International Surgery Journal
Alsuhaibani AA et al. Int Surg J. 2022 Jan;9(1):181-184
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20215153

Case Report

Curative treatment of pancreatic functioning insulinoma with stereotactic ablative radiation therapy: case report

Aws Abdulrahman Alsuhaibani[1]*, Abdullah Abdulrahman Alsuhaibani[2], Tareq Salah Hassan[2,3]

[1]Alfaisal University
[2]King Saud University, King Khalid University Hospital, Oncology center, Radiation Oncology Unit, Riyadh, Saudi Arabia
[3]Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt

Received: 06 December 2021
Revised: 20 December 2021
Accepted: 21 December 2021

***Correspondence:**
Dr. Aws Abdulrahman Alsuhaibani,
E-mail: aalsuhaibani@alfaisal.edu

ABSTRACT

Insulinoma is the most common pancreatic neuroendocrine tumor (NET). It is a rare disease account for 1-2% of pancreatic tumors and affect approximately up to 3 patients per million per year. complete surgical resection or debulking are standard of care option. However, surgery is associated with short and long-term post-operative morbidity and may not be appropriate for all patients. In This case we present management and cure of a case of functioning insulinoma with stereotactic ablative radiosurgery in an unfit patient for surgery.

Keywords: Insulinoma, Stereotactic radiation, SBRT, SABR, Radiation

INTRODUCTION

Insulinoma is the most common pancreatic NET. It is a rare disease account for 1-2% of pancreatic tumors. Although complete surgical resection or debulking are standard of care, surgery is associated with short and long-term post-operative morbidity and may not be appropriate for all patients. In This case we present management and cure of a case of functioning insulinoma with stereotactic ablative radiosurgery in an unfit patient for surgery.

CASE REPORT

57 years old male known case of hypertension on lisinopril 5 mg and bisoprolol 2.5 mg with past history of lymphoma diagnosed 35 years back treated with chemotherapy and radiotherapy.

History of cerebrovascular transient ischemic attack in July, 2018. Lead to slurred speech. After development of hypoglycemic attacks, CT scan (Figure 1) scan and MRI (Figure 2 and 3) of the abdomen showed bulky appearance of the uncinate process of the pancreas, concerning for pancreatic mass together with high serum insulin (4 folds of upper limit of normal value) and low serum blood glucose level and insulinoma was diagnosed on July 2018. After being evaluated by endocrine surgery, hepatobiliary surgery and radiation oncology and being discussed in tumor board, decision was patient counseling for Whipple's operation with high risk for morbidity and mortality versus stereotactic ablative radiation therapy (SABR). Patient refused surgery and decided not to go for surgery and decided to go for radiation. Patient received SABR 40 Gy over 4 fractions July 2021 using TrueBeam® with good tolerance (Figure 3).

Currently patient is under regular follow up with sustained improvement biochemically and clinically in the form of improvement of hypoglycemia and decrease

serum insulin levels (Figure 4) with no early or long-term complications.

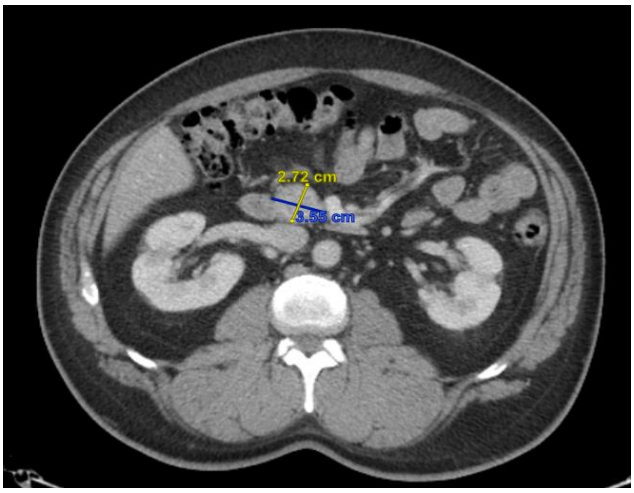

Figure 1: CT scan of the abdomen at presentation.

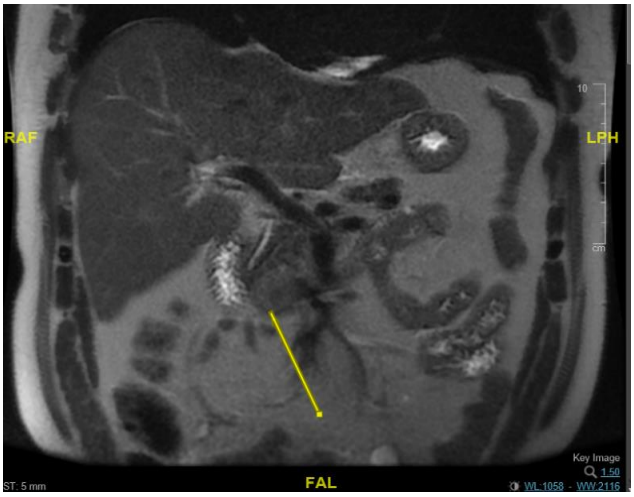

Figure 2: MRI abdomen at presentation.

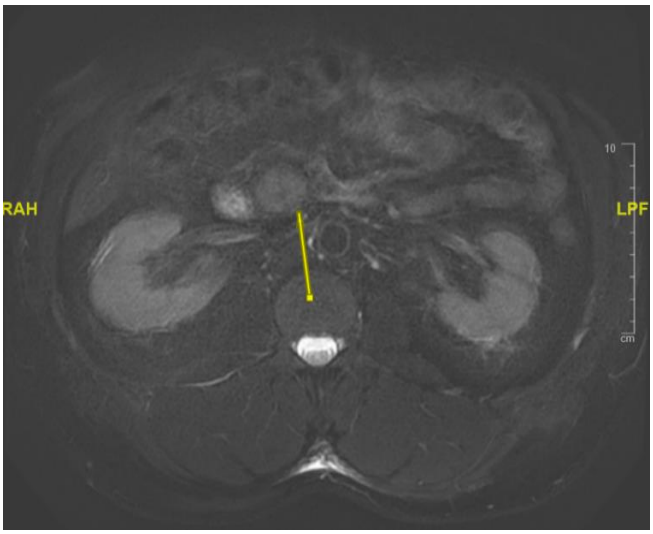

Figure 3: MRI abdomen at presentation.

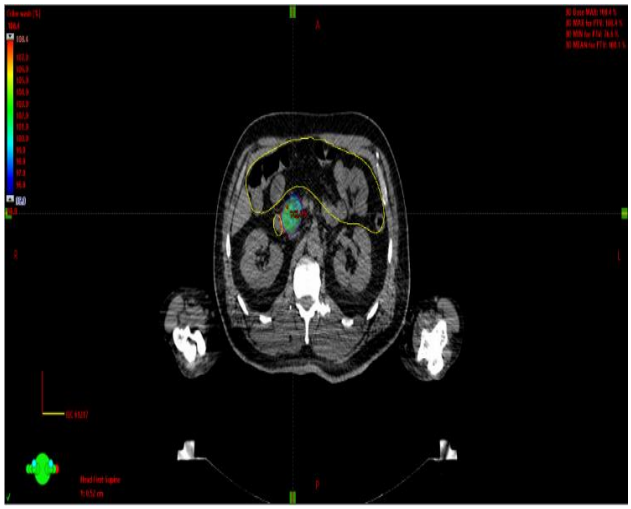

Figure 4: SABR treatment.

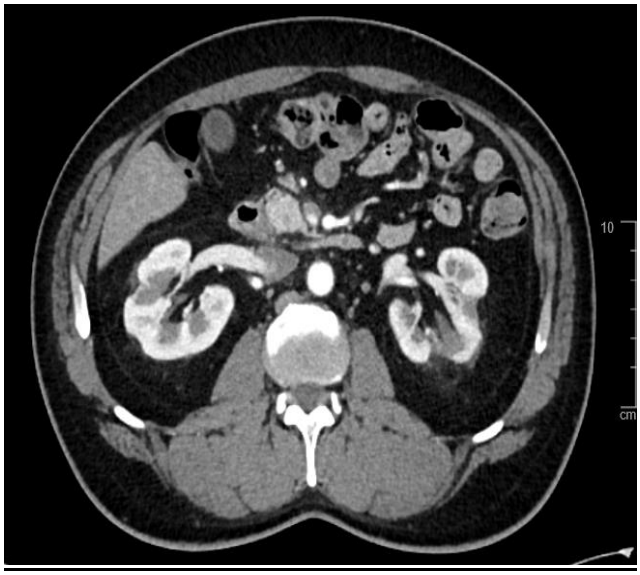

Figure 5: CT scan.

DISCUSSION

Insulinoma is the most common pancreatic NET. It accounts for 1-2% of pancreatic tumors and affect approximately up to 3 patients per million per year.[1,2]

May occur at any age, mainly during the 5th decade of life with slight female predominance.[3]

Histopathologically, Insulinomas are most commonly benign, well differentiated NETs, whereas malignant neoplasms account for approximately 5-10% of all cases.[4] It is derived from β-pancreatic islet cells that secrete insulin, and is associated with hypoglycemic neuroglycopenic and sympathetic-overstimulation symptoms.[5] Dysregulated hormonal production remains a challenge in the management of neuroendocrine neoplasms (NEN).[6] The great majority (>90%) of

insulinomas are nonmetastatic at presentation and can be surgically cured.[7]

Insulinoma malignancy is confirmed by presence of extra pancreatic locoregional, lymph-node or remote extension. Insulinoma is malignant in 4-14% of cases.[8]

Two other definitions, based on pathology results, are used in the current guidelines: insulinoma of uncertain prognosis (size greater than 2 cm or grade 2 based on the 2010 WHO classification, or vascular and/or perineural invasion or necrosis) and benign insulinoma if none of the above.[9]

Clinically, the diagnostic hallmark of insulinoma was first described by Whipple et al "Whipple's triad" or "triad of insulinoma" and consists of symptoms caused by hypoglycemia; low blood glucose level during the episodes; and symptoms relief upon blood glucose level normalization through glucose administration.[10] Hypoglycemic episodes caused by inappropriate insulin secretion are divided in two main categories, adrenergic and neuroglycopenic.[22,32]Adrenergic symptoms are caused by sympathetic nervous system (SNS) activation/catecholamines release and include diaphoresis, tremor, palpitations, anxiety, increased appetite and nervousness. Neuroglycopenic symptoms, caused by decreased central nervous system (CNS) glucose supply, include impaired mental status and cognition, visual disturbances, disorientation, memory deficits, stupor, seizures and coma.[11] Patients usually present with symptoms and signs precipitated during fasting periods, often upon awakening after the overnight fast or during exercise.[12]

Management includes conservative treatment with drugs targeting insulin-induced hypoglycemia, non-operative invasive procedures, as well as curative open or laparoscopic tumor resection.[2]

As the great majority (>90%) of insulinomas are nonmetastatic at presentation and can be surgically cured, complete surgical resection or debulking are standard of care option.[7,13] However, surgery is associated with short and long-term post-operative morbidity and may not be appropriate for all patients.[14]

In cases when the surgery may cause severe complications with the high risk of mortality, the physical non-surgical methods can be used.

There are data in literature about the different non-surgical modalities such as radiofrequency ablation, microwave ablation, cryodestruction, laser ablation, irreversible electroporation, photodynamic therapy, high-intensity focused ultrasound, cyberknife, and tumor alcoholization. No papers studied advantages and disadvantages of each method of treatment. Each method was used because of its availability in the hospital or department.[15] No full head-to-head comparison of different methods.

Stereotactic body radiation therapy (SBRT)

NETs are assumed to be highly radiosensitive based on data from Ahmed et al who reported on a multigene expression index for radiosensitivity correlated with response post SBRT to liver metastases. Based on this study, small bowel neuroendocrine malignancies were predicted to be highly radiosensitive, with pancreatic and large bowel neuroendocrine malignancies predicted to have the same radiosensitivity as colorectal metastases.[16]

SBRT offers an advantage both in image guidance and ablative radiation doses delivered directly to tumors with acceptable toxicity compared to conventional techniques in pancreatic cancer.[17] The concept of stereotactic radiotherapy was first described in the mid-20th century by Leksell which involves cranial stereotactic radiation by delivering large, precise doses of radiation to the brain, thus coining the term stereotactic radiosurgery (SRS).[18] 25 years later, in 1975 the gamma knife system became an alternative to surgical resection in treating brain metastasis using single ablative doses of radiation were delivered to brain metastases via using frame-based system, which was directly fixed to the skull.[19] By the early 1990s, by developing a body frame system using a linear accelerator, extracranial stereotactic radiotherapy started for treating to extracranial tumors, both primary and metastatic, involving the liver, lung, and the retroperitoneal space was developed.[19]

After being a standard option for early stage non-small cell lung cancer, SBRT had evolved to be tested for a variety of other malignancies.[20,21] Favorable results of SBRT for locally advanced pancreatic cancer (LAPC) has been achieved leading to the exploration of SBRT for other pancreatic cancer patients.[22] Kong was the first to use Cyberknife for pancreatic cancer treatment with increased body mass were observed in 100% of cases.[15,23] Phase I/II studies have demonstrated that CyberKnife radiosurgery is a safe and effective strategy for management of patients with locally advanced and metastatic pancreatic cancer. No significant toxicities were observed during or after treatment providing proof of concept that SBRT is an effective therapeutic strategy for functional neuroendocrine neoplasms.[24]

Huscher et al reported the first case report of the use of SBRT for an insulinoma, reporting excellent 3-year clinical control of symptoms.[25] Although small in number, reflective of the rarity of this disease, these reports demonstrate the clinical effectiveness of SBRT for NEN.

CONCLUSION

Stereotactic Body radiation therapy is a high precision treatment modality may be a valid option for treating

functioning pancreatic tumors in unfit patients for surgical resection due to comorbid illnesses with high safety and efficacy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. De Herder WW, Niederle B, Scoazec J-Y. Well-differentiated pancreatic tumor/carcinoma: insulinoma. Neuroendocrinology. 2006;84(3):183-8.
2. Okabayashi T, Shima Y, Sumiyoshi T. Diagnosis and management of insulinoma. World J Gastroenterol. 2013;19(6):829.
3. Bouslama K, Maghrebi H, Bedioui H, Bouslama KJJAHG. Pancreatic insulinoma: diagnostic approach and therapeutic modalities. BMC Res Notes. 2014;8:11-5.
4. Giannis D, Moris D, Karachaliou G-S. Insulinomas: from diagnosis to treatment. A review of the literature. J BUON. 2020;25(3):1302-14.
5. Metz DC, Jensen RTJG. Gastrointestinal neuroendocrine tumors: pancreatic endocrine tumors. Gastroenterology. 2008;135(5):1469-92.
6. Myrehaug S, Hallet J, Chu W. Proof of concept for stereotactic body radiation therapy in the treatment of functional neuroendocrine neoplasms. J Radiosurg SBRT. 2020;6(4):321.
7. De Herder WW, van Schaik E, Kwekkeboom D, Feelders RAJCe. New therapeutic options for metastatic malignant insulinomas. Mov Disord. 2011;75(3):277-84.
8. Zhao Yp, Zhan Hx, Zhang Tp. Surgical management of patients with insulinomas: result of 292 cases in a single institution. J Surg Oncol. 2011;103(2):169-74.
9. Baudin E, Caron P, Lombard-Bohas C. Malignant insulinoma: recommendations for characterisation and treatment. Ann Endocrinol (Paris). 2013;74(5-6):523-33.
10. Whipple AO, Frantz VKJAos. Adenoma of islet cells with hyperinsulinism: a review. Ann Surg. 1935;101(6):1299.
11. Nikfarjam M, Warshaw AL, Axelrod L. Improved contemporary surgical management of insulinomas: a 25-year experience at the Massachusetts General Hospital. Ann Surg. 2008;247(1):165.
12. Grant CSJBp, gastroenterology rC. Insulinoma. 2005;19(5):783-98.
13. Chan DL, Dixon M, Law CH. Outcomes of cytoreductive surgery for metastatic low-grade neuroendocrine tumors in the setting of extrahepatic metastases. Ann Surg Oncol. 2018;25(6):1768-74.
14. De Baere T, Deschamps F, Tselikas L. GEP-NETS update: Interventional radiology: role in the treatment of liver metastases from GEP-NETs. Eur J Endocrinol. 2015;172(4):R151-66.
15. Berelavichus SV, Kriger AG, Dugarova RS, Kaldarov ARJSCCM. Treatment of Insulinomas with Minimally Invasive Physical Procedure. Literature Review. 2019;1(2):104-12.
16. Ahmed KA, Caudell JJ, El-Haddad G. Radiosensitivity differences between liver metastases based on primary histology suggest implications for clinical outcomes after stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys. 2016;95(5):1399-404.
17. Ghaly M, Gogineni E, Saif MWJP. The Evolving Field of Stereotactic Body Radiation Therapy in Pancreatic Cancer. Pancreas (Fairfax). 2019;3(1):9.
18. Leksell LJAcs. The stereotactic method and radiosurgery of the brain. Acta Chir Scand. 1951;102:316-9.
19. Blomgren H, Lax I, Näslund I, Svanström RJAo. Stereotactic high dose fraction radiation therapy of extracranial tumors using an accelerator: clinical experience of the first thirty-one patients. Acta Oncol. 1995;34(6):861-70.
20. Videtic GM, Chang JY, Chetty IJ. ACR Appropriateness Criteria® Early-Stage Non-Small-Cell Lung Cancer. Am J Clin Oncol. 2014;37(2):201-7.
21. Kollar L, Rengan R. Stereotactic body radiotherapy. Paper presented at: Seminars in oncology. 2014.
22. Pollom EL, Alagappan M, Von Eyben R. Single- versus multifraction stereotactic body radiation therapy for pancreatic adenocarcinoma: outcomes and toxicity. Int J Radiat Oncol Biol Phys. 2014;90(4):918-25.
23. Koong AC, Le QT, Ho A. Phase I study of stereotactic radiosurgery in patients with locally advanced pancreatic cancer. Int J Radiat Oncol Biol Phys. 2004;58(4):1017-21.
24. Goodman KA, Koong AC. 26 Cyber Knife Radiosurgery for Pancreatic Cancer. 2005.
25. Huscher CGS, Mingoli A, Sgarzini G, Mereu A, Gasperi MJSi. Image-guided robotic radiosurgery (Cyber Knife) for pancreatic insulinoma: is laparoscopy becoming old? Surg Innov. 2012;19(1):NP14-7.

Cite this article as: Alsuhaibani AA, Alsuhaibani AA, Hassan TS. Curative treatment of pancreatic functioning insulinoma with stereotactic ablative radiation therapy: case report. Int Surg J 2022;9:181-4.