

RADIOLOGICAL INTERVENTIONS IN MALIGNANT BILIARY OBSTRUCTION**Bijoy Mathew and Hai-Bo Xu***

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ABSTRACT

Disorders affecting the biliary system is one of the major diseases affecting the population worldwide. In United States of America more than 20% of people who are older than 65 years of age are having gallstones and every year more than 1.1 million cases are diagnosed. There are many causes that contribute to biliary obstruction of which major role is played by cholelithiasis alone. According to recent studies the mortality rates associated with cholangio carcinoma and cancers involving pancreatic head are known to have very less survival rate. Maximum of 5 years survival are expected in western countries. Malignant biliary obstruction etiology is contributed by a variety of diseases but are commonly caused by gall bladder carcinomas, cholangio carcinoma and even by metastatic nodes. Interventional radiology plays a major contribution in this scenario. Radiological interventions are comparatively less invasive, and use imaging modalities in the diagnosis and treatment of the concerned diseases. The type and nature of malignancy, as well as stage of disease may be considered as the primary factors that helps the surgeon /radiologists in arriving at a decision whether the patient should be treated before the excision of the mass lesion or not. Here we are going to discuss about the etiology, symptoms, laboratory findings, diagnosis, indications and contraindications, diagnostic imaging, treatment modalities of malignant biliary obstruction.

KEYWORDS: Malignant biliary obstruction, stent, interventional radiology, bile, pancreas, liver, cholelithiasis, pancreatic carcinoma, cholangiocarcinoma, jaundice, diagnostic imaging.

INTRODUCTION

Understanding about the normal anatomy of biliary system also known as biliary tree or biliary tract is essential for further exploration. The bile system includes the gallbladder, bile ducts and certain cells inside and outside of the liver. The biliary system plays a crucial role in our body. It creates, moves, stores and helps in releasing bile into the duodenum to the body in order to digest foods. Bile is an important exocrine secretion of the liver and it is being produced frequently by hepatocytes.^[1] Bile mainly consists of cholesterol which is essential to maintain both membrane structural integrity and fluidity. It also contains many waste products such as bilirubin and bile salts. These are essential for digestion of fats. In case of malignant biliary obstructions, as the biliary tracts are occluded, there may be development of malignant jaundice. There are two processes involving the development of malignant jaundice. One due to infiltration with tumour cells directly or can indirectly develop due to the excessive compressibility by the tumour mass. The blockage involving the biliary confluence may be developed due to varying pathology. It can be due to neoplasms including both benign as well as malignant lesions. Well known pathologies involved in the development of massive biliary occlusion include

cholangio carcinoma, malignancies involving gall bladder and also pancreatic carcinomas. They are also seen in cases of metastatic lymphadenopathy. Other unusual causes which may be involved are carcinomas involving the liver, and end stage gastric carcinomas and also duodenal neoplasms.^[2] Interventional radiology departments are well known for its less invasive and widely used imaging techniques for the proper management of varying disorders. They are widely considered in the treatment of both operable as well as non operable cases. For the past 1-2 decades interventional radiology plays a major role in the treatment of these cases. There are many treatment modalities used nowadays for example application of per cutaneous trans hepatic biliary drains, embolisation of the portal vein before the surgical means and application of covered as well as uncovered stents in the biliary tract.^[3] Per cutaneous interventions still stand as the major modality in treating these kinds of patients. Proper drainage of bile fluids which is one of the highlights of interventional radiology management, may be effective in relieving symptoms in inoperable / older patient cases or may even be used as a treatment modality prior to surgery which may aid in improving liver enzymes and liver functions back to normal levels. There may be some adversities, that, are reported when drainage of bile

fluids are done before surgery such as infectious complications may supervene. In some cases the vice versa scenarios are also reported. There are some other interventions that are used frequently nowadays such as chole cystostomy and radiofrequency ablation. Regarding carcinoma involving pancreas, self-expanding metallic stents are considered to be better than plastic stents. The benefit of these stents are that, the decompression effect of these stents are long lasting. And there are less chances of occlusion associated with these stents. Where as regarding cholangio carcinoma, treatment modalities are different. Treatments done per cutaneously are used or naso biliary drainage of fluids are also done. These treatment methods are more effective than endoscope related stenting. And there are less chances of acquiring infections and even less chances of treatment failures. For patients suffering from either malignancy and diagnosed at an end stage may be given treatment for symptomatic relief only.^[4] And further treatments like stent placements may be done endoscopically taking into consideration about the life expectancy. The sole purpose of this review is to project the activities interventional radiology department implies in the proper management of malignant biliary obstruction cases.

Etiology

The main causes of malignant biliary obstruction are attributable to pancreatic ductal adeno carcinoma which presents with jaundice and is mostly seen painless. There are mainly 2 neoplasms that may cause biliary tract occlusion namely, pancreatic ductal adeno carcinoma and primary bile duct carcinoma also known as cholangio carcinoma.^[5] Ampullary carcinoma, primary duodenal adeno carcinoma, pancreatic neuroendocrine tumors may also lead to malignant biliary tree obstruction. Lymphadenopathy at the porta hepatis is also a major causation factor for the development of occlusion of the hepatic hilum and is commonly seen in metastatic colon cancer or even in lymphoma. There are some other factors also that may develop malignant biliary obstruction such as premalignant lesions.^[6] These can be namely biliary papillomatosis and others like autoimmune cholangiopathy. These may also manifest an obstructive picture similar to malignancy.

Clinical Manifestations

Mostly malignant biliary obstruction presents with few symptoms. Pancreatic carcinoma with a lesion in head of the gland - pancreas manifests with a painless jaundice which can be regarded as a classical sign.^[7] This can be classically seen as scleral icterus/ yellowness of skin. Whereas other neoplasms presents with symptoms like pruritis characterised by generalised itching of body which is a classical symptom. Dark urine can be visualised in some cases. Passing of light stools are also considered dangerous in elderly people more than 65 years of age. Right upper quadrant discomfort can also be seen with accompanying nausea. There are some non specific symptoms characterised mainly to malignancy

such as weight loss, anorexia etc. Night sweats also seen patients with malignancy.^[8]

Pancreatic cancer characteristically involves dull epigastric pain that radiates to the back due to pancreatic duct obstruction, palpable gallbladder would be palpable (Courvoisier's sign), generalised dyspepsia can be present in these patients. Pancreatic enzymes deficiency occurs hence gastric outlet obstruction and malabsorption occurs. Early satiety, new onset diabetes and acute pancreatitis supervenes. In 50% of patients abdominal pain predominantly in the right upper quadrant will be present.^[9] Pruritis (+) in 67% patients, weight loss in 57%. Peri hilar and distal bile duct lesions involve with mild jaundice. Whereas intra hepatic lesion involves pain.

Lab Investigations and Diagnostic Imaging

Serum bilirubin levels would be high as expected. Other parameters that can be considered are alkaline phosphatase and gamma glutamyl transpeptidase which can also be higher. Screening tests are done for a non specific CA19-9 which cannot be considered as a specific test and has a sensitivity of 80% and specificity of 83%. CA19-9 levels are elevated in many other cancers also namely, cholangio carcinoma, gastric cancer, esophageal cancer, hepatocellular carcinoma. It can be elevated in benign lesions like acute cholangitis or even acute pancreatitis. This test can show false positive in any biliary obstruction cases hence reducing the specificity of the test.

Cases arriving with the signs of jaundice preferably obstructive may be subject to computed tomography scan as well as other techniques such as magnetic resonance imaging associated by magnetic resonance cholangio pancreatography.^[10] Contrast CT scans and resonance imaging are highly beneficial in alarming the faculties about the levels and informing about the dilatation as well as defining the extent of the disease, thus providing a better platform to plan for further management. Pancreatography helps in providing sufficient information about the extent of biliary obstruction, levels of obstruction and presence of any variations suggesting pathology involving biliary confluence.

Jaundice is considered a major risk factor of malignant biliary obstruction. Jaundice induces impairment in cellular immunity thereby aids in tumour progression and hence metastatic spread. Bile availability would be greatly reduced in the enteric system as the flow is reduced due to bile obstruction. These all events affects absorption of vitamins. In vitamins lipid soluble vitamins are absorbed. Vitamin K which is a fat soluble vitamin is responsible for coagulation process. Deficiency of vitamin K leads to coagulopathy. These all factors make the patient unfit for surgery. Deficiency of vitamin K increases the risk of profused bleeding during surgery. As there is deficiency of vitamins changes occurs in the intestinal mucosa. This leads to increased susceptibility

to bacterial infections. Bacterial endotoxins translocate easily and lead to sepsis. SIRS is a well known complication.

Surgical Preparations

As soon as the doctors reach the appropriate diagnosis and the decision for further management is taken, the patient's coagulation profile is checked. The most important parameters involving the coagulation check-up are pro thrombin time and international normalised ratio. The levels of prothrombin test should always be less than 4 s. Whereas the international normalised ratio results should be less than 1.5.^[13] These parameters are very essentially maintained in order to avoid bleeding episodes. This is one of the major complications involving these cases. In patients with abnormal bleeding and coagulation profiles further management for correcting the coagulation issues should be undertaken. Vitamin K infusions are given for these kinds of patients. These can be done for more than three days. As soon as the patient tests results are within the normal range they can be considered for the procedure. Certain cases of emergencies are also reported which should be taken care of. For instance, a cholangitis patient with high risk of septicaemia. These types of patients are highly vulnerable and fresh frozen plasma should be administered prior to and even throughout the procedures. Drainage procedures are done in this patient as soon as the emergency situations are under control. Fresh frozen plasma should be collected and kept ready prior to the surgery as a precaution in case of any bleeding complications. The surgeon must make sure that antibiotics are administered prior to the surgery. Cephalosporin infusions are commonly given for these kinds of patients. Fasting is preferred for some patients before the surgery and not less than three hours is preferred.^[14] In the presence of certain contraindications percutaneous biliary drainage cannot be performed. For instance in presence of ascites, ascitic fluid should be drained prior to the procedure. A pre procedure ultrasound is of great use in providing knowledge about the approach needed to be used for the intervention.

Management

The clinical status and disease progression are the primary important deciding factors that contributes to the selection of nature and mode of the stent placement, including resectable disease, locally invading disease treated with help of neo adjuvant therapy, and metastatic progression in which only palliative option is the best.^[15] Other kinds of modalities that can be considered includes the following methods like per cutaneous drainage of fluids, ultrasound guided endoscopy procedures.

OPERABLE LESIONS

Percutaneous Transhepatic Biliary Drainage

Prior to surgical excision of the lesion, the biliary tree need to be decompressed. It is considered, the devastating effects of biliary blockage can be improved to a certain extent with decompression. The abnormal

bilirubin levels should be brought within the normal range. Bilirubin levels drops to a greater extent such that it reaches almost close to normal. This is highly essential as it reduces the effects of toxicity that are being expected from the chemotherapy. The liver enzymes should be monitored. In similar cases, percutaneous transhepatic external biliary drain should be considered. In order to limit the risk of ascending cholangitis the radiologist should make sure that the drain is externally placed as this may intervene the surgical excision. A per cutaneous trans hepatic cholangiogram is done by the help of a 21 G needle. This is obtained under ultrasound guidance. As the direct access into the biliary system is confirmed, contrast medium is injected under fluoroscopy surveillance. Thereby understanding the level of obstruction. A 0.021" micro wire is inserted through the 21 G needle into the biliary tree. A 0.035" coaxial system is also inserted over the same. 0.021" is made to exchange for 0.035" glide wire usually a stiff type is used for the purpose. If the patient is known to be non septic more contrast medium is injected. However if the patient is known to be septic the contrast injection should be very much limited as there is high chance for septicaemia. A multi hole all-purpose locking pigtail drain catheter is inserted on top of 0.035" guide wire. Which is later connected to an external bag. As there is high chance of dislodging, the drain should be firmly adhered to the skin. In some patients with difficulty to traverse the stricture, an external drainage catheter can be used with tip closer to the occlusion and followed by insertion episodes after a few days. These practices help in reducing the inflammation and related edema present. Regarding strictures not proximal to the hilar regions in which the primary biliary system is not occluded, the methods are comparatively easy and even a single drainage is more than enough. Drainage involving one or all two systems can be done when the primary biliary system is completely occluded. Whenever secondary confluence are also involved multiple insertions and drainage are required. If the histological pattern is not visualised under ultrasound guidance a transbiliary biopsy may be taken prior to drain insertion as access to the hepatic system is patent. There are many complications involved with percutaneous transhepatic biliary drainage like bleeding, sepsis etc. There are also reported cases of inflammation involving peritoneum and even biliary leakage. More than 5 % mortality chances are reported. There are many factors that may induce these complications. Increased levels of white cell count and C-reactive proteins are associated with increased mortality rates. Even reduced hemoglobin, and more bilirubin levels are also dangerous.

Portal Vein Embolization

Portal vein embolizations are considered only in cases of comparatively large obstructions, which involves excision of a larger portion of the liver parenchyma and are done supplementary to the removal of biliary system fluid. Portal vein embolization procedure gives way to increased cell growth of the opposite liver lobe and helps

achieve a sufficient pertaining percentage of liver parenchyma even after the excision of the mass.^[16] Initially an access is made into the portal system with the aid of percutaneous ultrasound guidance. This is made possible by using a 21 G needle and the system size is increased to 0.035". Portal vein embolization can be performed with the aid of coils and plugs. Or even particles or histo acryl glue may be used for the same purpose. Embolization may be performed as a continuous procedure or even as a dual stage procedure.^[17]

Non Operable Lesions

In inoperable obstruction cases placement of biliary stents are the chief mode of management. As the biliary tree is blocked and distended / dilated proper drainage of the biliary fluid is beneficial and is the initial goal of the treatment. This practice helps in retrieving the liver parenchyma and its functions back to normal. Thereby gives a sufficient symptomatic relief to the patient. And it also benefits in the application of chemotherapy. Few decades back laparotomy preferably exploratory was done as a palliative form of intervention.^[18] And it helped in giving a clear picture about the extend and level of the disease. But nowadays there are tremendous improvements in the case scenario as modern imaging techniques are used. More cross sectional imaging modalities are used. And they facilitate in the appropriate fixation of stents. There are two options for the placement of these stents, it can either be percutaneous or can also be placed by endoscopic means.

Stents

There are two kinds of stents than can be taken into consideration namely, polyethylene or plastic stents and self expanding metallic stents. Polyethylene made stents are used for the management of biliary confluence occlusion in most of the cases and are shown to be having excellent prognosis considering a short time span.^[19] A variety of stents in varying diameters are available nowadays. They include^[7] french upto (11.5) French in diameters. The merits for these kind of stents are the cost efficacy. Another is that they can be removed whenever in need such as during surgery. The nature of stent needed to be placed as the treatment modality depends on certain other crucial elements also such as life expectancy, and possibility of not being a benign lesion / mass. In hilar blockages the stents are applied laterally involving one side commonly which also happens in cases of percutaneous biliary tract drainage. In some cases stents are applied on both sides in which it becomes a necessity that both the stents are placed concurrently. This is important as it allows the two stents sufficient space to expand normally. It also gives an advantage of proper drainage of the concerned biliary tract. Few cases were also reported were opposite sides were also involved after placing stents on one side only. When surgeons come across these situations, managements are done by keeping the lowest portion of the prosthesis within the previously kept stent. This

practice gives way to proper expansion as well as sufficient removal of biliary tract fluid.

Bare - Stents

These kinds of stents came into use almost quarter a century ago. As the plastic stents are accompanied with many demerits these types of new modalities were preferred. First of all as a big lumen is made inside the liver and afterwards a polyethylene type stent is introduced into the lumen. When it is placed with the guidance of an endoscope 12- Fr sized plastic stent is used. This is the at most maximum allowable size.^[20] Similarly in case of a per cutaneously placed stent 14 Fr size is used. They are always a threat for proper sealing of the lumen. Fortunately, metallic nature stents are routinely placed using a 6 or even 7 Fr carrying catheter and they can be made to reach the specified lumen of even up to 30 Fr whenever is used. Metallic stents are always costly compared to other types of stents, but also due to their long standing patency they are considered effective in terms of money too. Numerous studies world wide had shown that compared to polyethylene stents metallic stents are less likely to get occluded. The efficacy of the metallic stents completely depend on the peculiar design. It is mostly made up of nitinol and also metallic stain less steel stents are available. They are usually made in a tubular design.

Covered Biliary Stents

These kind of stents have a peculiar design, in which, inspite of the tubular pattern mesh they are also made with a covering that is made of a thin membrane. The materials are usually made of polyurethane and silicone. There are some other stents which gives promising results by suppressing the tumour cell proliferation further. These are made of e PTFE / FEP. Commonly used carrying catheter of these stents are larger than ones used by metallic ones. In some cases before placing a covered stent a measuring pigtail is used. It is used for understanding the extend of the lesion. Depending on the site of placement of the stent there are some drawbacks particularly to covered stents. For instance when a covered stent is placed adjacent to cystic duct there is high chance for cholecystitis.^[21]

Lesions Associated With Hilum

The scenario changes when obstruction comes to the level of hilar regions. The access into the biliary tract need to be acquired from both the sides. The surgeon should make sure that both the stents should be kept concurrently. In common practice its done in a Y configuration. The types of stents placed in these cases are routinely bare ones. In a few cases covered types are also placed. These are for instance in biliary obstructions were cystic ducts are not involved. Seven configuration is used in some surgeries, these are not common and are done only in cases when entry into the biliary tract from even both sides are not possible. The seven type stents are manufactured in a peculiar fashion. They are delicately made in the central area of the mesh compared

to other types of stents. This is possible by reducing the mesh struts available in the center. This allows easy entry of another mesh.

Radio Frequency Ablation

Radiofrequency ablation is a specialised technique used in neoplasm treatment. In ablation technique alternating electric current is used widely. These currents are applied in high frequency and more rapidly to ensure that proper energy is produced.^[22] It is a complex process. The tumoral tissue is traversed under the proper guidance of an imaging modality. Thereby placing a particle in the tissue. This particle acts as an electrode such that energy is transferred with the help of this particle. Recently, many studies have been conducted in understanding the efficacy with devices for radio frequency ablation by traversing through the bile ducts. These experiments were first done on certain animals. Some live human cases were also considered for the study. It was found out that the device was efficient when the metal stents were applied in narrowed areas after frequency ablation procedure was done. Previously done endoscopic studies were not successful as compared to percutaneous placement of stents traversing the liver. More experiments are being undertaken in this modality nowadays.

Stent Occlusion

Whenever a stent is known to be occluded the procedure is needed to be repeated and proper drainage need to be done. If distal common bile duct is subject to occlusion and a stent is kept as a treatment modality there is high chance for blockage of the stent, even though the pathways may differ. Talking about polyethylene stents a bio - film synthesis is reported and also some colonies of bacterias are found in some cases. Whereas proliferation of some tissues that grows into the mesh at the level of the mass is the main origin of blockage in case of uncovered metallic stents.^[23] In case of partially covered / fully covered metallic stents the scenario is different. In these cases migration take place involving the stent. This give way to increased proliferation of tissue cells most commonly at the borders of the stent. In some previous studies it has been explained that some food particles from the duodenal lumen reergitate into the biliery confluence. These kinds of reverse back flow may also lead to blockage of the fixed stent. There are high chances of early blockage of these stents. This may be seen associated with stent application and leading to fractures involving the stent design.^[24] These kinds of malfunctions occur when dilatation procedures are done associated with ballooning. Whenever a stent is known to be occluded the procedure is needed to be repeated and proper drainage need to be done.

CONCLUSION

Radiological interventions plays an important role in the management of malignant biliary obstructions. They are comparatively less invasive, and use various imaging modalities in the diagnosis and treatment of the

concerned diseases. The type and nature of malignancy, as well as stage of disease may be considered as the primary factors that helps the surgeon /radiologists in arriving at a decision whether the patient should be treated before the excision of the mass lesion or not. In many cases drainage of biliary fluids prior to the surgical procedures are avoided as there may be high chances of pathological infections. In cases attributed to local lesions metallic stents (SEMS) are found to be the best available modality in strictures occurring not proximal to hilar regions whereas strictures involving the hilar regions are treated best with percutaneous drainage of biliary fluids(PTBD) as well as drainage through endoscopic guidance (ENBD). Other modalities such as photo dynamic therapy and radio frequency ablations are found to increase the prognosis. More researches and experiments are followed on ablation techniques. Best regards to all radiologists and surgeons working on further researches on malignant biliary obstruction.

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