Case Report

Primary Neuroendocrine Tumor of the Left Hepatic Duct: A Case Report with Review of the Literature

Ajay H. Bhandarwar, Taher A. Shaikh, Ashok D. Borisa, Jaydeep H. Palep, Arun S. Patil, and Aditya A. Manke

Division of GI and HPP Surgery, Department of Surgery, Grant Medical College & Sir JJ Group of Hospitals, Byculla, Mumbai 400008, India

Correspondence should be addressed to Ajay H. Bhandarwar, abhandarwar@yahoo.com

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1. Introduction

NET is derived from the embryonal neural crest cells called Argenta"ff"n or Kulchitsky cells and have a potential for secreting serotonin. This tumor can arise anywhere in the distribution of the Argenta"ff"n cell system. In addition to the most common sites of occurrence, namely, ileum and appendix these tumors have reported to occur in bladder, prostate, rectum, stomach, bronchi, pancreas, and biliary tree.

Primary Biliary Tract Neuroendocrine tumors (NET) are extremely rare tumors with only 77 cases been reported in the literature till now. We describe a case of a left hepatic duct NET and review the literature for this rare malignancy. To the best of our knowledge the present case is the first reported case of a left hepatic duct NET in the literature. In spite of availability of advanced diagnostic tools like Computerized Tomography (CT) Scan and Endoscopic Retrograde Cholangio Pancreatography (ERCP) a definitive diagnosis of these tumors is possible only after an accurate histopathologic diagnosis of operative specimens with immunohistochemistry and electron microscopy. Though surgical excision remains the gold standard treatment for such tumors, patients with unresectable tumors have good survival with newer biologic agents like Octreotide.

2. Case Report

A 69-years-old female presented with colicky pain in the right hypochondrium since 3 years. She had past history of open cholecystectomy done for gall stones 15 years back. On physical examination the patient was anicteric with soft abdomen. An Ultrasonography (USG) of the abdomen showed a hypoechoic lesion of size 3.5 cm × 4 cm in segment 4 of the liver. Computerized Tomography (CT) of the abdomen showed a 4.1 × 3.7 cm heterogeneously enhancing mass lesion in segment IV of liver abutting the left branch of portal vein (Figure 1). A Magnetic Resonance Imaging (MRI) of upper abdomen with Magnetic Resonance CholangioPancreatography (MRCP) showed a filling defect in the left hepatic duct with lesion in the adjacent part of liver in segment IV, suggestive of a left hepatic duct tumor with infiltration in the liver (Figure 2). Tumor marker serum alfa fetoprotein was mildly raised. Patient was worked up for left heptectomy. Intraoperatively a lesion arising from the left hepatic duct involving the left branch of portal vein and extending upto the portal confluence was found (Figure 3) rendering the tumor unresectable. A biopsy was
taken from the mass and procedure was abandoned in view of inoperability. Histopathology showed typical rosette appearance of a neuroendocrine tumor (Figure 4) and immunohistochemistry positive for CD56, Chromogranin and Synaptophysin (Figure 5). Ultrastructural study of the cell with electron microscopy (Figure 6) showed the presence of multiple neurosecretory granules with muscle tissue.

A whole body Positron Emission Tomography (PET) scan and an Octreotide labeled radionulceotide scan showed somatostatin receptor expressing lesion in the hepatobiliary system (Figure 7).

The patient was started on long-acting Octreotide therapy single dose every month. The patient has received 12 of such doses and is doing well after a 1-year followup without any complications. A follow up MRI (Figure 8) upper abdomen with MRCP at 1 year showed the absence of filling defect in the Left hepatic duct that was seen previously which showed tumor regression.
Figure 6: Electron microscopy picture showing multiple granules of varying sizes.

Figure 7: PET Scan (a) and Octreotide labelled (b) scan showing tumor limited to the hepatobiliary system.

Figure 8: Follow up MRCP at 1 year showing absence of any filling defect in the left hepatic duct.

3. Discussion

Primary Biliary-tract NETs are very rare. They account for 0.2–2% of all gastrointestinal NET [1, 2] reason being the paucity of enterochromaffin cells from which NETs arise in this area. Chronic inflammation of the bile duct epithelium is responsible for metaplasia of these enterochromaffin cells and formation of NET.

Davies [3] in 1959 reported NET of the distal bile duct and pancreatic duct which represented more of a periampullary NET rather than a biliary tract. Pilz [4] in 1961 was credited to report the first case of a Biliary Tract NET. After an extensive search of the Medline only 77 cases of Biliary Tract NET have been reported so far in the literature since 1961 (Table 1).

Till now no NET in the literature has been reported in the isolated left hepatic duct possibly making our case the first reported case of an isolated left hepatic duct NET.
### Table 1: Showing study of reported cases of Biliary tract NET.

| No. | Case reference       | Age | Sex | Complaint                      | Location |
|-----|----------------------|-----|-----|---------------------------------|----------|
| (1) | Pilz, [4] 1961       | 55  | F   | Weakness, RUQ pain, jaundice    | CBD      |
| (2) | Little et al., [5]   | 41  | F   | Autopsy finding, Jaundice, pain| Hilar    |
| (3) | Bergdahl, [6] 1976   | 79  | F   | Jaundice                        | Distal CBD |
| (4) | Judge et al., [7]    | 19  | M   | Jaundice                        | Hilar    |
| (5) | Gerlock and Muhletaler [8] 1979 | 32 | M   | Jaundice                        | CBD      |
| (6) | Vitaux et al., [9]   | 24  | M   | Jaundice                        | Distal CBD |
| (7) | Nakamuara et al. [10] 1981 | 58 | F   | Jaundice                        | CBD      |
| (8) | Abe et al., [11]     | 64  | M   | Jaundice                        | CBD      |
| (9) | Goodman et al., [12] | 28  | F   | RUQ Pain                        | Cystic duct |
| (10)| Jutte et al., [13]   | 62  | M   | Back Pain                       | CHD      |
| (11)| Nicolescu and Popescu, [14] 1986 | 50 | F   | RUQ pain                        | CBD      |
| (12)| Alexander et al., [15] 1986 | 64 | F   | Hematemesis                     | CBD      |
| (13)| Gastinger et al., [16] 1987 | 65 | F   | Jaundice, Pain                  | Hilar    |
| (14)| Reinhardt et al., [17] 1988 | 71 | F   | Jaundice, fever                 | CBD      |
| (15)| Chittal and Ra, [18] 1989 | 46 | F   | RUQ pain                        | Cystic duct |
| (16)| Fujita et al., [19] 1989 | 55 | F   | RUQ pain                        | CBD      |
| (17)| Bickerstaff and Ross [20] 1989 | 57 | F   | Jaundice                        | CBD      |
| (18)| Brown et al., [21] 1990 | 35 | F   | Jaundice                        | Hilar    |
| (19)| Bumin et al., [22] 1990 | 38 | F   | Jaundice                        | CBD      |
| (20)| Fellows et al., [23] 1990 | 30 | M   | Jaundice                        | CBD      |
| (21)| Besznyák et al. [24] | 13  | F   | Jaundice                        | Hilar    |
| (22)| Angeles-Angeles et al., [25] 1991 | 39 | F   | Jaundice                        | CBD      |
| (23)| Barron-Rodriguez et al., [26] 1991 | 36 | M   | Jaundice, RUQ pain             | CBD      |
| (24)| Newman et al., [27] 1992 | 15 | F   | N/A                             | CBD      |
| (25)| Dixon et al., [28] 1992 | 60 | F   | RUQ pain                        | CBD      |
| (26)| Rugge et al., [29] 1992 | 64 | F   | Jaundice, RUQ pain              | Cystic duct, CBD |
| (27)| Gembala et al., [30] 1993 | 28 | M   | Jaundice                        | Hilar    |
| (28)| Mandujano-Vera et al., [31] 1995 | 53 | F   | Jaundice                        | CBD      |
| (29)| Sankary et al., [32] 1995 | 47 | F   | Jaundice                        | Hilar    |

### Table 1: Continued.

| No. | Case reference       | Age | Sex | Complaint                      | Location |
|-----|----------------------|-----|-----|---------------------------------|----------|
| (30)| Hao et al., [33] 1996 | 47  | M   | Incidental finding              | CBD      |
| (31)| Kopelman et al., [34] 1996 | 44 | M   | Jaundice                        | CBD      |
| (32)| Belli et al., [35] 1996 | 78  | M   | Jaundice                        | CBD      |
| (33)| Bembeneck et al., [36] 1998 | 12 | F   | Jaundice                        | Hilar    |
| (34)| Nahas et al., [37] 1998 | 61  | F   | Jaundice                        | Hilar    |
| (35)| Ross et al., [38] 1999 | 65  | F   | Jaundice                        | CBD      |
| (36)| Chamberlain and Blumgart [39] 1999 | 37 | F   | Itching                         | Hilar    |
| (37)| Chamberlain and Blumgart [39] 1999 | 67 | F   | Itching                         | Hilar    |
| (38)| Hermina et al., [40] 1999 | 69 | M   | RUQ pain                        | Cystic duct |
| (39)| Perakath et al. [42] 2000 | 36 | F   | Jaundice, Pain                  | CHD      |
| (40)| Chan et al [41] 2000 | 14  | M   | Jaundice                        | Hilar    |
| (41)| Maitra et al., [42] 2000 | 53 | F   | Jaundice                        | CBD      |
| (42)| Maitra et al., [42] 2000 | 61 | F   | Jaundice, itching               | Hilar    |
| (43)| Jutturi et al., [43] 2000 | 43 | M   | Jaundice, itching               | CBD      |
| (44)| Turrion et al., [44] 2002 | 51 | F   | Jaundice, itching               | Hilar    |
| (45)| Pawlik et al., [45] 2003 | 59 | M   | Jaundice                        | Hilar    |
| (46)| Podnos et al., [46] 2003 | 65 | F   | Choledocholithiasis, CBD        | CBD      |
| (47)| Podnos et al., [46] 2003 | 27 | M   | Jaundice, itching               | CBD      |
| (48)| Volpe et al., [47] 2003 | 19 | M   | Jaundice, pain                  | CBD      |
| (49)| Menezes et al., [48] 2005 | 30 | M   | Jaundice                        | CHD      |
| (50)| Ligato et al., [49] 2005 | 33 | F   | Irritable bowel                 | Hilar    |
| (51)| Hubert et al., [50] 2005 | NA | M   | Jaundice                        | CBD      |
| (52)| Hubert et al., [50] 2005 | NA | M   | Jaundice                        | CBD      |
| (53)| Hubert et al., [50] 2005 | NA | F   | Jaundice                        | CBD      |
| (54)| Nesi et al., [51] 2006 | 30 | M   | Jaundice, diarrhoea             | CBD      |
| (55)| Kim et al., [52] 2006 | 67  | F   | Jaundice                        | CBD      |
| (56)| Caglikulecki et al., [53] 2006 | 40 | F   | Jaundice                        | Hilar    |
| (57)| Honda et al., [54] 2006 | 76 | M   | Jaundice, pain                  | CBD      |
Table 1: Continued.

| No. | Case reference | Age | Sex | Complaint | Location |
|-----|----------------|-----|-----|-----------|----------|
| (58) | Todorki et al., [55] 2007 | 73 | M | Jaundice, Fever | CBD |
| (59) | Sethi et al., [56] 2007 | 51 | M | ERCP finding | CHD with Cystic |
| (60) | Stavridi et al., [57] 2007 | NA | NA | NA | Cystic duct |
| (61) | Jiménez et al., [58] 2007 | 60 | M | Jaundice | Hilar |
| (62) | Ferrone et al., [59] 2007 | NA | NA | NA | NA |
| (63) | Nafidi et al., [60] 2008 | 31 | F | RUQ pain | CBD |
| (64) | Gusani et al., [61] 2008 | NA | NA | NA | CBD |
| (65) | Schmitt et al., [62] 2008 | NA | NA | NA | Hilar |
| (66) | Costantini et al., [63] 2008 | NA | NA | NA | CHD |
| (67) | Felekouras et al., [64] 2009 | 60 | F | Jaundice | Cystic duct |
| (68) | Price et al., [65] 2009 | NA | NA | Jaundice | CBD |
| (69) | Price et al., [65] 2009 | NA | NA | Jaundice | CBD |
| (70) | Price et al., [65] 2009 | NA | NA | Jaundice | Hilar |
| (71) | Tonnhofer et al., [66] 2010 | 6 | F | Jaundice | CBD |
| (72) | Zhan et al. [67] 2010 | 10 | M | NA | CBD |
| (73) | Squillaci et al., [68] 2010 | 52 | M | Jaundice | CBD |
| (74) | Squillaci et al., [68] 2010 | 70 | M | Jaundice | CBD |
| (75) | Tsalis et al., [69] 2010 | 77 | M | Incidental | Hilar |
| (76) | Lee et al., [70] 2011 | 59 | M | Jaundice | CBD |
| (77) | Athanasopoulos et al., [71] 2011 | 43 | M | Jaundice | CBD |
| (78) | Present case | 69 | F | Pain | Left hepatic duct |

CHD: common hepatic duct, CBD: common bile duct, Hilar at the common bile duct bifurcation.

The most common site of malignancy in the biliary tract was common bile duct (57.14%) followed by the hilar confluence (27.28%), the cystic duct (9.1%), common hepatic duct (5.12%) and finally the left hepatic duct (1.23%).

The mean age of presentation was 47 years (range 6 years to 79 years).

The male to female ratio is 1:1.23 showing that the biliary NET has a preponderance for female.

By far the most common symptom in patients of Biliary tract NET is Jaundice (63.4%) followed by Pain (14.1%), jaundice with pain (12.7%) and remaining nonspecific symptoms like weight loss.

The incidence of a Carcinoid syndrome in patients of Biliary Tract NET is very rare. Only 4 cases which include a single case published by Nesi et al. [51] in 2006 with symptoms of diarrhea due to secretion of serotonin and 3 cases by Price et al. [65] in 2009 with features of Zollinger Ellison syndrome due to secretion of gastrin from tumor in CBD.

4. Conclusion

Biliary Tract NET are rare tumors that typically present with jaundice and pain. As compared to its counterpart Cholangiocarcinoma Biliary NET occurs in a younger age group with a female preponderance [39]. Biliary NET usually are nonsecreting tumor. Preoperative diagnosis of these tumors require a high index of suspicion and accurate histopathological diagnosis which must include a immunohistochemistry study and electron microscopy. Biliary tract NET are slow-growing indolent tumor which have a limited propensity for local and metastatic spread. Surgical resection aimed at complete tumor excision with bilo-enteric continuity offers the best cure and high survival rates. Patients who have undergone resection have a long term survival. Even in inoperable patients chemotherapy with newer biologic agents like Octreotride have a favorable outcome on the patient’s survival.

Conflict of Interests

The authors declare that they have no conflict of interest.

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