Case report

Diagnostic problem of Primary Hepatic Neuroendocrine Tumor in 18-year-old woman: A case report

Jessica Andriani a,*, Vicky Sumarki Budipramana b, Cindy Sadikin c

a Emergency Department, Premier Surabaya Hospital, Indonesia
b Department of Surgery, Premier Surabaya Hospital, Indonesia
c Department of Radiology, Premier Surabaya Hospital, Indonesia

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ABSTRACT

Introduction and importance: Primary Hepatic Neuroendocrine Tumor (PHNET) is a very rare case and it’s quite challenging to diagnose and treat. There are approximately 300 cases reported. Among them, only two giant PHNET cases were found in children under 20 years old.

Case presentation: We reported an unusual giant PHNET that was found in 18 years old female followed by intratumoral bleeding, which was initially misdiagnosed as Hemangioma. Abdominal Computed Tomography (CT) imaging showed a large liver mass with the peripheral enhancing nodular solid part in the delayed phase, which resembled Hemangioma.

Clinical discussion: Preoperative diagnosis of a Primary Hepatic Neuroendocrine Tumor is difficult as the liver often becomes the site of Neuroendocrine Tumor metastasis from other gastrointestinal organs, rarely occurred in people under 20 years of age, and the CT scan looks like Hemangiomas. The clinical symptoms are not typical, so other specific diagnostic tools for Neuroendocrine Tumor such as Chromogranin A level and 24-hour 5-hydroxyindoleacetic acid urine test are not performed. The indication of hepatic resection is made based on the preoperative diagnosis of other conditions such as large tumor size or tumor complications. Intraoperative diagnosis is also not typical for PHNET, so the definitive diagnosis of PHENT is made from post-resection histopathology.

Conclusion: The preoperative diagnosis of this rare tumor is still a big challenge. The physicians should be alert when finding Giant Hemangioma of the Liver, and Neuroendocrine Tumor should be the differential diagnosis. Blood Chromogranin A, urine 5-hydroxyindoleacetic acid test, and Positron Emission Tomography (PET) scan should also be considered.

1. Introduction

Neuroendocrine Tumor (NET) is rare heterogeneous neoplasms that derived from the neuroendocrine system with varying clinical syndromes [1,2]. It was first described by Oberndorfer in 1907 in the term Karzinoide [3]. The incidence of NET is around 2–4 cases in 100,000 population per year and about 0.66% of all types of malignancy [4]. NET is rarely found in children under 20 years old, but commonly found in people above fifty years old [5]. Neuroendocrine Tumor mainly occurs in the gastrointestinal system, with 44.7% in the small intestines, 19.6% in the rectum, 16.7% in the appendix, 10.6% in the colon, and 7.2% in the stomach [6]. Even though metastatic liver lesion derived from primary gastrointestinal NET is common, the Primary Hepatic Neuroendocrine Tumor is rarely found in the population and only present at 0.3% of all NETs [3]. Only two giant PHNETs were found in children under 20 years old [7]. Therefore, the diagnosis and treatment of this disease have many difficulties. Preoperative diagnosis of a Primary Hepatic Neuroendocrine Tumor is difficult as the liver often becomes the site of Neuroendocrine Tumor metastasis from other gastrointestinal organs, rarely occurred in people under 20 years of age, and the CT scan looks like Hemangiomas. The clinical symptoms are not specific, so other specific diagnostic tools for Neuroendocrine Tumor such as Chromogranin A level and 24-hour 5-hydroxyindoleacetic acid urine test are not performed. The indication of hepatic resection is made based on the preoperative diagnosis of other conditions such as large tumor size or tumor complications. Intraoperative diagnosis is also not typical for PHNET, so the definitive diagnosis of PHENT is made from post-resection histopathology.

Conclusion: The preoperative diagnosis of this rare tumor is still a big challenge. The physicians should be alert when finding Giant Hemangioma of the Liver, and Neuroendocrine Tumor should be the differential diagnosis. Blood Chromogranin A, urine 5-hydroxyindoleacetic acid test, and Positron Emission Tomography (PET) scan should also be considered.

* Corresponding author at: Jalan Nginden Intan Barat No. B, Surabaya, Jawa Timur, Indonesia.
E-mail address: jessicaandriani95@gmail.com (J. Andriani).

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hydroxyindoleacetic acid urine test are not performed. The indication of hepatic resection is made based on the preoperative diagnosis of other conditions such as large tumor size or tumor complications. Intraoperative diagnosis is also not typical for PHNET, so the definitive diagnosis of PHNET is made from post-resection histopathology. In this case report, we present the diagnostic problem of a rare case of Giant Primary Hepatic Neuroendocrine Tumor in a patient under 20 years of age.

This work has been reported according to the SCARE criteria [8].

2. Case presentation

An Indonesian female, 18 years old, was admitted to our hospital with persistent right upper quadrant abdominal pain, hypotension, and anemia. The pain was felt for around one month, primarily when the patient took a deep breath. Sometimes the patient also felt nauseous and vomiting. There were no other remarkable symptoms. There was also no remarkable history of past illness and history of family illness. The patient was referred to our hospital in stable condition. However, when the patient got admitted to our hospital, the hemoglobin level gradually decreased, from 9 to 8.5 within one day. Tumor markers were in the normal range. No other remarkable laboratory examination was found.

The first imaging performed on this patient was abdominal ultrasonography and an enhanced homogeneous echo intensity large liver mass was found. After the patient got hypotension, the patient underwent an enhanced abdominal CT scan at the former hospital (Fig. 1), and it was found that the liver was enlarging, and there was a large lobulated slight hypodense liver mass (size $15 \times 16 \times 18$ cm), predominantly with the necrotizing area. The mass had its feeding artery from the right hepatic artery's branches. In the delayed phase, it showed peripheral enhancing nodular solid part resembling Hemangioma. Post embolization imaging showed that the vascularization of the mass had decreased significantly. Two days after embolization, the mass was evaluated using abdominal Doppler ultrasonography, and it was found that there was no vascularization intra and perilesional. The bleeding also decreased. Two days later, an abdominal CT scan was performed (Fig. 2). It was found that the large mass covered almost all the right lobe of the liver, with an overall density of 25–29 Hounsfield Unit. There was no significant arterial feeder and no portal thrombus. But there was a suspicious necrosis area with a thin wall. Concerned that the thin wall could cause a spontaneous rupture, the patient was then decided to receive surgical treatment, and the patient agreed.

A preoperative diagnosis was Liver Hemangioma with intratumoral bleeding and rupture. Complete resection of the mass was successfully performed by a senior digestive surgeon to segment V-VI-VII liver with margin width of around 2 cm. No enlarged lymph nodes were found. Gross dissection of the resected showed a huge tumor with a solid wall and blood-filled cavity, and blood clot, closely resembling the presentation of Hemangioma (Fig. 3). There was no suspicion that led to Neuroendocrine Tumor. Unexpectedly, the postoperative pathology demonstrated malignant small round cell tumor with differential diagnosis hepatoblastoma and neuroendocrine carcinoma, further verified by immunochemistry assays showing Synaptophysin (+), Chromogranin A (+), Neuron-Specific Enolase (+), Alpha-fetoprotein (−), Glypican 3 (−). The final diagnosis was Primary Hepatic Neuroendocrine Tumor. The patient received postoperative care in the Intensive Care Unit, then the patient recovered well from surgery, and was discharged after approximately one month of admission. The patient then received long-acting somatostatin analog for further treatment. The patient was doing well during six months follow up, and there is no significant complaint.

3. Discussion

Neuroendocrine Tumor arises primarily in the gastrointestinal tract and bronchus. The appendix is the most common site of NET [9]. Meanwhile, Primary Hepatic Neuroendocrine Tumor is a rare case, and it’s quite challenging to diagnose and treat. Most PHNET cases were occurred in adults above fifty years old [5]. Only a few patients were diagnosed when they are less than eighteen years old [9]. According to Pastrian et al., the size of a giant PHNET is more than 8 cm. Until 2019, there were 300 reported cases of PHNET, only less than 30 cases are considered giant PHNET. Only two cases were found in children under 20 years old, which is similar to our case [7].

The Neuroendocrine Tumor can synthesize and release vasoactive

Fig. 1. A CT scan 3 days before embolization showed liver mass feeding artery was from the right hepatic artery's branches. In the delayed phase, it showed peripheral enhancing nodular solid part resembling Hemangioma.
amines and regulatory peptides such as serotonin, bradykinin, substance P, prostaglandins E and F, dopamine, and histamine. The increase of serotonin and bradykinin can cause flushing and diarrhea in Neuroendocrine Tumor patients [9]. But it was not found in our patient, so it was unlikely that the liver mass was diagnosed with Neuroendocrine Tumor at first. Primary Hepatic Neuroendocrine Tumor does not have any specific clinical presentation, and it is just reported that abdominal pain is the most common complaint, followed by weight loss, jaundice, and palpable right upper quadrant mass. It is difficult to differentiate from other liver tumors [3]. The definitive diagnosis of PHNET is made from post-resection histopathology [5]. Nevertheless, preoperative diagnosis is essential to decide further treatment, so we need to utilize laboratory and imaging tests for accurate preoperative diagnosis.

Tumor markers such as Alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), and Cancer Antigen (CA) are not helpful for diagnostic [3]. They were also found in our patients within the normal level. Meanwhile, Chromogranin A was considered the most helpful marker to confirm the diagnosis of NET [3]. It has high sensitivity (87–100%) and high specificity (92%) for diagnosed NET, but it is rare to do a serum Chromogranin A test because the case of PHNET is very rare [10]. Another non-invasive test that can be used to diagnose is 5-hydroxyindoleacetic acid from urine for 24 h (sensitivity 95–100%) [11]. Unfortunately, we didn’t perform Chromogranin A level and 5-hydroxyindoleacetic acid urine test because initially, no suspicion led to the Neuroendocrine Tumor. At seven days after surgery, when the pathological report concluded that the tumor was a Neuroendocrine Tumor, we did not measure the Chromogranin A level and 5-hydroxyindoleacetic acid urine test due to the decreased concentration after hepatic tumor resection.

The diagnosis of PHNET can be confused with other hepatic masses, based on radiological imaging. In the US imaging, it will show hypoechoic, hyperechoic, or mixed echogenic lesions with rings around them, and in the color US, it can lead to misdiagnosing of Hemangioma because it will show a bloodstream echo signal within lesions. Abdominal CT imaging shows multiple well-circumscribed, heterogeneous, hypodense masses, and no lesions showed significant calcification. However, in our patient, abdominal CT showed peripheral enhancing nodular solid part, which resembled Hemangioma and leads to misdiagnosis [12,13]. Magnetic Resonance (MR) images of PHNET show well-circumscribed, lobulated, or multiple nodular of high signal intensity on T2W1 and DWI, also heterogeneous and hypointense masses on T1W1 [12,14]. Identification of somatostatin receptor overexpression using radiolabeled somatostatin analog is being used to differentiate PHNET from other types of liver tumors. Several modalities can be used, such as Octreoscan using 111In-labeled DTPA-octreotide and PET Scan. PET Scan has better accuracy and sensitivity (97%) compared to CT scan (61%) and Octreoscan (52%). There are two commonly used tracers for NET, such as serotonin precursor 11-C-5-hydroxytryptophan and somatostatin analog 68Ga-DOTA peptides. Therefore, a PET Scan could also evaluate tumor susceptibility to somatostatin analog therapy [11]. The optimal treatment for PHNET that was published until now is complete resection. For unresectable cases, palliative hepatic resection combined with transcatheter arterial chemoembolization (TACE) is recommended [11,14].

4. Conclusion

Primary Hepatic Neuroendocrine Tumor is a very rare tumor, especially in children under 20 years old, so it’s quite challenging to make an accurate preoperative diagnosis. The rarity of the case, lack of suspicion in the clinical findings, and the similarity of the radiological features of this tumor with Hemangiomas make the physicians misdiagnose the case. The physicians should be alert when finding Giant Hemangioma of the Liver, and Neuroendocrine Tumor should be the differential diagnosis. Blood Chromogranin A, urine 5-hydroxyindoleacetic acid test, and PET Scan should also be considered.

List of abbreviations

| Abbreviation | Definition                  |
|--------------|-----------------------------|
| AFP          | Alpha-fetoprotein           |
| CT           | Computed Tomography         |
| MR           | Magnetic Resonance          |
| NET          | Neuroendocrine Tumor        |
| NSE          | Neuron-Specific Enolase     |

Fig. 2. CT scan result 4 days after embolization showed a decrease in bleeding.

Fig. 3. Resected tumor sample showing liver mass with necrosis and hemorrhage.
Consent

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

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Guarantor

Jessica Andriani, Emergency Department, Premier Surabaya Hospital.

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CRediT authorship contribution statement

Jessica Andriani: conceptualization, data curation, investigation, writing - original draft.

Vicky Sumarki Budipramana: conceptualization, formal analysis, investigation, writing - review & editing, supervision.

Cindy Sadikin: data curation, resources, investigation, visualization.

Declaration of competing interest

No conflict of interest.

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