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SIMULTANEOUS HEPATOCELLULAR CARCINOMA AND ESOPHAGEAL CANCER: A CASE REPORT OF DUAL MALIGNANCY WITH REVIEW OF LITERATURE

Dr. Siddhant Mehta* Senior Resident, Department of Gastroenterology, AIIMS Rishikesh - 249203*Corresponding Author

Dr. Rohit Gupta Additional Professor and HOD, Department of Gastroenterology, AIIMS Rishikesh - 249203

Dr. Anand Sharma Assistant Professor, Department of Gastroenterology, AIIMS Rishikesh - 249203

ABSTRACT Simultaneous occurrence of hepatocellular carcinoma and esophageal cancer is rare. We report such a case with review of the literature. A total of 8 reports describing 12 cases were found. Most cases were reported from Japan and occurred synchronously. Most cases of EC were of squamous cell variant. Metastasis was noted in three patients. HCC was solitary in 10 patients and underlying liver disease was predominantly alcohol related. Five patients were managed surgically with success and six patients were alive beyond one year.

KEYWORDS : Hepatocellular carcinoma, Esophageal carcinoma, Multiple primaries, dual malignancy.

Introduction

Multiple primary neoplasm's occur rarely in India, reported in 177 patients over 40 years— . They not only pose a diagnostic challenge, but may have profound implications on the management of the patient. Hepatocellular carcinoma (HCC) occurring simultaneously with Esophageal carcinoma (EC) may be mistaken for metastasis. We describe the first case of simultaneous esophageal carcinoma and HCC to be reported from India with a comprehensive literature review.

Case presentation

A 60-year-old male presented with constant dull aching pain in the right hypochondrium, abdominal distension, and swelling of legs for two months. He also noticed gradually progressive difficulty in swallowing for one month and could swallow only liquids at the time of presentation. He did not have jaundice, altered sensorium, hematemesis or melena, oliguria, dilated abdominal wall veins, cough, fever, night sweats, shortness of breath, palpitations, odynophagia. He denied history of tuberculosis, blood transfusion, major surgeries, alcohol intake, corrosive ingestion or chronic medical comorbidities. He smoked 20 pack years. He was diagnosed elsewhere with a liver lesion and referred to us for further management.

Examination revealed pallor, generalized loss of muscle mass, moderate ascites, bipedal edema, normal blood pressure, respiratory rate and jugular venous pulse. He had firm hepatomegaly palpable 6 cm below right costal margin.

Blood investigations (Table 1) revealed iron deficiency anemia, hypoalbuminemia, high alfa-feto protein (AFP) levels and portal hypertensive ascites with no evidence of peritonitis. He was also Hepatitis C virus (HCV) antibody positivity with high HCV RNA levels. Computed tomography (CT) scan revealed 10cmx8cmx7cm lesion in the right lobe of the liver which showed enhancement in the arterial phase and washout in the delayed venous phase. Enhancing thrombus was noted in the main portal vein at bifurcation, right hepatic vein, suprahepatic inferior vena cava along with heterogeneously enhancing celiac and left gastric nodes. CT of thorax showed asymmetric thickening of distal esophagus and gastro-esophageal junction with loss of fat planes with diaphragm and multiple enhancing soft tissue nodules in both lungs (Figure 1). Esophagogastroduodenoscopy revealed small esophageal varices and ulceroproliferative lesion involving gastro-esophageal junction extending 2cm into the lesser curvature (Figure 2A-2B). Biopsy of the esophageal lesion was suggestive of mucin secreting adenocarcinoma (Figure 2C-2D).

Table 1. Investigations on admission

Investigations	Value
Haemoglobin (g/dl)	6.7
Platelets (per microfiber)	1,86,000
Creatinine (mg/dl)	0.7
Sodium (mEq/L)	136
Potassium (mEq/L)	3.6
International normalised ratio	1
Total bilirubin (mg/dl)	1.6
Aspartate aminotransferase (IU/L)	22
Alanine aminotransferase (IU/L)	107
Alkaline Phosphatase (IU/L)	271
Gamma glutamyl transpeptidase (U/L)	113
Protein (g/dl)	5.7
Albumin (g/dl)	2.3
Vitamin B12 (pg/ml)	545
Ascitic fluid cell count (per microliter)	120
Ascitic fluid protein(g/dl)	1.65
Ascitic fluid albumin(g/dl)	0.89
Alfa-feto protein (ng/ml)	12550

Figure 1: Imaging characteristic of our patient with HCC and Esophageal malignancy.

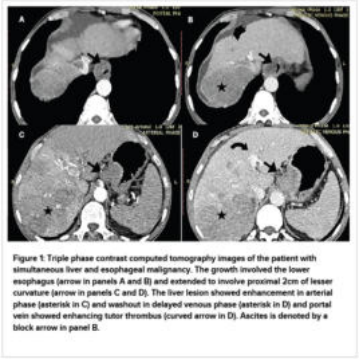

Figure 1: Triple phase contrast computed tomography images of the patient with simultaneous liver and esophageal malignancy. The growth involved the lower esophagus (arrow in panels A and B) and extended to involve proximal 2cm of lesser curvature (arrow in panels C and D). The liver lesion showed enhancement in arterial phase (asterisk in C) and washout in delayed venous phase (asterisk in D) and portal vein showed enhancing tutor thrombus (curved arrow in D). Ascites is denoted by a block arrow in panel B.

Figure 2: Endoscopic and Histology characteristic of our patient with HCC and Esophageal malignancy.

Figure 2: Endoscopic images showing growth(arrow in panels A and B) extending from gastroesophageal junction (A) to 2cm in proximal lesser curvature (B). Histology showing tumor cells (Arrow in panels C and D) alongside normal gastric mucosa (curved arrow in C) and floating among extracellular mucin (asterisk in D)

Based on above investigations, he was diagnosed with synchronous HCC [Barcelona classification of liver cancer stage C] and metastatic esophageal adenocarcinoma. Esophageal stenting was offered, but was deferred due to financial constraints. In view of advanced HCC, he was deemed unfit for chemotherapy and was started on supportive treatment.

Discussion and Review of literature

We searched Pub Med/MEDLINE since inception till 1st January 2021 using the terms ('liver' OR 'hepatic' OR 'hepatocellular' OR 'hepatoma') AND ('cancer' OR 'malignancy' OR 'neoplasm' OR 'carcinoma' OR 'tumour') AND ('esophageal' OR 'gastroesophageal junction').

We also searched the references of the selected articles for any additional articles. Only manuscripts in English were included.

We found 8 articles reporting 12 patients. (Table 2)

Most of the cases (10/12) were reported from Japan. The median age was 70(range 54-84) years and all patients were males. Except in one patient, all were synchronous(2). The diagnosis of EC preceded that of HCC in 6 patients(3–5) and followed HCC in four (2,5–7).

There is no clear hypothesis in literature explaining co-existence of these malignancies, though male gender, smoking and alcohol are shared risk factors. Of the 6 patients in whom EC was diagnosed first, only three were symptomatic. Squamous cell carcinoma (SCC) was the predominant histological subtype of EC.

Two patients had multicentric HCC (4,6). Alcohol was the predominant etiology for the underlying chronic liver disease (CLD), seen in five patients (2,4). Child class could be ascertained in nine patients (Child class A-7; Child class B-2) (2–7). AFP levels were available in five patients (2,3,5,6) and were below 400ng/ml.
One patient had sigmoid colon adenocarcinoma diagnosed synchronously with the other two lesions.

Treatment of Malignancies:

Five patients underwent surgical management and two had post-operative complications. The first patient had simultaneous resection of both cancers with bleeding into the thoracic cavity (5). The second patient developed pneumonia and liver failure in the post-operative period of a two-step surgery. Both were managed successfully. Non surgical management was offered due to Child class B status in two patients, lung metastasis and multicentric HCC in one patient each (4). The contraindication to surgery was not mentioned in the rest. The surgical approach in the operated patients was influenced by HCC being most advanced of the two malignancies, esophageal resection and reconstruction being a more extensive procedure, with associated bleeding into the thoracic cavity necessitating the use of positive end expiratory pressure with consequent compromised portal blood flow.
One year survival was available 10 patients. Most of the deaths were related to EC.

Table 2: Summary of the manuscripts (including our case) fulfilling the inclusion Criteria as explained the text

Study	N (patients)	Age (yrs) /Sex	Synchronous or Metachronous	Malignancy diagnosed first	Treatment	follow up	Outcome
Jager et al,1981(6)	1	71/M	Synchronous	HCC	Chemotherapy for esophageal carcinoma and TAE for HCC	7 months	Dead (Non response to chemotherapy)
Kanemstsu et al, 1992 (8)	1	54/M	Synchronous		Radiotherapy for esophageal carcinoma and TAE for HCC	7 months	Alive
Shimizu et al,1993(9)	1	73/M	Synchronous	HCC	Hepatic segmentectomy followed later by transthoracic subtotal esophagectomy and substernal cervical esophagogastrostomy	22 months	Alive
Morita et al,1994 (4)	4	68/M	Synchronous	Esophagus	HCR for esophageal carcinoma and Lipiodolisation for HCC	24 months	Alive
		70/M	Synchronous	Esophagus	HCR for esophageal carcinoma and Lipiodolisation and TAE for HCC	25 months	Dead (Blee
		67/M	Synchronous	Esophagus	HCR for esophageal carcinoma and Lipiodolisation for HCC	12 months	Dead (aspiration pneumoni
		84/M	Synchronous	Esophagus	Radiotherapy for esophageal carcinoma and Lipiodolisation for HCC	4 months	Dead (bleeding from esophageal
Nagahama et al,1996 (5)	2	72/M	Synchronous	Esophagus	Subtotal resection of esophagus and hepatic segmentectomy performed simultaneously	18 months	Dead (Bon
		68/M	Synchronous	HCC	Subtotal resection of esophagus and hepatic segmentectomy performed simultaneously	27 months	Alive
Pelloni et al,2001 (9)	1	68/M	Synchronous		Hepatic segmentectomy followed later by transhiatalesophagectomy		
Takahashi et al, 2005(2)	1	69/M	Metachronous	HCC	TAE and partial liver resection for HCC and EMR for esophageal carcinoma	6 years	Alive
Akiyama et al,2015(3)	1	73/M	Synchronous	Esophagus	Laparoscopic assisted sigmoidectomy and open partial liver resection in one stage followed a month later by thoracoscopicesophagectomy	7 months	Alive

Our patient	1	60/M	Synchronous	Esophagus	Sorafenib and palliative therapy		Alive

Our patient had biopsy proven EC. Though the HCC was diagnosed radiologically, the classical imaging findings, background cirrhosis and high AFP levels left little doubt with the diagnosis. We deferred liver biopsy due to the risk of complications and unlikely impact on management. Our review has certain limitations. Firstly, our review excluded Japanese language though Japan has been found to have the highest association of EC and HCC. Secondly, the information on the liver function and stage of cancers was heterogenous. This may be because the reports were scattered in time and the understanding of the pathology and treatment of these malignancies evolved over time.

The recent advances might lead to better understanding of the pathophysiology, early detection of lesions, and availability of potent therapeutic options leading to improved outcome of such cases.

Conclusion

Simultaneous HCC and EC occurs rarely, mostly diagnosed synchronously. Liver lesions in a patient with EC should be evaluated, though metastasis is more common than a second primary in such situations. Surgical management was possible in less than 50% patients. The management decision and outcome may be influenced by the surgical risks due to liver dysfunction and the advanced stage of the liver malignancy.

REFERENCES:

1. Vyas, J. J., Deshpande, R. K., Sharma, S., & Desai, P. B. (1983). Multiple primary cancers in Indian population: metachronous and synchronous lesions. Journal of surgical oncology, 23(4), 239-249.
2. Takahashi, K., Yoshida, H., Mamada, Y., Taniai, N., Nakamura, Y., Mizuguchi, Y., ... & Tajiri, T. (2005). A Case Report of Metachronous Hepatocellular Carcinoma and Early Esophageal Cancer. Journal of Nippon Medical School, 72(3), 187-190.
3. Akiyama, Y., Iwaya, T., Konosu, M., Shioi, Y., Endo, F., Katagiri, H., ... & Sasaki, A. (2015). Curative two-stage resection for synchronous triple cancers of the esophagus, colon, and liver: report of a case. International Journal of Surgery Case Reports, 13, 1-4.
4. Morita, M., Kuwano, H., Toh, Y., Matsuda, H., Matsumata, T., & Sugimachi, K. (1994). The clinical characteristics of patients with synchronous squamous cell carcinoma of the esopohagus and hepatocellular carcinoma. Surgery today, 24, 803-808.
5. Nagahama, T., Goseki, N., Kato, S., Maruyama, M., & Endo, M. (1996). Esophageal carcinoma and coexisting hepatocellular carcinoma resected simultaneously. Archives of Surgery, 131(2), 208-210.
6. Jager, R. M., & Max, M. H. (1981). Association of squamous carcinoma of the esophagus with a synchronous primary hepatocellular carcinoma. Journal of Clinical Gastroenterology, 3(1), 73-78.
7. Shimizu, R., Murakami, T., Wadamori, K., Yano, K., & Suzuki, T. (1993). The surgical management of synchronous hepatocellular carcinoma and thoracic esophageal carcinoma. Surgery Today, 23, 63-67.
8. Kanematsu, M., Imaeda, T., Yamawaki, Y., Hirose, Y., Inoue, A., Goto, H., & Doi, H. (1992). Hepatocellular carcinoma with extrahepatic primary neoplasms. Gastrointestinal radiology, 17, 53-57.
9. Pelloni, A., Guerra, A., & Gertsch, P. (2001). Surgical treatment of synchronous hepatocellular and esophageal carcinoma: case report and review of literature. Hepato-gastroenterology, 48(39), 684-686.