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Simultaneous Parathyroidectomy & Distal Pancreatectomy for MEN1 Patient

Sherin A Hussein[1,*], Raafat Alturfi[2]

[1]*M.B.ch.B, FIB, MS (Medical oncology) Oncology Department, Alyarmok teaching hospital, Iraq*

[2]*Assistant professor, MD, CABS, FIBMS (Dig Surgery), FACS, FRCS(Glasgow), Gastroenterology and hepatology Teaching Hospital, Medical City, Baghdad, Iraq*

ABSTRACT

Aim: report a rare case of Multiple endocrine neoplasia type1(MEN 1), with rare way of presentation&surgical treatment. **Background:** MEN1 is autosomal dominant disease characterized by a predisposition to the parathyroid glands, anterior pituitary, and pancreatic islet cells tumors. **Case description:** a female patient with MEN 1 syndrome presented with symptoms of hypoglycemia and hypercalcemia due to pancreatic insulinoma & parathyroid tumor, treated by simultaneous left sided pancreatectomy & subtotal parathyroidectomy due to severe both symptoms, with excellent outcome. **Conclusion:** hyperglycemia & hypercalcemia can present in severe form as well as at the same time in MEN1 patient, and require urgent management for both. Clinical **significance:** pancreatectomy & parathyroidectomy can be done at same time by rather expert surgical team, with good outcome.

Keywords: MEN1, Parathyroidectomy, Pancreatectomy, Case Report.

BACKGROUND

Multiple endocrine neoplasia type 1 or Werner syndrome, is a rare autosomal dominant disease characterized by a predisposition to tumors of the parathyroid glands (90%), anterior pituitary (30% to 40%), and pancreatic islet cells (30% to 70%) [1]. prevalence of MEN1 is 2 per 100,000 in the general population [2]. MEN1 can present in a wide age range, from age 5 to 81 years, with biochemical and clinical manifestations, usually of primary hyperparathyroidism, in 85% of patients [1].

In 1997, a clone of the gene causative of MEN1 that consists of 10 exons encoding a 610-amino acid protein referred to as menin was identified (Gen Bank Accession No: U93236.1) [3]. As a tumor suppressor gene, the MEN1 gene functions mainly as loss of heterozygosity at the menin locus of chromosome 11q13 [4,5] and present genetic testing for the MEN1 gene focuses on detection of the polymorphic markers in this region [3].

Genetic diagnosis of MEN1 has clinical importance for reducing disease-related morbidity and mortality of index cases and their relatives [3]. In particular, early biochemical surveillance for genetically affected asymptomatic relatives can help to detect MEN1-related tumors even 10 years before clinically evident disease [6]. In contrast, the negative result

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***Corresponding Author**

Dr. Sherin A Hussein

PM.B.ch.B, FIB, MS (Medical oncology) Oncology Department, Alyarmok teaching hospital, Iraq, Phone: 009647709204547

Email: Sherin.ali.h82@gmail.com

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of genetic testing for MEN1 mutations can eliminate the psychological burden of possible MEN1 in patient relatives [3]. Thus, genetic testing is recommended in first-degree relatives of index patients [1].

Presentation

Age of onset of endocrine tumors is usually in the teenage years but symptoms from these tumors may not appear for several years and the diagnosis is frequently delayed until the fourth decade of life [7].

Tumors may hyper secrete hormone, causing hypercalcemia and recurrent nephrolithiasis due to hyperparathyroidism(HPT), Zollinger-Ellison syndrome (hypergastrinaemia), hypoglycaemia (hyperinsulinemia), amenorrhea (hyperprolactinemia) or acromegaly (excess growth hormone) [7].

Tumors of the pituitary gland may cause symptoms by mass effects [7].

Angiofibromas, collagenomas, cutaneous manifestation and lipomas do not typically cause symptoms, and they are mostly of cosmetic concern [7].

Diagnosis

Parathyroid carcinoma is difficult to diagnose preoperatively [8]. Most parathyroid carcinomas are diagnosed at surgery; however, some are not diagnosed until local recurrence or metastases [8]. This is because there are no definitive histopathologic features to differentiate carcinoma from adenoma. FNA is inappropriate for diagnosis [8].

Treatment: Surgery Treatment consists of parathyroidectomy with enbloc resection of tumor and involved structures [9]. This may include the ipsilateral lobe of thyroid. Radical lymph node dissection is not recommended. Recurrent tumor and oligo metastases should also be resected [9].

This is a case report of MEN1 patient presented with frequent attacks of sever hypoglycemia and hypocalcemia treated by the same session.

CASE DESCRIPTION

A forty-three year old female, presented with frequent attacks of confusion, sweating, fainting and disturb level of consciousness, during the last 3 months, the condition relieved by taking sweet fluid or eating. She had weight gain about 10kg during the same period. Her blood sugar was always below 50mg/dL. She underwent seventy-two hour fasting test but she develops severe hypoglycemic attack after 4 hours that treated by hypertonic glucose water. Her blood analysis was normal apart from elevation of serum calcium, insulin, proinsulin, parathyroid hormone and hypoglycemia.

Abdominal computed tomography (CT) SCAN: demonstrated a well-defined mass 4.3x 3.7cm at tail of pancreas with another mass 1.5 x1.2 cm posterior to previous one, suggesting pancreatic islet cell tumor (Figure 1).

Chest and pelvic CT scan demonstrated multiple osteolytic lesions involve ribs and pelvic bones, the largest one is 46x29 mm seen at anterolateral right 3rd rib, and picture goes with bone brown tumors due to hyperparathyroidism. The diagnosis of MEN 1 syndrome was made, and sends for neck CT scan, which demonstrated 17mm enhancing nodule seen related to the left lobe and another enhancing nodule 19x18 mm seen inferior to the right lobe of the thyroid gland the picture goes with multiple parathyroid adenoma. Brain MRI revealed no significant pituitary pathology.

During multi-disciplinary team (MDT) discussion the decision was made to deal with parathyroid and pancreatic tumors at the same time because of severe both symptoms. The informed consent was taken from the patient, after full explanation to her about her disease and the surgical planning with possible complications.

Through cervical collar incision, 3 glands (right inferior, left superior& inferior) in addition to ectopic one near the thymus. All were removed in addition to left hemithyroidectomy, keeping the normal right upper parathyroid gland intact (subtotal thyroidectomy) (Figure 2).

Then and at the same time, through upper midline incision distal pancreato-splenectomy was done (Figure 3). The histopathology revealed parathyroid hyperplasia of all resected glands. And regarding the pancreas, it contains 4 nodules the largest one 42mm which showed well differentiated neuroendocrine tumor WHO grade I. Post operatively the patient developed transient hyperglycemia and discharged well after five days with normal blood glucose and serum calcium.

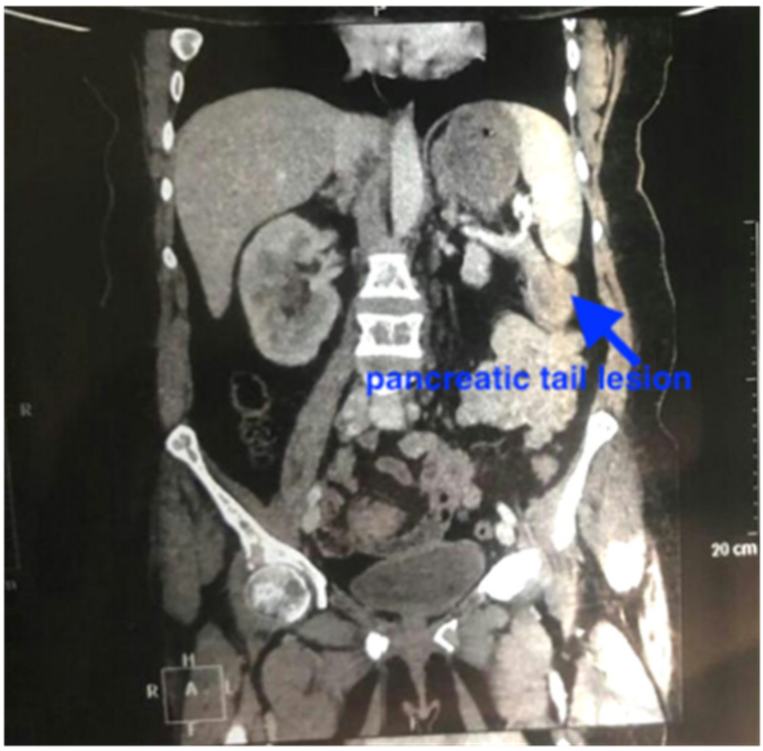

Figure 1. Abdominal CT scan showed enhancing pancreatic tai lesion.

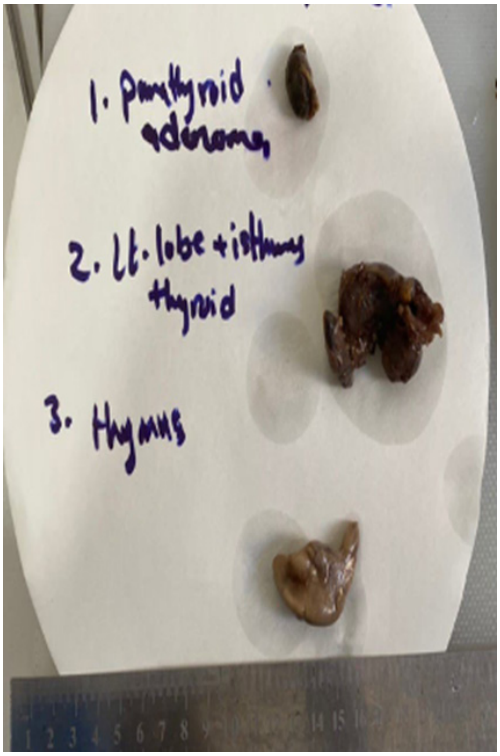

Figure 2. Showed extent of parathyroidectomy.

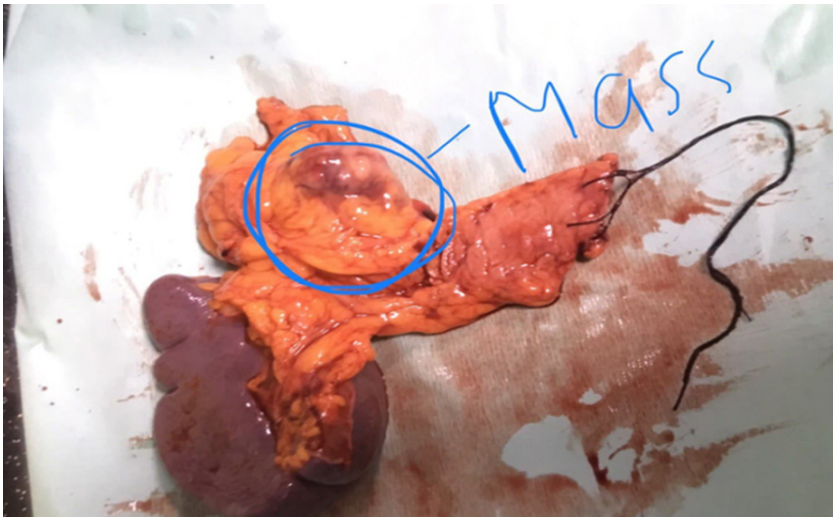

Figure 3. Left sided pancreato-splenectomy.

DISCUSSION AND CONCLUSION

The treatment of this case with MEN I is unique, inform of that she had two functional endocrine tumors at the same time. So the dilemma was whether to start with pancreas because of severe symptom of hypoglycemia or to start with parathyroid because of high serum calcium with multiple osteolytic lesions? The decision was made in MDT meeting to do simultaneous surgery for both, especially the surgical team has good experience to deal with pancreatic as well as with parathyroid surgery.

The surgical indication for primary hyperparathyroidectomy (PHPT) is obvious in patients with symptoms with severe hypercalcemia; and in these circumstances there appears to be a good risk/ benefit balance [9]. Surgery is not recommended in young asymptomatic patients in whom the serum calcium values are less than 1 mg/dl over the upper-normal limit and whose bone mineral density values are greater than–2.5 T-score because early parathyroidectomy predisposes the patient to an earlier recurrence of hyperparathyroidism [9].

Regarding PHPT in MEN I, it is associated with multi-glandular hyperplasia and an increased incidence of supernumerary or ectopic glands [10] (like what was found in this case). The goals of surgery are to achieve and maintain eucalcemia for the longest time possible, to avoid iatrogenic hypoparathyroidism and to minimize the need for future surgery.

Because of all parathyroid glands are affected in MEN1, the surgical management requires removal of all abnormal tissue using an open bilateral exploration. Debate remains over the most appropriate operation, that is, subtotal parathyroidectomy (extirpation of 3.5 glands) or total parathyroidectomy with or without auto transplantation to achieve this goal

The decision to perform a subtotal parathyroidectomy or a total parathyroidectomy with autotransplantation should be made with the risk of recurrent or persistent disease and the risk of permanent hypoparathyroidism in mind.

Some authors perform a 4-glands exploration and a 3.5-gland parathyroidectomy with bilateral cervical thymectomy leaving the remnant gland in situ. The choice of which gland to leave as a remnant is made based on visualization of the smallest or most normal-appearing gland after frozen section biopsy confirms it is in fact parathyroid tissue [10].

Pancreatic neuroendocrinal tumors (pNET) s in patients with MEN1 has a number of unique features, which have markedly complicated the therapeutic approach. First, non-functioning (NF)-pNETs occur microscopically in 80–100% of MEN1 patients, are invariably multiple, throughout the pancreas, and it is estimated in only 0–13% of patients do they become symptomatic [11].

Of all pancreatic endocrine tumors two- thirds are functional but in patients with MEN-1 most are nonfunctional. Among MEN-1 patients with functioning a pancreatic endocrine tumor, gastrinoma is the most commonly observed malignant tumor [12], insulinoma occurs in 10% of patients [10].

The result of this multiplicity of NF-pNETs and gastrinomas is that it is now generally recognized that these patients cannot be cured completely of all pNETs tumors without very aggressive surgical resections (complete pancreatectomy for NF-pNET) [11]. However, increasing evidence suggest that patients with small lesions (<1.5–2 cm) have an excellent prognosis without surgery in most cases [11,12].

So, Recent guidelines from a number of organizations (like NANET&ENET) for the treatment of pNETs in MEN1 recommend a conservative approach to patients with MEN1/ Zollinger-Ellison syndrome or NF-pNETs with imaged pNETs <1–2 cm [11].

Also, in patients with NF-pNETs, because of the multiplicity of small adenomas, a total pancreatectomy would be required, which because of its morbidity, is not recommended [11].

CLINICAL SIGNIFICANT

MEN 1 syndrome patient, presented with symptoms of hypoglycemia and hypercalcemia due to pancreatic insulinoma & parathyroid tumor, treated by simultaneous left sided pancreatectomy & subtotal parathyroidectomy due to severe both symptoms, with excellent outcome.

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None.

CONFLICT OF INTERESTS

The authors declare that there is no interest conflict.

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