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Successful resection of a centrally located primary hepatic neuroendocrine tumor

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ABSTRACT

INTRODUCTION: Primary neuroendocrine tumors (NETs) of the liver are rare tumors that are challenging to diagnose.

PRESENTATION OF CASE: A 41-year old woman presented with a four-month history of moderate abdominal pain in the right upper quadrant. A computed tomography scan of the abdomen revealed a large hypervascular liver lesion measuring 14 × 10 × 15 cm occupying segments IV and VIII and part of segment V of the liver. A liver biopsy revealed findings consistent with a well-differentiated NET. Transarterial chemoembolization was offered to the patient; however, the procedure was unsuccessful. Surgical management was therefore considered and resulted in a favorable outcome.

DISCUSSION: Primary hepatic NETs are thought to originate from NET cells that may subsequently propagate to the intrahepatic biliary tree and become cancerous. These tumors are often missed during an initial evaluation due to a low clinical index of suspicion. In some cases, nonspecific symptoms such as abdominal pain and bloating may be an indication of early disease. No guidelines have been developed for the treatment of primary hepatic NETs; nevertheless, surgical resection remains the treatment of choice and plays a potentially curative role.

CONCLUSION: Surgical resection may be beneficial in the management of a primary NET of the liver even when the procedure appears to be challenging, such as in the case of a centrally located liver tumor.

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1. Introduction

Neuroendocrine tumors (NETs) are rare malignancies that originate from the neuroendocrine system. These tumors can secrete monoamines and are categorized based on features pertaining to their biological behavior, including tumor grade, degree of differentiation, and tumor stage [1]. According to previous reports, these tumors primarily arise in the lungs, pancreas, and gastrointestinal tract, albeit they can arise in several body organs and thereby cause a wide range of symptoms [2]. Nevertheless, NETs are usually reported as metastatic hepatic neoplasms, although the liver itself is seldom reported as the primary tumor site.

Primary hepatic NETs are extremely rare, with less than 100 cases reported in the English medical literature since they were first described in 1958 [3]. Additionally, most primary hepatic NETs are generally located in the right liver lobes [4]. When located in the center of the liver, NETs may present a challenging clinical situation because resection must be performed carefully to preserve the left

and right lobes and maintain liver function. We present a case of primary hepatic NET in the center of the liver. The work has been reported in line with the SCARE criteria [5].

2. Presentation of case

A 41-year-old Saudi female with known bronchial asthma and non-insulin-dependent diabetes mellitus presented to the emergency department complaining of a four-month history of moderate abdominal pain in the right upper quadrant. The pain was colicky in nature, aggravated by food intake, relieved by analgesia, and associated with nausea. She reported no history of vomiting, bowel habit change, weight loss, or fever. She also had no family history of malignancy or a personal history of radiotherapy or smoking.

On examination, she was conscious, oriented, alert and did not show signs of respiratory distress, pallor, or cyanosis. However, she was underweight. A review of the systems was unremarkable. Cardiovascular and chest examination were unremarkable. An examination of her abdomen was soft on palpation and revealed an enlarged liver span. Her abdomen was not tender to palpation and her bowel sounds were normal.

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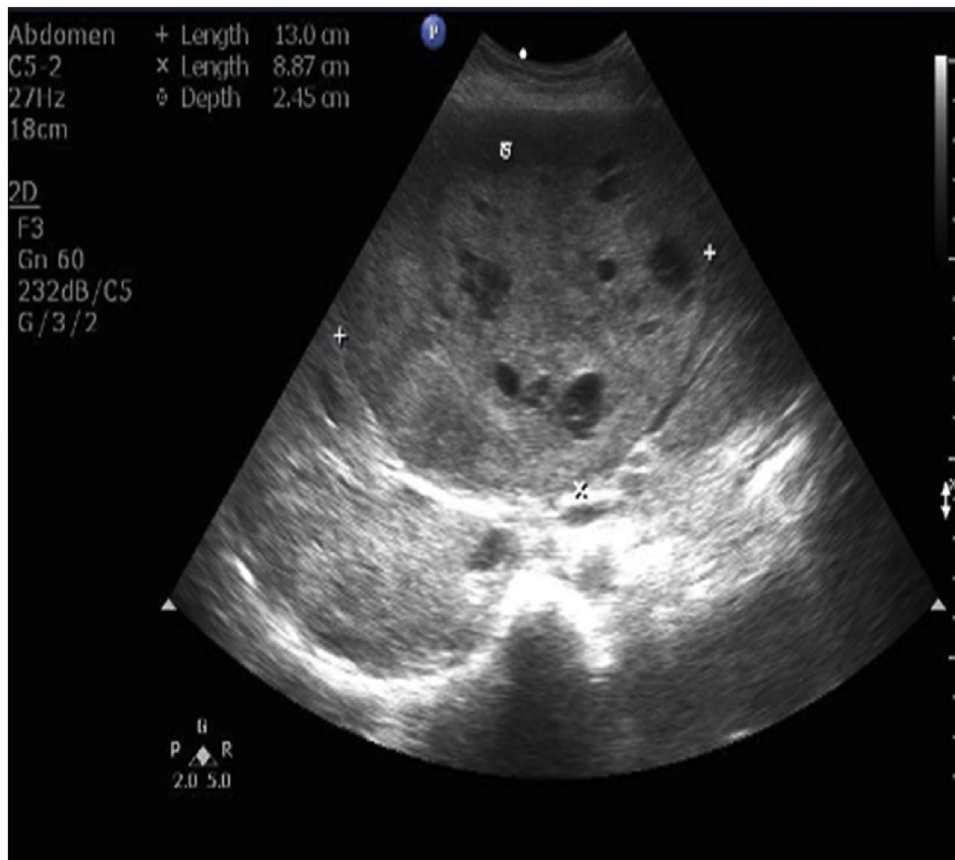


Fig. 1. Abdominal ultrasound showing a large lesion in the liver.

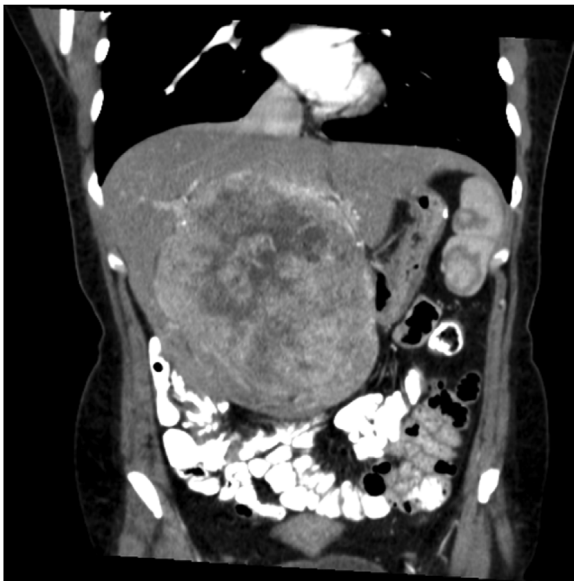


Fig. 2. A computed tomography scan of the abdomen (coronal view) showing a large hypervascular liver lesion measuring approximately 14 × 10 × 15 cm.

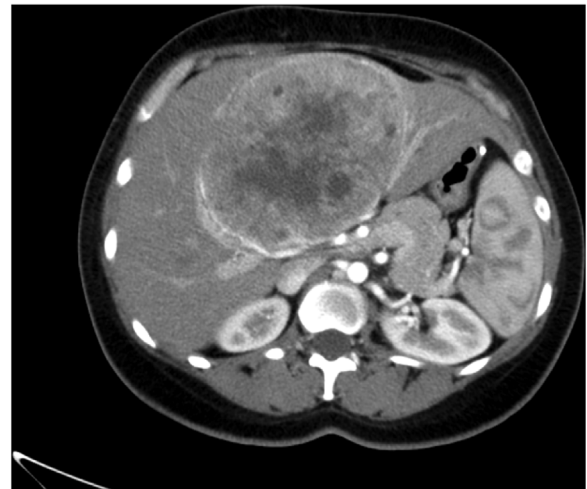


Fig. 3. A computed tomography scan of the abdomen (axial view) showing a large hypervascular liver lesion in segments IV and VIII and part of segment V that displaced the right and left portal veins.

Her initial workup included the following: white blood cell count $7.2 \times 10^9/L$, hemoglobin concentration 10.6 g/dL, platelet count $289 \times 10^9/L$, albumin level 40 g/L, total bilirubin 1.7 $\mu\text{mol/L}$, alanine transaminase 17 u/l, alkaline phosphatase 84 u/l, carbohydrate antigen 19-9 level 16 $\mu\text{g/L}$, carcinoembryonic antigen (CEA) level 0.6 $\mu\text{g/L}$, alpha-fetoprotein (AFP) 2 kiu/L, 5-hydroxyindoleacetic acid (5-HIAA)/creatinine 4 mg/gCrea,

creatinine (enzymatic) 18.1 mmol/L, and chromogranin A 170 $\mu\text{g/L}$.

An abdominal x-ray revealed a normal distribution of bowel gas, whereas an abdominal ultrasound revealed a large lesion in the liver (Fig. 1). A computed tomography (CT) scan of the abdomen revealed a large hypervascular liver lesion measuring 14 × 10 × 15 cm occupying segments IV and VIII and part of V (Figs. 2 and 3). The masses displaced the right and left portal veins, mild intrahepatic biliary duct dilatation and normal liver

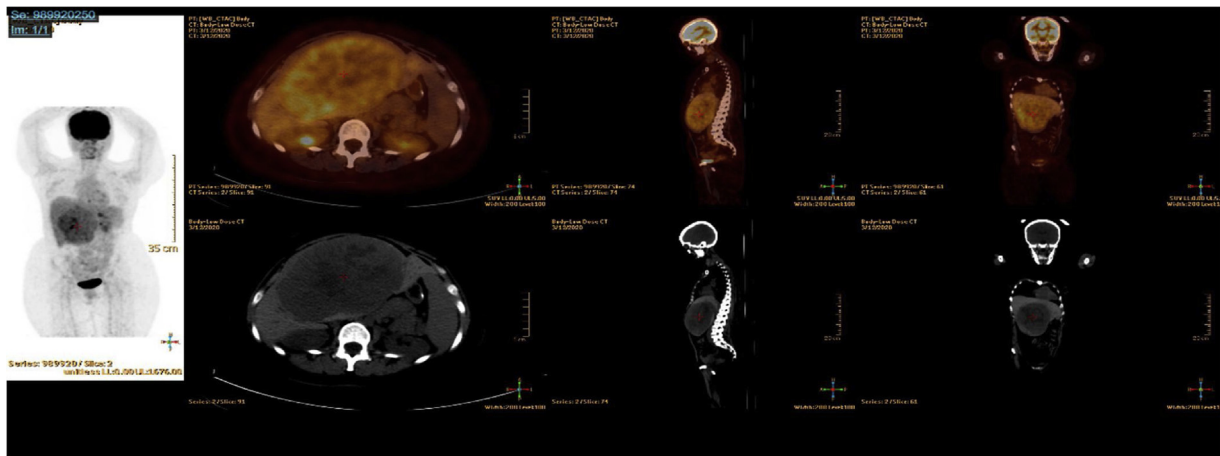


Fig. 4. A positron emission tomography scan showed a large, globular, moderately hypermetabolic mass involving the central hepatic region sparing small portions of the right and left lobes that measured approximately $14.7 \times 15.1 \times 10.2$ cm.



Fig. 5. A post-transarterial chemoembolization computed tomography scan of the abdomen (axial view) showing 40% necrosis of the mass.

volume. A positron emission tomography (PET) scan showed a large, globular, moderately hypermetabolic mass measuring $14.7 \times 15.1 \times 10.2$ cm in the central hepatic region. The mass spared small portions of the right and left lobes superiorly and both liver lobes (Fig. 4). A liver biopsy showed a well-differentiated NET with papillary configuration, and it was positive for chromogranin, synaptophysin, and pancytokeratin; its Ki-67 proliferation index was 5%.

The case was discussed in the tumor board, and the initial plan was to offer transarterial chemoembolization (TACE). Four weeks after the procedure, a repeat abdominal CT scan showed stability of the large hypervascular liver lesion, with 40% necrosis of the mass (Fig. 5). Surgical management was therefore considered. An inverted L-shape incision was made and both liver lobes were mobilized, and the Pringle maneuver was applied to avoid bleeding during mobilization. Using a cavitron ultrasonic surgical aspirator, parenchymal division was done with gradual clipping and transfixing of crossing vessels and ducts. After complete removal of the tumor and the gall bladder, the methylene blue test was performed, and all leaking areas were sutured except the left lateral segment

of the biliary drainage was reconstructed by hepatico-jejunostomy using a Roux-en-Y loop (Fig. 6).

The patient's post-operative course was uneventful, and she was discharged after four days. A histopathology examination of the tumor revealed a well-differentiated, unifocal, neuroendocrine tumor measuring about 15 cm. Tumor necrosis was observed, and the parenchymal margin was infiltrated by the tumor while the vascular margin was not.

A follow up CT scan performed after two weeks showed surgical bed fluid collection measuring about $2.6 \times 4.3 \times 7.2$ cm. The fluid was suctioned under CT guidance with only three milliliters of pus aspirated; no drain was placed after aspiration. Laboratory investigations of the fluid revealed a bilirubin level of $52 \mu\text{mol/L}$. Culture of her abdominal fluid showed mild growth of *Klebsiella pneumoniae*, which responded to extended spectrum beta lactamase producer (ESBL). The patient was started on intravenous imipenem for two weeks.

A repeat abdominal CT scan performed after one month showed a stable surgical bed fluid collection measuring $7.2 \times 1.4 \times 2$ cm



Fig. 6. Intraoperative finding of a large, encapsulated mass occupying most of the central hepatic region.

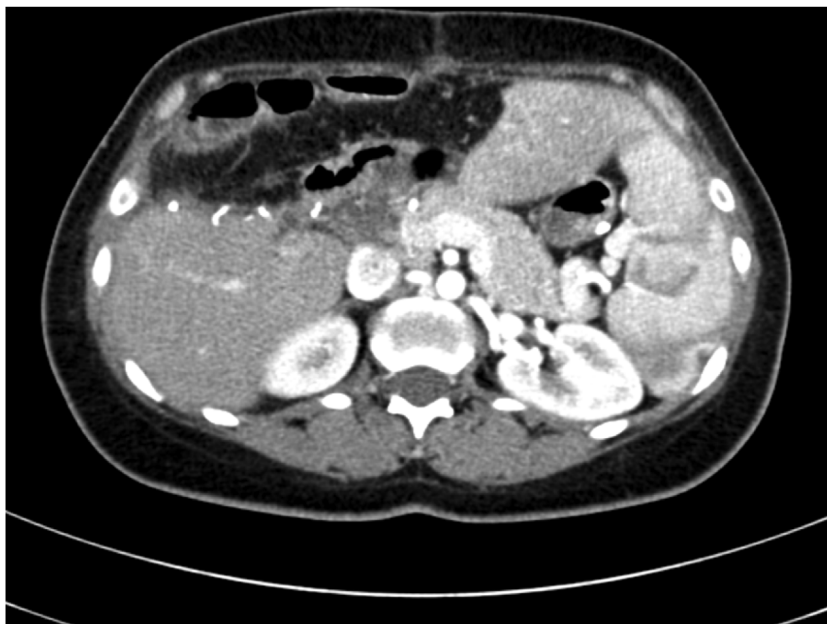


Fig. 7. A post-operative computed tomography scan of the abdomen (axial view) showing a surgical bed fluid collection measuring about 2.6 × 4.3 × 7.2 cm.

(Fig. 7). The patient was regularly followed up at the outpatient clinics and did not present any complaints.

3. Discussion

Primary hepatic NETs are thought to originate from NET cells that may subsequently propagate to the intrahepatic biliary tree and become cancerous [6]. Additionally, some investigators have suggested that transdifferentiation of cancerous stem cells into NET cells may cause the cells to undergo neuroendocrine differentiation [7]. The World Health Organization classifies NETs of the liver into three grades: type I or well-differentiated tumors, which have a good prognosis; type II or moderately differentiated tumors; and type III or poorly differentiated tumors, which carry a poor prognosis.

Primary hepatic NETs are often missed during an initial evaluation due to a low clinical index of suspicion. In some cases, nonspecific symptoms such as abdominal pain and bloating may be an indication of early disease. However, because most patients with primary hepatic NETs are asymptomatic, early-stage diagnosis may be challenging. In addition to the nonspecific nature

of initial symptoms, early diagnosis is further complicated by the slow-growing nature of these tumors. The patient in our case had a four-month history of moderate abdominal pain in the right upper quadrant, which can be confused with visceral causes such as acute pyelonephritis or cholecystitis, thereby delaying diagnosis.

Most NETs of the liver are typically located in the right liver lobe and slowly metastasize to the left lobe [4]. Some patients have multifocal hepatic NETs, but these have been reported to be solitary space-occupying lesions of the liver [4]. The lesion in our patient's case was in the central region of the liver. A histopathological examination of the tumor revealed findings consistent with a well-differentiated NET, and immunohistochemical staining showed that the tumor was positive for chromogranin, synaptophysin, and pancytokeratin, which are all indicative of a primary hepatic NET. Some investigators have also reported a PET/CT-guided biopsy combined with histopathological analysis and immunohistochemistry to be useful modalities for preoperative diagnosis [8]. In our case, we used CT, PET, biopsy, and immunohistochemistry to reach a preoperative diagnosis. Although PET and CT did not help make a definitive diagnosis, these modalities were helpful in identifying the liver mass.

Surgery was not initially explored in our patient because the size of the tumor would have complicated the procedure. Consequently, TACE was offered and it was successful as a repeat abdominal CT scan showed 40% necrosis of the mass, prompting the team to consider surgical management. Previously, it was reported that neither TACE nor liver protection significantly prolonged survival in patients with primary NETs [9]. Unfortunately, no guidelines have been developed for the treatment of primary hepatic NETs. Nevertheless, surgical resection remains the treatment of choice and plays a potentially curative role [10]. In our patient, the tumor occupied liver segments IV and VIII and part of segment V. One of the main concerns of performing standard resection in our patient was inadequate residual hepatic volume after resection, which could have resulted in decreased liver function. Postoperative chemotherapy is mandatory in cases with progressive disease, which was not the case in our patient.

4. Conclusion

Primary hepatic NETs are rare tumors that may be challenging to diagnose due to their nonspecific clinical features and slow progression. Given that they are potentially metastatic and life-threatening, it is essential for clinicians to be able to identify and manage them. Patients with centrally located hepatic tumors may be challenging to manage, as there are no specific techniques proposed for the management of these tumors. Surgery may be beneficial and result in a favorable outcome, albeit the risk of inadequate residual volume after surgery should be considered.

Declaration of Competing Interest

All of authors have no conflict of interest.

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Ethical approval

In our institute, ethical approval is exempted, depend on acquired patient consent.

Consent

Written informed consent was obtained from the guardian on behalf of the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author's contribution

All authors contributed to manuscript preparation, manuscript editing, manuscript review.

Registration of research studies

We don't need to register this work.

Guarantor

The Guarantor is DR. Ashwag Alharbi.

Patient perspective

Patient was satisfied with the treatment.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

- [1] M.J. Raphael, D.L. Chan, C. Law, S. Singh, Principles of diagnosis and management of neuroendocrine tumours, *CMAJ* 189 (2017) E398–E404, <http://dx.doi.org/10.1503/cmaj.160771>.
- [2] J.M. van der Zwan, A. Trama, R. Otter, N. Larrañaga, A. Tavilla, R. Marcos-Gragera, A.P. Dei Tos, E. Baudin, G. Poston, T. Links, Rare neuroendocrine tumours: results of the surveillance of rare cancers in Europe project, *Eur. J. Cancer* 49 (2013) 2565–2578, <http://dx.doi.org/10.1016/j.ejca.2013.02.029>.
- [3] H.A. Edmondson, Tumors of the liver and intrahepatic bile ducts, n.d.
- [4] A. Gurung, E.M. Yoshida, C.H. Scudamore, A. Hashim, S.R. Erb, D.L. Webber, Primary hepatic neuroendocrine tumour requiring live donor liver transplantation: case report and concise review, *Ann. Hepatol.* 11 (2012) 715–720, [http://dx.doi.org/10.1016/S1665-2681\(19\)31449-8](http://dx.doi.org/10.1016/S1665-2681(19)31449-8).
- [5] R.A. Agha, M.R. Borrelli, R. Farwana, K. Koshy, A. Fowler, D.P. Orgill, For the SCARE Group, The SCARE 2018 statement: updating consensus Surgical CAse REport (SCARE) guidelines, *Int. J. Surgery* 60 (2018) 132–136.
- [6] Sugi RV, Jeswanth S, Prabhakaran R, Senthil Kumar P, Sugumar C, Ravichandran P, Primary hepatic neuroendocrine tumor: an usual tumor at an unusual site, *J. Liver Dis. Transplant.* 2018 (2018), <http://dx.doi.org/10.4172/2325-9612.1000163>.
- [7] H.L. Waldum, K. Öberg, Ø.F. Sørđal, A.K. Sandvik, B.I. Gustafsson, P. Mjones, R. Fossmark, Not only stem cells, but also mature cells, particularly neuroendocrine cells, may develop into tumours: time for a paradigm shift, *Therap. Adv. Gastroenterol.* 11 (2018), <http://dx.doi.org/10.1177/1756284818775054>.
- [8] A.K.R. Gorla, R.K. Basher, L. Kaman, A. Bal, A. Bhattacharya, B.R. Mittal, 68Ga-DOTATATE PET/CT in primary hepatic neuroendocrine tumor, *Clin. Nucl. Med.* 42 (2017) 118–120, <http://dx.doi.org/10.1097/RLU.0000000000001510>.
- [9] Z.-M. Zhao, J. Wang, U.C. Ugwuowo, L. Wang, J.P. Townsend, Primary hepatic neuroendocrine carcinoma: report of two cases and literature review, *BMC Clin. Pathol.* 18 (2018) 3, <http://dx.doi.org/10.1186/s12907-018-0070-7>.
- [10] D.S. Foster, R. Jensen, J.A. Norton, Management of liver neuroendocrine tumors in 2018, *JAMA Oncol.* 4 (2018) 1605–1606, <http://dx.doi.org/10.1001/jamaoncol.2018.3035>.

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