

GB malignancy accounts for 80-90% of all biliary tract cancers. It is an aggressive malignancy with poor overall survival. An SCF, in the case of carcinoma gall bladder, is exceedingly rare with only 3 cases of SCF in patients with GB cancer are reported to date.

In addition to GB wall thickening on imaging, which was suspicious of malignancy, the patient had palpable supraclavicular nodes that were metabolically active on a whole-body PET scan without any metabolic activity in regional abdominal lymph nodes. In this case, metastatic involvement of supraclavicular nodes will make the tumour unresectable. Given suspicion for metastasis, USG guided supraclavicular lymph node FNAC was done. However, when FNAC was done, metabolic activity seen on PET scan in the supraclavicular was indeed due to tubercular lymphadenitis with the presence of granulomas. We previously described the association of tuberculosis in cases of GB cancer, which can influence staging and further management. Seven patients had tuberculosis in association with carcinoma gall bladder. Two patients had supraclavicular lymph nodes, two patients were detected to have TB in inter aortocaval nodes, and one had peritoneal tubercular nodules. Two patients had tuberculosis in dissected hepatoduodenal ligament lymph nodes. At least five of the seven patients would have been deemed unresectable if sampling of nodes was not done. Hence, FNAC and lymph nodes sampling need to be done when IAC or left supraclavicular nodes are involved in a case of carcinoma gallbladder in an otherwise resectable disease.⁵

The patient had a decrease in GB mass metabolic activity, after which the patient underwent definitive surgical resection after initiating ATT and starting NACT. This is the only reported case of SCF associated with adenocarcinoma GB, which has been treated with definitive surgical resection. It has been eight months since the diagnosis of malignancy has been established, and the patient has completed four months of postoperative follow-up and is recurrence-free.

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Nasobiliary Drainage for Intrahepatic Cholestasis and Pruritus Refractory to Medical Therapy: A Series of Three Cases

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Benign recurrent intrahepatic cholestasis (BRIC) and acute viral hepatitis (AVH) are two examples of conditions that can result in intrahepatic cholestasis. Antihistaminics and cholestyramine are generally used for managing pruritus. Some cases have severe pruritus refractory to

all medical therapies. Pruritus may be associated with severely impaired quality of life and inability to sleep. We present two cases of BRIC and one case of AVH in which the patients had pruritus refractory to medical therapy.

Case Series

Case 1: A 40-year-old male presented with yellow discoloration of eyes and high colored urine associated with severe pruritus for 2 weeks. A liver biopsy was done after negative viral and autoimmune markers. The liver biopsy showed bland cholestasis consistent with BRIC. As the patient had severe pruritus refractory to medical therapy with impaired quality of life, the option of NBD was discussed, and NBD placement was done. NBD was removed subsequently after 3 weeks at a Bilirubin level of 5.5 mg/dl. No complication was noted.

Case 2: A 32-year-old male with history of cholestatic jaundice twice in past, presented with 2 weeks history of jaundice and severe pruritus with consequent insomnia and impaired quality of life. Liver biopsy showed bland cholestasis consistent with BRIC. The option of NBD was discussed in view of severe pruritus refractory to medical therapy. NBD was removed subsequently after 16 days at a Bilirubin level of 20.6 mg/dl. No complication was noted.

Case 3: A 27-year-old male diagnosed with acute hepatitis A infection had prolonged cholestasis for 8

weeks and presented with severe pruritus refractory to medical management. NBD placement was done at bilirubin level of 42.3 mg/dl. The patient had fever after NBD placement, which improved on antibiotics. NBD was removed subsequently after 1 month at a bilirubin level of 18.5 mg/dl.

These patients received ursodeoxycholic acid, hydroxyzine and cholestyramine. One patient also received naltrexone and steroids. These patients presented four to 8 weeks after the onset of jaundice with increasing bilirubin levels and pruritus refractory to medical therapy. All patients were seen at several sites before coming to our center; however, none of them had previously been offered the option of naso-biliary drainage. In our centre, the potential complications of ERCP were explained and the alternative of NBD was given to the patient. A 7 Fr NBD was placed after selective cannulation of the common bile duct. Endoscopic papillotomy was not done since it would have increased the procedure-related risk of pancreatitis. **Table 1** shows the clinical and biochemical parameters of 3 patients. All the three patients had negative work up for underlying auto-immune disease (anti-nuclear antibody, anti-mitochondrial antibody, anti-smooth muscle antibody, and anti-liver kidney microsomal antibody). MRCP showed normal appearance of the biliary tree in all patients. All the patients had remarkable improvement of pruritus after 48 to 72 hours of NBD insertion.

Table 1: Clinical characteristics of patients with cholestatic hepatitis.

Characteristic	Case 1	Case 2	Case 3
Age (years)/ Sex	40, M	32, M	27, M
Bilirubin (T/D) (mg/dL)*	22.5 / 20.1	32.5 / 29.7	42.3 / 33.5
AST / ALT (U/L) at NBD placement	61 / 76	22 / 29	35 / 28
SAP (U/L)	289	201	177
GGT (U/L)	89	79	92
Viral markers**	Negative	Negative	IgM anti-HAV reactive
MRCP	Normal	Normal	Normal
Liver biopsy	Bland cholestasis	Bland cholestasis	Not done
Clinical diagnosis	BRIC	BRIC	Acute viral hepatitis A
Time to normalization of LFTs	9 weeks	16 weeks	11 weeks
NBD duration	21 days	16 days	1 month

* Liver function test at the time of NBD placement, ** included HBsAg, anti HCV, IgM anti HAV and IgM anti HEV, MRCP: magnetic resonance cholangiopancreatography, BRIC: benign recurrent intrahepatic cholestasis, LFTs: liver function tests.

Discussion

Bile salts are the main agents thought to cause pruritus associated with jaundice. Biliary drainage is the most effective treatment for pruritus and itching subsides very soon following NBD placement. The relief in pruritus occurs prior to a significant decrease in serum bilirubin concentration. Several pharmacological agents have been tried; however, occasionally, pruritus remains refractory to these medications.^{1,2} NBD interrupts the entero-hepatic circulation of bile salts and leads to improvement of pruritus. Stapelbroek *et al* used NBD in 3 patients with BRIC associated pruritus and demonstrated improvement within 24 hours.³

Singh *et al* used NBD in six patients with cholestatic acute viral hepatitis and intractable pruritus prospectively. The authors noted that naso-biliary drainage hastened the recovery in these patients.⁴ Hedage *et al* analyzed retrospective data from five European centres. Pruritus was quantified using a visual analogue scale (VAS). 27 patients (59% females) underwent 29 nasobiliary drainage procedures. The median duration of NBD was 7 days. NBD decreased pruritus in 89.6% of cases (VAS from 10.0 to 0.3, $p < 0.0001$). The median percentage decline in pruritus was 94% and 33% of patients were free of pruritus within 24 hours. The duration of treatment response was independent of duration of drainage and bile output. The authors also noted significant improvements of serum alkaline phosphatase and serum bilirubin.⁵ Yakar *et al* used NBD in 16 patients (25 NBD procedures) with BRIC and refractory pruritus while 17 patients were managed by medications. The authors noted longer clinical remissions in the NBD group.⁶ It is important to note that ERCP can lead to pancreatitis. Mild post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis occurred in 31% of cases in series by Hedage *et al*.⁵ Yakar *et al* also noted pancreatitis in one out of 16 patients.⁶ A small size NBD catheter and avoidance of papillotomy can decrease risk of ERCP associated pancreatitis.⁷

Conclusion

We have presented above a series of 3 cases with refractory pruritus secondary to intrahepatic cholestasis, all of whom had remarkable improvement after NBD placement. NBD can be a very useful modality in such cases but it is rarely used due to lack of awareness.

Acknowledgements: Mr Yogesh Saini (research coordinator)

Funding: none.

Conflict of interest: none

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