**A Rare Case Report on Hepatic Neuroendocrine Tumour with Multifocal Hepatocellular Carcinoma**

**ABSTRACT**

Neuroendocrine tumors (NETs) are uncommon cancers that arise from neuroendocrine cells and are typically found in the gastrointestinal tract, pancreas, and lungs. Hepatic involvement is usually due to metastases, though primary or widespread NETs of the liver are very uncommon and occasionally misdiagnosed. We describe a rare instance of a 52-year-old woman who developed lower limb edema and subsequently developed multifocal hepatocellular carcinoma, a neuroendocrine liver tumor. Imaging revealed extensive, multifocal liver lesions, which were confirmed by histopathology and immunohistochemistry. These cases are uncommon and challenging to diagnose because of the patient's atypical presentation, absence of systemic symptoms, and concurrent primary hepatic cancer. For an accurate diagnosis and appropriate treatment of rare hepatic NETs, comprehensive imaging and pathological evaluation are essential.

**Keywords:** Tumours, Neuroendocrine Tumours (NETs), Benign, Malignant, Liver Metastases, Prevalence, Incidence.

**INTRODUCTION**

Clusters of aberrant cells that resemble lumps or growths are called Tumours. Any of the trillions of cells that make up our bodies can be the starting point for them. Depending on whether a Tumour is precancerous, benign, or malignant, it will develop and act differently [1]. Neuroendocrine Tumours (NETs) are Tumours made of cells that react to a signal from the neurological system by releasing hormones into the circulation. Hormone production may be increased in neuroendocrine Tumours compared to normal, leading to a variety of symptoms. These growths could be malignant or benign [2]. Neuroendocrine neoplasms (NENs) are a diverse group of Tumours with unique morphological and biological characteristics [3]. Due to its non-specific clinical appearance and highly diverse radiologic characteristics, it is often misdiagnosed as another hepatic Tumour. Furthermore, the most effective therapeutic approach for raising survival rates is still surgical excision with well-defined margins [4]. NETs, a subset of extremely rare cancers account for 0.46% of gastrointestinal and bronchopulmonary malignancies [5]. Metastases from NENs primarily damage the liver [6]. Liver metastases caused by neuroendocrine disorders are often numerous and vary in size. Although miliary seeding across the liver is rare, both liver lobes are typically afflicted [7]. As hepatocytes may metabolize neuroactive amines and peptide hormones and lessen their effects, most cancers really originate in the portal venous drainage. Hepatic venous drainage, however, provides unchanged Tumour products with direct access to the systemic circulation once secondary hepatic illness manifests [3]. Merely 0.5% of all cancers are neuroendocrine Tumours. The prevalence is roughly 2/100,000, and because of the appendiceal position, there is a female preponderance under 50 years of age. The lung (22-27%) and gastrointestinal system (62–67%) are the two main primary locations.12–22% of cases involve a presentation with metastatic illness [8]. Over a 15-year period, there has been a noticeable increase in the frequency of NETs, accompanied by a drop in the proportion of cases with metastatic presentation. This suggests that the notable increase in incidence may be explained by increased detection [5].

**CASE REPORT**

A 52-year-old female, Mrs. X presented with the chief complaints of lower limb swelling for 1 month, she had no history of abdominal pain /fever/loss of appetite/loss of weight. She has a known case of type 2 diabetes mellitus and hypertension for 10 years and a heterogenous lesion of the liver. She had a past medication history of T. Glirum ½ tablet 1-0-1, T.Telma 1tablet 0-0-1, T. Ironforte and T. Prenerve 75mg 0-1-0. On general examination, her temperature was found to be 98.4℉, BP was 130/90mmHg, pulse rate was 86 beats per minute, and respiratory rate was 20 breaths/min. She had no history of allergies. Alpha Fetoprotein:2.55IU/mL. USG whole abdomen report showed a multifocal lesion seen in the liver, the largest in the right lobe of the liver- a complete cystic lesion measuring 16x15x18 cm. Vascularity seen within the solid components to meet out metastasis and bulky uterus with heterogeneous myometrial junction with adenomyosis of uterus and a heterogenous lesion measuring 3.6x3.5 seen in the right lateral wall. Abdomen Triple Phase Report showed gross hepatomegaly, large mass lesions in segments 4a, 4b, and 8, and multiple liver lesions in the wall of the liver segments. F/S/O Multifocal hepatocellular carcinoma, multiple lymph nodes at portal hepatitis, hepatoduodenal ligaments, along left gastric vessel, common hepatic artery and upper retroperitoneum, no ascites, no peritoneal deposit, no omental thickness; bilateral grade I hydronephrosis, bulky uterus with adenomyosis.

Histopathology Report showed liver space-occupying lesion, core needle biopsy: well-differentiated hepatocellular carcinoma, well-defined neuroendocrine Tumour, identified through immunohistochemistry (IHC). PET CT whole body screen report showed a large non-FDG heterogeneously enhancing centrally necrotic mass lesion involving segments ivA, ivB, v, and viii of the liver, 13.8x12.7x19.1 cm suggestive of HCC. Suggested HPE & IHC correlation. The right and left branches of the portal vein are splayed around the lesion. No filling defect was noted in the mass portal vein and the branches. The middle hepatic vein appears exerted by the main lesion; right hepatic vein appears displaced posteriorly. the lesion is seen to compress the intrahepatic IVC. Inferiorly the mass is seen to displace the gall bladder. There is compression of the right and left hepatic duct, causing mild bilateral CHBRD. Mechanically the lesion is abutting the D1& D2 segment of the duodenum and displacing it to the left. Multiple non-FDG avid gastrohepatic periportal and peripancreatic lymph nodes are noted, the largest measuring 23x14 mm- likely metastasis. Low-grade FDG avid sub cranial lymph node is noted- likely inflammatory. No other abnormal hypermetabolic lesion was seen.

Based on subjective and objective evidence, the patient was diagnosed with Neuroendocrine Tumour of the Liver with Multifocal Hepatocellular Carcinoma and was planned for the TACE procedure along with nuclear medicine. The treatment chart includes T, Telma-AM HS, T. Ironfast-2 OD, T. Prenerve OD, T. Methylprednisolone 4mg OD, and T. Montek FX HS. No Drug interactions were found.

**DISCUSSION**

Neuroendocrine Tumours originate in neuroendocrine cells, which produce hormones in response to electrical signals from nerves. Neuroendocrine cancer that originates in the liver is exceptionally rare. It tends to progress slowly and is often not diagnosed until it reaches an advanced stage [9]. Neuroendocrine Tumours are cancers that can develop wherever endocrine cells are present. They are distributed throughout the body, but the most common sites for Tumours to develop from them are the lungs, small intestines, and pancreas. The symptoms of neuroendocrine Tumours can be categorized into hormonal and mechanical symptoms. Hormonal symptoms include severe diarrhoea, severe gastric ulcers, or uncontrolled blood sugar that responds poorly to treatment. The hormones produced can vary depending on the location in the body where the Tumour originates. On the other hand, mechanical symptoms are related to the physical impact of the tumour on the body, such as a small bowel obstruction or localized pain due to pressure on a specific structure.[10] Functioning neuroendocrine Tumours are known for releasing biologically active polypeptides or amines, leading to specific clinical symptoms. Therefore, it is essential to identify the hormone or amine that is being overproduced. Currently, four non-invasive imaging studies are used to detect and assess the spread of neuroendocrine liver metastases. The hyper vascular nature of neuroendocrine metastases may cause them to appear isodense with the normal liver tissue during computerized tomography (CT) scans when a contrast infusion is used. Magnetic resonance imaging (MRI) with appropriate pulse sequences is equally effective as CT in detecting liver metastases in patients with neuroendocrine Tumours. Somatostatin receptor scintigraphy (SRS) is useful for locating primary neuroendocrine Tumours, especially those originating in the foregut, and for detecting metastatic disease, particularly outside the liver. Selective hepatic arteriography can detect liver metastases with a sensitivity of 65% and is capable of visualizing lesions smaller than 5 mm in diameter. However, due to its invasive nature, it has been largely replaced by the less invasive modalities mentioned above [11]. Liver metastases from NETs usually involve both lobes of the liver and manifest as multiple, variable-sized lesions [7] .

Around 12% to 27% of all patients with NETs are diagnosed with distant metastasis, with the liver being the most common site for NET metastasis regardless of the primary site. The percentages of patients with pancreatic, cecal, colonic, and small bowel NETs presenting with distant disease are 64%, 44%, 32%, and 30% respectively. Metastatic disease has a negative impact on survival, with patients presenting with distant metastases having a 4-fold increased risk of death compared to those with localized disease [12].As long as the tumor is resectable and the tumor load is not too high, Bhutiani et al. proposed a literature-based therapy protocol that prioritizes surgical resection for low-grade NELMs13. But because so many diverse parts of our patient were impacted, curative excision was not an option. Rather, transarterial chemoembolization (TACE) was intended to reduce tumor development and alleviate symptoms. Current strategies for unresectable NELMs, which concentrate on tumor control and symptom relief, align with this approach.

**CONCLUSION**

In conclusion, neuroendocrine Tumours (NETs) present a complex and challenging clinical scenario, with origins in neuroendocrine cells found throughout the body, particularly in the gastrointestinal tract and lungs. While primary neuroendocrine cancer in the liver is rare, its optimal management remains elusive due to limited understanding and late-stage diagnosis. Symptoms of NETs encompass hormonal and mechanical manifestations, reflecting the diverse array of hormones produced and the physical impact of Tumour growth. Accurate diagnosis is crucial, often relying on non-invasive imaging modalities such as CT, MRI, somatostatin receptor scintigraphy (SRS), and selective hepatic arteriography. The incidence of NETs has risen substantially over the years, attributed partly to improved diagnostic techniques.

Treatment options, including surgical resection, ablation, and liver transplantation, aim not only to eradicate Tumours but also to alleviate symptoms and improve patient selection for curative procedures.

**Consent**

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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