Histopathological examination following side-by-side placement of metal stents for malignant hilar biliary obstruction

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A B S T R A C T

Background: Endoscopic-guided placement of metal stents for unresectable malignant hilar biliary obstruction (UMHBO) is performed using partial stent-in-stent or side-by-side (SBS) techniques. The latter involves placing sequential stents within the bile duct. Excessive dilation of the bile duct during stent placement can have serious effects on the surrounding organs.

Methods: This study details seven cases of SBS placement of 8.0 mm metal stents for UMHBO. Histopathological examinations were performed to identify the effects on the bile duct and surrounding tissues.

Results: The mean post-placement diameter of the bile ducts was 13.86 mm, and no compression necrosis or thrombi were observed in surrounding tissues. Cholangitis occurred in five cases, and death occurred as a result of cholecystitis in one case.

Conclusion: The use of 8.0-mm stents for SBS is unlikely to have major negative effects on peribiliary tissues and blood vessels. However, post-placement cholecystitis can result in increased mortality; thus, gallbladder drainage should be considered.

Keywords: Autopsy; Bile duct obstruction; Cholangiocarcinoma; Cholangiopancreatography, endoscopic retrograde

Introduction

Endoscopic biliary drainage for unresectable malignant hilar biliary obstruction (UMHBO) is performed via bilateral drainage, unilateral drainage,1,2 or placement of either plastic or metal stents3 depending upon the facility and attending physician. For metal stent placement for UMHBO, partial stent-in-stent (PSIS) and side-by-side (SBS) techniques are the major procedures. During the SBS procedure, a thin 6-Fr delivery system is used to advance two guidewires to the right and left intrahepatic ducts (targets), allowing simultaneous placement of two metal stents.4,5 Thus, the SBS procedure is easier than the PSIS procedure. However, Naitoh et al6 reported that while no differences were observed in terms of stent placement success rate and patency duration, the SBS technique was associated with increased procedural accidents such as hepatic abscess and cholecystitis. Additionally, since the SBS technique involves sequential placement of two metal stents in the extrahepatic biliary duct, over-dilation of the duct can lead to mucosal damage and thrombi in the portal vein, which runs parallel to the duct.7,8 Thus, histopathological investigation of the biliary ducts and peribiliary tissue is necessary following SBS stent placement. Herein, we examined the safety and associated problems of indwelling stents with the SBS procedure using autopsy cases.

Methods

Seven individuals were examined who had died because of primary disease despite having undergone metal stent placement in the biliary duct using SBS procedure at our hospital and related facilities. The subjects’ families provided written consent to perform pathological autopsy. Table 1 shows the subjects’ background information. The metal stent utilized was a Zilver 635 biliary metallic stent with a diameter of 8.0-mm (Cook Medical, Bloomington, IN, USA).
The delivery system of this stent is thin at 6 Fr, it is possible to allow simultaneous placement of two metal stents. It is a laser-cut type metal stent and made of nitinol, and it is characterized by being able to place a stent at a target part because there is almost no shortening. Two stents with a length of 6.0 cm were used in three cases; two stents with a length of 8.0 cm were used in two cases; and in two cases in which the stricture length was 6.0 cm and 8.0 cm, two stents each (total of four stents) were used in parallel, respectively. In all cases, the end of the stent on the ampulla side was placed within the bile duct. In all cases, endoscopic sphincterotomy was performed when placing the stents. There were no cases of procedural complications, such as pancreatitis, hemorrhage, or perforation, associated with stent placement. There were four cases (57.1%) with stent obstruction after placement. The mean duration between placement and obstruction was 109 days, with a range of 14 to 204 days. In three cases (42.9%), an additional 8.0 mm stent was placed within the original stent due to obstruction associated with intra-stent invasion of the tumor. Mean duration of stent placement was 186 days but ranged from 30 to 518 days.

We investigated maximum extrahepatic bile duct diameter after stent placement, intra-stent tumor invasion, overgrowth, and formation of biliary sludge and granulation. Furthermore, items related to the lateral side of the stent; namely, stent wire depth, compression necrosis and thrombi formation in the tumor and surrounding tissues, intrahepatic cholangitis, intrahepatic cholecystitis, and hepatic abscess; were investigated. Histopathology or macro-inspection was conducted.

This study is a retrospective case series, and the ethics committee of our hospital is a study that was judged not to be reviewed.

### Results

Table 2 shows the autopsy results. The mean maximum bile duct diameter after stent placement was 13.86 mm. Fig. 1 presents...
macro-observation findings of the extrahepatic bile duct in Cases 3 and 5, respectively. In Case 5, thrombosis in the extrahepatic portal vein, which runs parallel to the extrahepatic bile duct, was observed. A thrombus due to repeated endoscopic sclerotherapy for esophageal varices caused by liver cirrhosis was determined to have existed before stent placement.

Although stents placed in tumor sites were patent in all cases during autopsy, tumor invasion into the stent lumen was observed in five cases (71.4%), while overgrowth was observed in one case (14.3%). Fig. 2A presents macro-observations and Fig. 2B presents histopathological findings of the tumor site in Case 2. The degree to which the stent wire was embedded into the biliary wall differed with site and thus was not uniform; however, in all cases, the fibromuscular layer was the deepest level. Histopathological findings at the tumor site in Case 3 (Fig. 3) indicated that the stent wire was embedded into the fibromuscular layer. Histopathological findings at the non-tumor and tumor sites in the extrahepatic bile duct in Case 5 (Fig. 4A) and Case 4 (Fig. 4B), respectively, indicated that although the stent wire pushed the submucosal layer aside and allowed penetration into the fibromuscular layer, it did not affect the hepatic artery or portal vein. Histopathological findings for the non-tumor site of the intrahepatic bile duct where the stent was placed in Case 4 (Fig. 4C) indicated that although the stent wire extended to the portal vein region of the fibrous tissue, compression necrosis of hepatic cells was not observed.

In all cases, macro-observation of the bile sludge accumulation was observed within the bile ducts. Cholestasis in the intrahepatic bile duct was observed in four cases (57.1%), intrahepatic cholangitis in five cases (71.4%), and liver abscess in four cases (57.1%). The direct cause of death was cancer in six cases and gallbladder perforation due to cholecystitis in one case. Autopsies revealed cholecystitis in two patients (28.6%), who experienced cystic duct obstruction due to tumor invasion. In Case 1, intrahepatic cholangiocarcinoma invaded directly from the hilar bile duct into the hepatoduodenal ligament, the cystic duct and was occluded.
Discussion

The techniques of PSIS and SBS do not differ in terms of procedural complications; however, the SBS technique carries the risk of procedural complications caused by over-dilation of the bile duct. Matsui et al. carried out histopathological investigation of 15 cases in which either a single metal stent or covered and uncovered metal stents were placed using the PSIS technique. This maintained good patency of the bile duct lumen; consequently, no compression necrosis of the biliary tissue nor vascular obstruction were observed. Hanada et al. suggested that a high frequency of portal vein thrombosis was caused by pressure displacement along the short axis of the metal stent in cases of hilar cholangiocarcinoma in which uncovered metal stents were placed using the PSIS technique. However, these reports did not include cases in which stent placement was performed using the SBS technique.

The course of the extrahepatic bile duct runs parallel with the portal vein and hepatic artery, which run within the hepatoduodenal ligament. Thus, bile duct expansion may affect the surrounding vessels. However, although all cases showed displacement of the stent wire into the fibromuscular layer, no resultant effect on the portal vein or hepatic artery was observed. There were no cases of thrombus formation in the portal vein or hepatic artery after stent placement. However, the use of metal stents with 10.0 mm diameters requires care so that stent placement does not affect surrounding tissues. These stents are primarily used with further dilation of the extrahepatic bile duct and when three or more metal stents are used in parallel.

Herein, intrahepatic cholangitis and liver abscess occurred simultaneously in two cases, and tumor invasion led to cystic duct obstruction. In these cases, cholecystitis also occurred; and in one case, gall bladder rupture was the direct cause of death. Risk factors for cholecystitis following metal stent placement include stent placement with strong axial force and tumor invasion into the gall bladder. Recently, metal stents with strong expansive force along the short axis and covered stents have been used when performing the SBS technique. However, in such cases, attention must be paid to possible cholecystitis following stent placement. In cases where cholecystitis progresses to fatality; gall bladder drainage should be considered as early as possible.

Various metal stents might be placed using the SBS technique in the future. Since the metal stent diameter, number of metal stents required, and the expansive force all have different effects on the extrahepatic bile duct, the SBS technique should be performed in more cases to identify safe stent placement procedures.

Our study limitation is that few cases were examined because autopsy cases were used. Future studies should evaluate the safety of stent placement using the SBS method in many cases.

In conclusion, placement of an 8.0-mm diameter metal stent using the SBS technique has little effect on the peribiliary tissues and vessels through excessive dilation. However, as cholecystitis in cases of tumor invasion in the cystic duct can lead to fatality, early re-intervention for drainage and other procedures should be considered at cholecystitis onset.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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