biopsy, CBD bx	Yes
			10. Periportal LN TB, bile duct-no evidence of malignancy	-ve	Hepaticojejunostomy with frozen section	Yes

Table 1. Summary of cases of hepato-pancreato-biliary cases in literature (continue)

No	Study (Reference no.)	No of cases	Diagnosis	Pre-operative evidence for TB (FNAC/biops/brush cytology)	Management (all patients have received ATT as part of management)	Post-operative biopsy +ve for TB
			11. Pancreatic TB	-ve	Distal pancreatectomy, splenectomy with choledochojejunostomy	Yes
			12. Peripancreatic LN TB	-ve	Pancreaticoduodenectomy	Yes
			13. Pancreatic and peripancreatic LN TB	-ve	Pancreaticoduodenectomy	Yes
			14. Pancreatic and peripancreatic LN TB	-ve	Pancreaticoduodenectomy	Yes
			15. Pancreatic TB	FNAC from right supraclavicular LN and pancreatic head mass +ve for TB	ATT only	NA
			16. Pancreatic TB	FNAC from pancreatic head mass +ve for TB	ATT only	NA
			17. Pancreatic TB	FNAC from pancreatic head mass +ve for TB	ATT only	NA
			18. Bile duct TB	Brush cytology +ve for TB	ERCP stenting, ATT	NA
7.	Padhiari et al. (33)	5	1. Pseudotumor of CBD	No	Surgical (procedure NA)	Yes
			2. Pseudotumor of CBD	No	Surgical (procedure NA)	Yes
			3. CBD stricture	Brush cytology +ve for TB	ERCP stenting	NA
			4. CBD stricture	Brush cytology +ve for TB	ERCP stenting	NA
			5. CBD stricture	PCR of bile aspirate +ve for TB	ERCP stenting	NA
8.	Alsawat et al. (27)	1	Obstructive jaundice with distal CBD stricture	Mediastinal LN +ve for TB, brush cytology-inconclusive	ATT only	NA
9.	Sanabe et al. (34)	1	Pancreatic TB	-ve	Distal pancreatectomy with total gastrectomy with partial resection of transverse colon	Yes
10.	Prasad et al. (14)	1	Obstructive jaundice with hilar stricture	-ve	Cholecystectomy with T tube placement	Yes (frozen biopsy)
11.	Lee et al. (35)	1	Obstructive jaundice with hilar stricture	Bile aspirate +ve for TB, lung nodule +ve for TB	PTBD	NA
12.	Govindswamy et al. (5)	7	Duodenal perforation with pericholedochal and para aortic lymphadenopathy	-ve	Perforation closure, GJ, FJ	Yes
			Pancreatic TB	-ve	Cholecystectomy, HJ	Yes
			Obstructive jaundice with hilar stricture	-ve	Cholecystectomy, HJ	Yes
			Obstructive jaundice with hilar stricture	-ve	Cholecystectomy, HJ	Yes
			GB TB with portal vein thrombosis	-ve	Cholecystectomy, GB biopsy	Yes

Table 1. Summary of cases of hepato-pancreato-biliary cases in literature (continue)

No	Study (Reference no.)	No of cases	Diagnosis	Pre-operative evidence for TB (FNAC/biops/brush cytology)	Management (all patients have received ATT as part of management)	Post-operative biopsy +ve for TB
			GB TB with Mirrizzi's syndrome type II with cholecystoduodenal fistula	-ve	Cholecystectomy, duodenal repair, GJ	Yes
			GB TB	-ve	Cholecystectomy, HJ, GJ, JJ	Yes
13.	Ando et al. (36)	1	Obstructive jaundice with left hepatic duct stricture and enlarged hilar LN	EUS FNAC of hilar LN +ve for TB	ERCP stenting, ATT	NA
14.	Iwai et al. (37)	1	Obstructive jaundice with hilar stricture	PCR of bile +ve for TB	PTBD, ATT	NA
15.	Yeh et al. (38)	2	Obstructive jaundice with hilar stricture	-ve	HJ	Post op biopsy +ve for TB
			Obstructive jaundice with hilar stricture	PCR of bile +ve for TB, brush cytology -ve	PTBD, ATT	NA
16.	Kok et al. (39)	4	Obstructive jaundice with distal CBD stricture	FNAB +ve for TB	ERCP stenting, ATT	NA
			Obstructive jaundice with hilar stricture	Brush cytology +ve for TB	Left cholangio-jejunostomy	NA
			Obstructive jaundice with CBD stricture	-ve	Open biliary stenting	Yes (frozen biopsy)
			Obstructive jaundice with hilar stricture	-ve	HJ	Yes (frozen biopsy)
17.	Hickey et al. (6)	1	Obstructive jaundice with CBD and hilar stricture	Inguinal LN +ve for TB	ERCP stenting	NA
18.	Valeja et al. (40)	1	Obstructive jaundice with CBD stricture	-ve	HJ	Yes (frozen biopsy)
19.	Inal et al. (41)	1	Obstructive jaundice with CBD stricture	Biopsy via PTBD	PTBD stenting	NA
20.	Behera et al. (42)	1	Obstructive jaundice with CBD stricture	-ve	HJ	Yes (frozen biopsy)
21.	Bearer et al. (43)	1	Obstructive jaundice with CBD stricture	ERCP assisted bile cytology	ERCP stenting	NA
22.	Ratanarapee et al. (44)	1	Obstructive jaundice with CBD stricture	-ve	T-tube drainage	Yes (frozen biopsy)
23.	Fan et al. (13)	1	Obstructive jaundice with CBD stricture	-ve	PTBD stenting	Yes (frozen biopsy)
24.	Abascal et al. (45)	1	Obstructive jaundice with multiple CBD stricture	-ve	Laparotomy and biopsy Died of sepsis	Yes (frozen biopsy)

AFB: Acid-fast bacilli, ATT: Anti-tubercular treatment, BCG: Bacilli Calmette-Guerin, CBD: Common bile duct, ERCP: Endoscopic retrograde cholangio-pancreatography, EUS: Endoscopic ultrasound, FJ: Feeding jejunostomy, FNAB: Fine needle aspiration biopsy, FNAC: Fine needle aspiration cytology, GB: Gall bladder, GJ: Gastrojejunostomy, HJ: Hepaticojejunostomy, LN: Lymph node, NA: Not available, PCR: Polymerase chain reaction, PTBD: Percutaneous transhepatic biliary drainage, TB: Tuberculosis.

being relieved by ATT exist, but surgery remains the mainstay of treatment given the diagnostic dilemma and the presence of mechanical biliary obstruction in majority of the cases (27). Furthermore, fibrotic strictures are less prone to respond to ATT alone. Sometimes, these biliary lesions may become fibrotic in response to ATT further exacerbating the jaundice. Cholecystectomy and hepaticojejunostomy are the most commonly performed procedures for biliary TB. T-tube drainage of the CBD may be considered in these cases (5).

Isolated GB TB may mandate cholecystectomy with on-table frozen section, extended (radical) cholecystectomy, or a cholecystectomy with bile duct resection and reconstruction in the

form of a bilio-enteric anastomosis. Various surgeries ranging from pancreatoduodenectomies to distal pancreatosplenectomy have been performed for pancreatic TB, with a suspicion of malignancy in the absence of a conclusive pre-operative or intraoperative diagnosis (8). Sometimes, multi-visceral resection may be contemplated if the suspicion for malignancy is high (5).

HIV and HPB TB

Immunocompromised patients, like those with HIV/AIDS, have more severe manifestations of TB besides being more susceptible to TB reactivation and dissemination (6). EPTB is more common in these patients. Co-existent HIV infection must be actively sought in all patients with HPB TB. A higher degree of clinical suspicion coupled with a regular follow up may help detect patients with HPB TB in presence of HIV/AIDS early thereby avoiding the associated morbidity. The WHO recommends starting anti-retroviral therapy (ART) 2-8 weeks after starting ATT, especially in drug-resistant cases (28). Both ART and ATT may have complex drug interactions which must be kept in mind while treating these patients.

CONCLUSION

Hepato-pancreato-biliary TB is rare even in areas where TB is still common. It may present with varied signs and symptoms and the non-specific findings of biochemical and imaging investigations may contribute to the diagnostic conundrum, especially with HPB cancer, and it is almost impossible to make a pre-operative diagnosis of HPB TB. It is a great mimic of other benign or malignant HPB lesions. It should be considered as a differential diagnosis, especially in areas where TB is still endemic. Certain features that may hint towards the diagnosis of HPB TB are long duration of symptoms, pain out of proportion to the mass, mild (cf. deep in malignancy) jaundice, a history of TB, other systemic manifestations of TB like pulmonary or generalized lymph node involvement, associated involvement of other abdominal organs. Surgical interventions are frequently required in the absence of a definitive pre-operative diagnosis of TB and suspicion of malignancy. A high index of suspicion coupled with streamlined investigations may help identify these patients especially in endemic areas as TB is completely curable with medical management with ATT in most of the cases. The co-existence of HPB TB and HIV must be actively searched for in all cases.

Author Contributions: Concept - VKK; Design - VKK; Supervision - VKK; Fundings - VKK; Materials - VKK; Data Collection and/or Processing - PV; Analysis and/or Interpretation - PV; Literature Search - PVS; Writing Manuscript - PV, VKK; Critical Reviews - VKK.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. *Rodriguez-Takeuchi SY, Renjifo ME, Medina FJ. Extrapulmonary tuberculosis. Pathophysiology and imaging findings. Radiographics 2019; 39(7): 2023-37. https://doi.org/10.1148/rg.2019190109*
2. *Amarapurkar D, Patel N, Amarapurkar A. Hepatobiliary tuberculosis in western India. Indian J Pathol Microbiol 2008; 51(2): 175-81. https://doi.org/10.4103/0377-4929.41644*
3. *Franco-Paredes C, Leonard M, Jurado R, Blumberg HM, Smith RM. Tuberculosis of the pancreas: Report of two cases and review of the literature. Am J Med Sci 2002; 323(1): 54-8. https://doi.org/10.1097/00000441-200201000-00010*
4. *Niyogi D, Goel M, Shinde RS, Patkar S. Primary hepatic tuberculosis: A rare occurrence. Ann Hepato-Biliary-Pancreatic Surg 2019; 23(1): 80. https://doi.org/10.14701/ahbps.2019.23.1.80*
5. *Govindasamy M, Srinivasan T, Varma V, Mehta N, Yadav A, Kumaran V, et al. Biliary tract tuberculosis - a diagnostic dilemma. J Gastrointest Surg 2011; 15(12): 2172-7. https://doi.org/10.1007/s11605-011-1685-5*
6. *Hickey N, McNulty JG, Osborne H, Finucane J. Acute hepatobiliary tuberculosis: A report of two cases and a review of the literature. Eur Radiol 1999; 9(5): 886-9. https://doi.org/10.1007/s003300050761*
7. *de Melo VA, de Melo GB, Silva RL, Piva N, Almeida MLD. Tuberculosis of the cystic duct lymph node. Braz J Infect Dis 2004; 8(1): 112-4. https://doi.org/10.1590/S1413-86702004000100009*
8. *Saluja SS, Ray S, Pal S, Kukeraja M, Srivastava DN, Sahni P, et al. Hepatobiliary and pancreatic tuberculosis: A two decade experience. BMC Surg 2007; 9: 1-9. https://doi.org/10.1186/1471-2482-7-10*
9. *Panic N, Maetzel H, Bulajic M, Radovanovic M, Löhr JM. Pancreatic tuberculosis: A systematic review of symptoms, diagnosis and treatment. United Eur Gastroenterol J 2020; 8(4): 396-402. https://doi.org/10.1177/2050640620902353*
10. *Chaudhary P, Bhadana U, Arora MP. Pancreatic Tuberculosis. Indian J Surg 2015; 77(6): 517-24. https://doi.org/10.1007/s12262-015-1318-4*
11. *Nagar AM, Raut AA, Morani AC, Sanghvi DA, Desai CS, Thapar VB. Pancreatic tuberculosis: A clinical and imaging review of 32 cases. J Comput Assist Tomogr 2009; 33(1): 136-41. https://doi.org/10.1097/RCT.0b013e31816c82bc*
12. *Noyal M, Harish BN, Bhat V, Parija SC. Neonatal melioidosis: A case report from India. Indian J Med Microbiol 2009; 27(3): 260-3. https://doi.org/10.4103/0255-0857.53213*
13. *Fan ST, Yan KW, Lau WY, Wong KK. Tuberculosis of the pancreas: A rare cause of massive gastrointestinal bleeding. Br J Surg 1986; 73(5): 373. https://doi.org/10.1002/bjs.1800730517*
14. *Prasad A, Pandey KK. Tuberculous biliary strictures: Uncommon cause of. 2001; 45(3): 365-8. https://doi.org/10.1046/j.1440-1673.2001.00940.x*
15. *Chong VH, Lim KS. Hepatobiliary tuberculosis. Singapore Med J 2010; 51(9): 744-51.*
16. *Dou Y, Liang Z. Pancreatic tuberculosis: A computed tomography imaging review of thirteen cases. Radiol Infect Dis 2019; 6(1): 31-7. https://doi.org/10.1016/j.jrid.2018.04.004*
17. *Rana SS, Sharma V, Sampath S, Sharma R, Mittal BR, Bhasin DK. Vascular invasion does not discriminate between pancreatic tuberculosis and pancreatic malignancy: A case series. Ann Gastroenterol 2014; 27(4): 395-8.*

18. *Woodfield JC, Windsor JA, Godfrey CC, Orr DA, Officer NM. Diagnosis and management of isolated pancreatic tuberculosis: Recent experience and literature review. ANZ J Surg 2004; 74(5): 368-71. https://doi.org/10.1111/j.1445-1433.2004.02996.x*

19. *Gupta V, Vishnu KS, Yadav TD, Sakaray YR, Irrinki S, Mittal BR, et al. Radio-pathological correlation of 18F-FDG PET in characterizing gallbladder wall thickening. J Gastrointest Cancer 2019; 50(4): 901-6. https://doi.org/10.1007/s12029-018-0176-2*

20. *Diaz ML, Herrera T, Lopez-Vidal Y, Calva JJ, Hernandez R, Palacios GR, et al. Polymerase chain reaction for the detection of Mycobacterium tuberculosis DNA in tissue and assessment of its utility in the diagnosis of hepatic granulomas. J Lab Clin Med 1996; 127(4): 359-63. https://doi.org/10.1016/S0022-2143(96)90184-5*

21. *Alcantara-Payawal DE, Matsumura M, Shiratori Y, Okudaira T, Gonzalez R, Lopez RA, et al. Direct detection of Mycobacterium tuberculosis using polymerase chain reaction assay among patients with hepatic granuloma. J Hepatol 1997; 27(4): 620-7. https://doi.org/10.1016/S0168-8278(97)80078-5*

22. *Vadwai V, Boehme C, Nabeta P, Shetty A, Alland D, Rodrigues C. Xpert MTB/RIF: A new pillar in diagnosis of extrapulmonary tuberculosis? J Clin Microbiol 2011; 49(7): 2540-5. https://doi.org/10.1128/JCM.02319-10*

23. *Maulahela H, Simadibrata M, Nelwan EJ, Rahadiani N, Renesteen E, Suwarti SWT, et al. Recent advances in the diagnosis of intestinal tuberculosis. BMC Gastroenterol 2022; 22(1): 89. https://doi.org/10.1186/s12876-022-02171-7*

24. *Mallery JS, Centeno BA, Hahn PF, Chang Y, Warshaw AL, Brugge WR. Pancreatic tissue sampling guided by EUS, CT/US, and surgery: A comparison of sensitivity and specificity. Gastrointest Endosc 2002; 56(2): 218-24. https://doi.org/10.1016/S0016-5107(02)70181-8*

25. *Cheng VCC, Ho PL, Lee RA, Chan KS, Chan KK, Woo PCY, et al. Clinical spectrum of paradoxical deterioration during antituberculosis therapy in non-HIV-infected patients. Eur J Clin Microbiol Infect Dis 2002; 21(11): 803-9. https://doi.org/10.1007/s10096-002-0821-2*

26. *Breen RAM, Smith CJ, Bettinson H, Dart S, Bannister B, Johnson MA, et al. Paradoxical reactions during tuberculosis treatment in patients with and without HIV co-infection. Thorax 2004; 59(8): 704-7. https://doi.org/10.1136/thx.2003.019224*

27. *Alsawat KE, Aljebreen AM. Resolution of tuberculous biliary stricture after medical therapy. World J Gastroenterol 2006; (7): 1153-6. https://doi.org/10.3748/wjg.v12.i7.1153*

28. *WHO. WHO consolidated guidelines on tuberculosis. Module 4: Treatment - drug-resistant tuberculosis treatment. Online annexes. WHO. 2020. p. 1-120.*

29. *Narayan KS, Kumar M, Padhi S, Jain M, Ashdhir P, Pokharna RK. Tubercular biliary hilar stricture: A rare case report. Indian J Tuberc 2018; 65(3): 266-7. https://doi.org/10.1016/j.ijtb.2017.06.013*

30. *Eso Y, Takai A, Arasawa S, Ueda Y, Seno H. Hepatobiliary and pancreatic: Granulomatous hepatitis due to disseminated bacillus Calmette-Guérin disease. J Gastroenterol Hepatol 2017; 32(9): 1538. https://doi.org/10.1111/jgh.13831*

31. *Jethwani U, Singh G, Kandwal V, Saroha R, Chouhan J, Bansal N, et al. Tuberculosis of biliary tract: A rare cause of common bile duct stricture. OA Case Reports 2013; 2(6): 53. https://doi.org/10.13172/2052-0077-2-6-640*

32. *Durairajan S, Lakshmanan A, Rehman A, Jameel A, Durairaj S, Amudhan A, et al. Biliary tract tuberculosis: An enigma. Tropical Gastroenterol 2017; 38(2): 132-4. https://doi.org/10.7869/tg.415*

33. *Padhiari RK, Ramesh MK, G P P, Ahmed N. Tuberculosis biliary stricture simulating as cholangiocarcinoma. J Clin Diagn Res 2015; 9(3): PL01-2. https://doi.org/10.7860/JCDR/2015/11266.5706*

34. *Sanabe N, Ikematsu Y, Nishiwaki Y, Kida H, Murohisa G, Ozawa T, et al. Pancreatic tuberculosis. J Hepatobiliary Pancreat Surg 2002; 9(4): 515-8. https://doi.org/10.1007/s005340200065*

35. *Lee SY, Kang CY, Low SC, Chow KH. Tuberculous biliary stricture. Clin J Gastroenterol 2012; 5(1): 53-8. https://doi.org/10.1007/s12328-011-0278-x*

36. *Ando N, Iwata K, Yamazaki K, Shimizu S, Sugihara J, Katayama M, et al. A case of liver hilar tuberculous lymphadenitis complicated by biliary stricture diagnosed by endoscopic ultrasound-guided fine-needle aspiration. Clin J Gastroenterol 2019; 12(1): 57-62. https://doi.org/10.1007/s12328-018-0898-5*

37. *Iwai T, Kida M, Kida Y, Shikama N, Shibuya A, Saigenji K. Biliary tuberculosis causing cicatricial stenosis after oral antituberculosis therapy. World J Gastroenterol 2006; 12(30): 4914-7. https://doi.org/10.3748/wjg.v12.i30.4914*

38. *Yeh TS, Chen NH, Jan YY, Hwang TL, Jeng LB, Chen MF. Obstructive jaundice caused by biliary tuberculosis: Spectrum of the diagnosis and management. Gastrointest Endosc 1999; 50(1): 105-8. https://doi.org/10.1016/S0016-5107(99)70357-3*

39. *Kok KY, Yapp SK. Tuberculosis of the bile duct: A rare cause of obstructive jaundice. J Clin Gastroenterol 1999; 29(2): 161-4. https://doi.org/10.1097/00004836-199909000-00012*

40. *Valeja R, Pal S, Mann MS, Hadke NS, Bhardwaj M. Isolated common bile duct tuberculosis. Indian J Gastroenterol 1999; 18(3): 125-6.*

41. *Inal M, Aksungur E, Akgül E, Demirbaş O, Oğuz M, Erkoçak E. Biliary tuberculosis mimicking cholangiocarcinoma: Treatment with metallic biliary endoprosthesis. Am J Gastroenterol 2000; 95(4): 1069-71. https://doi.org/10.1111/j.1572-0241.2000.01944.x*

42. *Behera A, Kochhar R, Dhavan S, Aggarwal S, Singh K. Isolated common bile duct tuberculosis mimicking malignant obstruction. Am J Gastroenterol 1997; 92(11): 2122-3.*

43. *Bearer EA, Savides TJ, McCutchan JA. Endoscopic diagnosis and management of hepatobiliary tuberculosis. Am J Gastroenterol 1996; 91(12): 2602-4.*

44. *Ratanarapee S, Pausawasdi A. Tuberculosis of the common bile duct. HPB Surg 1991; 3(3): 205-8. https://doi.org/10.1155/1991/42843*

45. *Abascal J, Martin F, Abreu L, Pereira F, Herrera J, Ratia T, et al. Atypical hepatic tuberculosis presenting as obstructive jaundice. Am J Gastroenterol 1988; 83(10): 1183-6.*

BÜTÜNLEYİCİ DERLEME-ÖZET
Turk J Surg 2024; 40 (2): 95-103

Hepato-pankreato-biliyer tüberküloz

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ÖZET

Hepato-pankreato-biliyer (HPB) tüberküloz (TB), tanısal bir ikilem oluşturan ve maligniteyi maskeleyen nadir bir ekstra pulmoner TB formudur. Neredeyse her zaman tedavi edilebilse de varlığını belgelemek için yüksek derecede şüphe ve doğrulayıcı kanıtlar gerektirir. Medline/PubMed'de "hepatic", "liver", "biliary" ve "pancreatic" anahtar kelimeleri "tuberculosis" ile birlikte aranmıştır. Veriler toplanmış ve analiz edilmiştir. Hepato-pankreato-biliyer TB'nin yaygın semptomları arasında sarılık, kilo kaybı, karın ağrısı ve maligniteden ayırt edilemeyen diğer semptomlar yer almaktadır. Ultrasonografi, bilgisayarlı tomografi, manyetik rezonans görüntüleme gibi görüntüleme yöntemleri dilate intrahepatik safra kanalları, kütleyi ve safra yolu darlığını veya genişlemiş nekrotik lenf nodlarını ortaya çıkarabilir. İnce iğne aspirasyon sitolojisi/biyopsisi, fırça biyopsisi, aside dirençli basil (AFB) boyaması ve moleküler testler tanıyı kesinleştirmeye yardımcı olabilir. Vakaların çoğunda biliyer drenaj ve anti-tüberküloz tedavinin (ATT) başlatılması gerekirken, medikal olarak dirençli vakalar veya fibrotik striktürler için cerrahi uygulanmaktadır. Bununla birlikte, çoğu vakada ameliyat öncesi tanı malignite iken ameliyat sonrası histopatoloji ile tanı konmaktadır. Yüksek bir şüphe endeksi ve kolaylaştırılmış incelemeler, vakaların çoğunda tıbbi tedavi ile TB tamamen iyileştirilebilir olduğundan ATT ile yönetilecek hastaların ameliyat öncesinde belirlenmesine yardımcı olabilir.

Anahtar Kelimeler: Hepato-pankreato-biliyer, sarılık, tümörler, tüberküloz

DOİ: 10.47717/turkjsurg.2024.6338