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Giant insulinoma in a 15-year-old man: A case report

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ABSTRACT

INTRODUCTION: Giant insulinomas are extremely rare pancreatic neuroendocrine tumor.
PRESENTATION OF CASE: A 15-year-old man presenting with acute onset of lightheadedness was found to have serum glucose of 1.5 mmol/L. The blood collected from the hypoglycemic episode showed an inappropriately high insulin and C-peptide level. Abdominal computerized tomography showed a 12.5 cm well-defined, lobulated hypervascular mass at pancreatic tail, without any evidence of metastasis. En bloc resection with distal pancreatectomy, and splenectomy was successfully performed. The pathological examination confirmed insulinoma, with benign characteristics. Follow-up after the procedure revealed neither hypoglycemic, nor hyperglycemia.
CONCLUSION: We report the youngest case of a giant insulinoma. Despite the size of the tumor, the pathological report confirmed the benign characteristics. However, long-term follow-up is still essential to detect recurrence in the future.

1. Introduction

Insulinomas are rare neoplasms with a reported incidence of 4 cases per million population-year [1]. The majority of patients are above 50 years of age and is slightly more common in women than men [2]. Insulinomas are usually very small, with 80% being less than 2 cm in diameter [3]. Giant insulinomas (>9 cm in diameter) are even extremely rare. Less than 40 cases were reported since 1927 [4–6]. Mean age at the presentation was 54 years, with the youngest reported case at 29 years. Most giant insulinomas showed metastatic features at the time of diagnosis. We report an exceptional case of a 12.5 cm insulinoma in a 15-year-old patient with benign characteristics.

1.1. Presentation of case

A 15-year-old man was seen at emergency department with acute onset of lightheadedness, diaphoresis, and palpitations in the evening after fasting for 7 h. He had experienced repetitive episodes of dizziness for 2 months without any weight change. His serum glucose level was 1.5 mmol/L. His symptoms resolved after dextrose administration. He had no family history of insulinoma or multiple endocrine neoplasia type 1 (MEN-1). Physical exams showed a large palpable mass at left upper quadrant of the abdomen.

The subsequent analysis of the blood collected from the hypoglycemic episode showed an inappropriately high insulin level of 13.34 μU/mL (normal <3 μU/mL), and a high C-peptide level of 2.2 ng/mL (normal < 0.6 ng/mL). Abdominal contrast-enhanced computed tomographic (CT) scan showed a large well-defined, lobulated hypervascular mass with areas of low attenuation and calcifications at pancreatic tail, measuring 12 cm in largest diameter. The mass was adjacent to stomach, spleen, and left kidney. There were no pancreatic duct dilatation, no liver mass and no significant abdominal lymphadenopathy (Fig. 1). Serum intact parathyroid hormone (iPTH), calcium, and prolactin level were all normal.

The patient was admitted for continuous glucose infusion and frequent meals intake. The plasma glucose was maintained between 3.5–5 mmol/L by average glucose infusion at 10 g/hour. Esophagogastroduodenoscopy (EGD) was performed to exclude gastrointestinal tract invasion. Ten days after his admission, the patient underwent surgical exploration. Careful palpation demonstrated splenic attachment but not kidney. Therefore, en bloc resection with distal pancreatectomy, together with splenectomy was performed. The patient did not receive vaccination 2-week prior to surgery due to the urgency of the operation. The gross appearance showed 12.5 × 10.0 × 8.3 cm mass located at the pancreatic tail. Cut sections of the mass showed gray tan surface with

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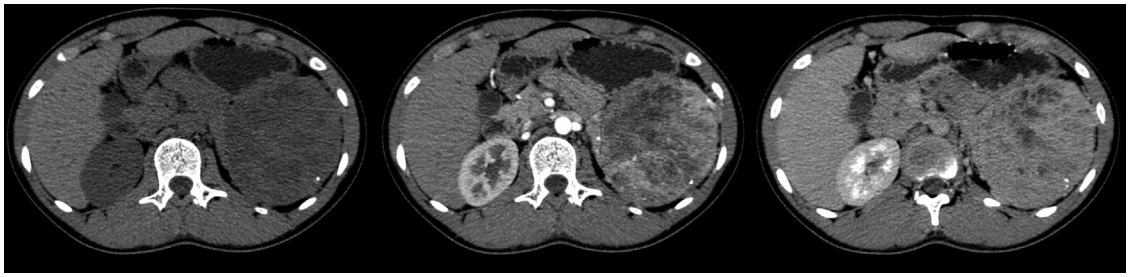

Fig. 1. CT of the abdomen showing the pancreatic mass in (from left to right, respectively) pre-contrast, arterial, and portal phase.

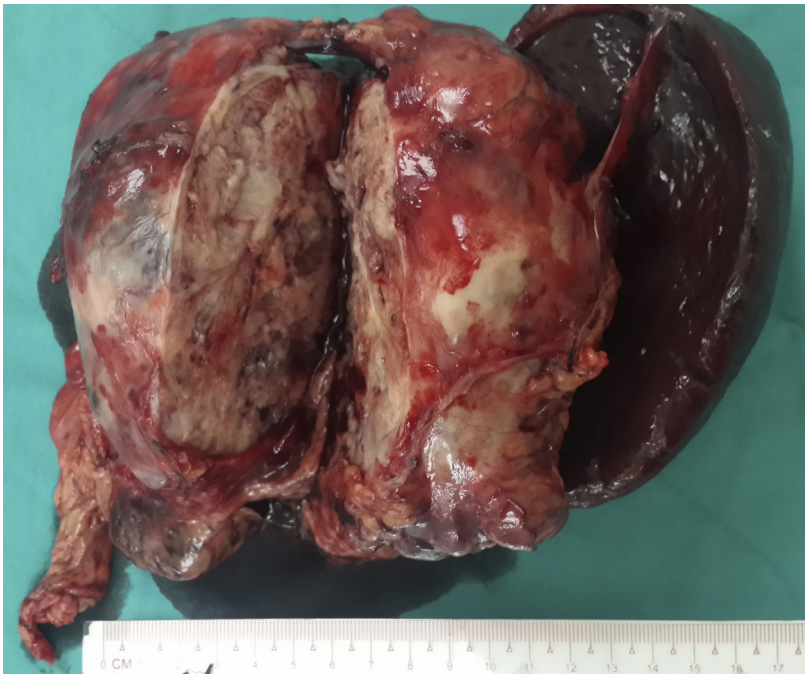

Fig. 2. Gross pathology.

focal hemorrhage. The mass was attached with the splenic capsule without splenic invasion (Fig. 2).

Histopathological examination revealed complete fibrous encapsulated mass composed of neoplastic cells arranging in cord, nest, insular and trabecular pattern (Fig. 3A–C). Immunological staining was positive for chromogranin, synaptophysin, insulin. Ki67 nuclear staining was positive at about 1–2%. Staining for Congo red, glucagon, and somatostatin was negative (Fig. 3D–H). The neoplastic cells had uniformed round nuclei with stippled nuclear chromatin and indistinct nucleoli without angiolymphatic or perineural invasion. Mitotic figures were 3–4/10 high power field (HPF). The tumor was confined in pancreas without splenic capsular invasion. All three resected lymph nodes showed no sign of metastasis.

Postoperative cause was uneventful. The latest follow-up of the patient (6 months after the procedure) revealed neither hypoglycemic, nor hyperglycemia. Post-splenectomy vaccination was performed.

2. Discussion

Insulinomas are rare pancreatic neuroendocrine tumors (PNET), which are mostly small at diagnosis. Giant insulinomas (>9 cm diameter) are even rarer. A giant insulinoma measuring 12.5 cm found in a 15-year-old man is very atypical. Our patient presented with typical Whipple triad. He reported only 2 month duration of symptoms before the diagnosis. High serum C-peptide and insulin level, in contrast with low plasma glucose level, confirmed the endogenous hyperinsulinemia. From these laboratory findings, the differential diagnosis was insulinoma, malignant insulinoma, ectopic insulin secreting tumor, and noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS). The mass palpable in this patient might represent intraabdominal insulin-secreting tumor such as insulinoma, and malignant insulinoma. In extremely rare cases, some malignancies were also previously reported to secrete insulin, such as gastrointestinal stromal tumor [7]. NIPHS could cause hypoglycemia from endogenous hyperinsulinism, but palpable mass in this patient could not explain this syndrome. Tumor was easily localized at pancreas by abdominal CT due to the large size. The CT result helped rule out NIPHS and made ectopic insulin secreting tumor unlikely. The diagnosis of insulinoma was confirmed by the positive staining for insulin while being negative for other hormones.

Diagnosing an insulinoma in youths as in our patient should raise the concern for genetic diseases. A case of giant insulinoma was previously reported to be associated with MEN-1 [8]. Yet, normal serum intact PTH, calcium and prolactin level helped exclude MEN-1 syndrome in this patient.

Surgical excision is the treatment of choice for insulinomas. In the small ones, simple enucleation or a distal pancreatectomy could be done. More aggressive surgical procedure is needed for larger tumors, requiring Whipple or total pancreatectomy

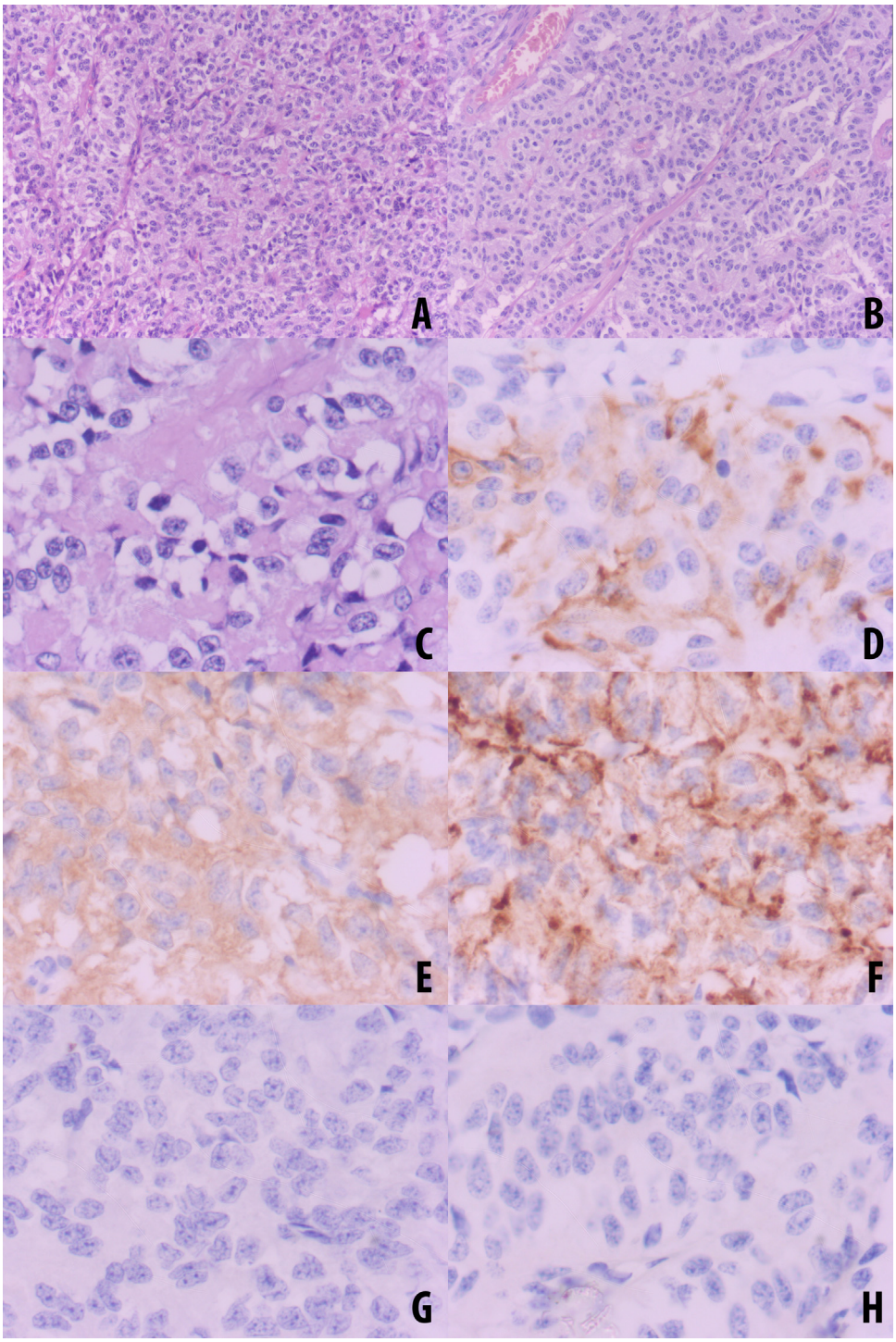

Fig. 3. Histopathology of the pancreatic mass (H&E): Low magnification shows neoplastic cells arranging in cord, nest, insular and trabecular pattern (A). The neoplastic cells are intervened by capillary networks (B). The neoplastic cells had uniformed round nuclei with stippled nuclear chromatin and indistinct nucleoli (C). Immunohistochemical study demonstrates the neoplastic cells with positive immunoreactivity to insulin antibody (D), the neuroendocrine marker synaptophysin (E), chromogranin (F), and none of the tumor cells with immunoreactivity for Glucagon (G) and Somatostatin (H).

techniques. Tumor invasion should also be considered. Stomach, spleen, and left kidney adjacency was shown by CT in this patient. Preoperative EGD helped exclude stomach invasion, thus partial gastrectomy might be unnecessary in this patient. However, whether to perform partial nephrectomy or splenectomy could not be determined preoperatively. Some noninvasive procedures such as fluorine-18-L-dihydroxyphenylalanine positron emission tomography (18F-DOPA PET), could help localize and verify adjacent organ invasion [9]. Nevertheless, these studies are limited in some patients [10], are not available in our institute, and have very limited availability in Thailand. Exploration was therefore performed to determine the organ invasion. After perioperative findings, en bloc resection with distal pancreatectomy was considered to ensure tumor-free margins. Splenectomy was also performed because of the splenic attachment.

From pathological report, the tumor confinement in the pancreas without local invasion, less than 2% Ki67 positive staining, uniformed round nuclei, regular distribution of nuclear chromatin, indistinct nucleoli, present of chromogranin and synaptophysin, and the absent of angiolymphatic or perineural invasion displayed the favourable benign findings; however, more than two mitoses per 10 HPF slightly increased the risk of malignancy [11]. Due to the large size of tumor, more than 60% of patients with giant insulinomas present metastatic features or evidence of local invasion at the time of the diagnosis [4]. This is much higher than the 4–13.6% reported in most insulinoma series [1,3]. Therefore, our patient is now currently scheduled for the life-long follow-up.

Our patient is interesting because of the extreme age at presentation, which is the youngest reported case of a giant insulinoma. Despite the huge size of the tumor and the splenic attachment, the pathological report confirmed the benign characteristics.

Conflicts of interest

All authors have no conflict of interest.

Funding

All authors have no funding of research.

Ethical approval

Ethical approval was not required for this case report.

Consent

Written informed consent was obtained from the patient and his parent for publication of this case report and accompanying images.

Author contribution

Vasin Vasikasin: author of the case report, the physician involving with the patient during admission and follow-up. Jirawat Watthanatham: the surgeon responsible for tumor resection. Prateep Napatharatip: the radiologist providing imaging detail in this report. Sumeth Termmathurapoj: the pathologist discussing the histopathology aspect in this report.

Guarantor

Vasin Vasikasin.

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