

Unusual Pathologic Findings Associated with Multiple Endocrine Neoplasia Syndrome-1: Undescended Parathyroid Gland Hyperplasia and Mesenteric Cyst

Multipl Endokrin Neoplazi Sendrom-1 ile İlgili Alışılmadık Patolojik Bulgular: İnmemiş Paratiroid Hiperplazi ve Mezenterik Kist

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CASE REPORT
OLGU SUNUMU

ABSTRACT
ÖZET

Although gastro-entero-pancreatic tumors constitute main clinical features of multiple endocrine neoplasia type 1 (MEN1), mesenteric cyst has not previously been recognized clinically as part of this syndrome. We report here a woman who presented with combination of mesenteric cyst that was removed surgically and undescended hyperplastic parathyroid gland located in the superior cervical region. This case illustrates that mesenteric cyst, like other gastro-entero-pancreatic tumors, may be part of MEN1. Superior cervical and submandibular areas should be investigated carefully for any uptake when evaluating patients with sestamibi scintigraphy for parathyroid diseases because of potential conflict with salivary glands uptake of sestamibi.

Key words: Mesenteric cyst, multiple endocrine neoplasia Type 1, parathyroid glands, scintigraphy

Gastro-enteropankreatik tümörler Multipl Endokrin Neoplazi 1'in (MEN1) başlıca klinik bulgusu olmasına rağmen mezenterik kist daha önce bildirilmemiştir. Bu yazıda, MEN1'li bir kadın hastada cerrahi olarak çıkarılan mezenterik kist ile nadir olarak görülen süperiyor servikal yerleşimli inmemiş hiperplastik paratiroid bezi birlikteliğini sunuyoruz. Bu olgu sunumu MEN1'in olağan olmayan klinik sunumu hakkında olup diğer gastroenteropankreatik tümörler gibi mezenterik kistin de MEN1'in birer komponenti olabileceğini göstermektedir. Paratiroid hastalıkları için sestamibi ile yapılan bir paratiroid sintigrafisinde tükrük bezlerindeki fizyolojik tutulumlar nedeniyle değerlendirilmesi zor olan süperiyor servikal ve submandibular alanlar, inmemiş paratiroid bezler açısından özellikle aranmalıdır.

Anahtar kelimeler: Mezenterik kist, multipl endokrin neoplazi Tip1, paratiroid bezi, sintigrafi

Introduction

MEN1 is a rare autosomal dominant hereditary cancer syndrome presented mostly by tumours of the parathyroids, endocrine pancreas and anterior pituitary (1, 2). Associated with this syndrome, other endocrine and non-endocrine lesions, such as adrenal cortical tumours, carcinoids of the bronchi, gastrointestinal tract and thymus, meningiomas, lipomas, angiofibromas, collagenomas can also occur in varying combinations (3-6). Parathyroid gland hyperplasia or adenomas are the most common clinical manifestation of MEN1. Sestamibi parathyroid scintigraphy is used to provide the surgeon with the best anatomical information. Radio-guided parathyroidectomy is useful in re-operation for persistent or recurrent hyperparathyroidism and ectopic adenomas. We presented a MEN1 case with ectopic parathyroid gland sited in the submandibular area and mesenteric cyst in the abdomen.

Case Report

A 41-year-old woman presented at the endocrinology outpatient clinic with the complaints of dizziness, nausea and amenorrhea which had lasted four months. The patient had had an operation for right near total thyroidectomy 11 years ago.

Histopathology revealed a benign nodular goiter. Since the patient was treated with dopamine agonist therapy that reduced the prolactin levels to normal (parlodel for 7 years and kabergolin for last two years), an adenoma 3 mm in diameter was confirmed in the pituitary gland by pituitary magnetic resonance (MR). After therapy the patient had regular menstrual cycles without galactorrhea, and laboratory tests showed a lower limit of normal prolactin hormone (4.7 ng/mL; normal range 4.79-23.3 ng/mL).

During the follow up, elevated calcium levels (11.2 mg/dL; normal range: 8.5-10.2 mg/dL) and elevated PTH (285 pg/mL; normal range, 15-65 pg/mL) suggested hyperparathyroidism. The ultrasound indicated no evidence of a parathyroid adenoma. She had normal bone mineral density. Nasopharynx MR revealed a well-demarcated, contrast enhanced 9 mm nodule located in the anatomic area of the right submandibular salivary gland, including no discrimination from the lymphoid tissue.

Tc-99m sestamibi dual phase parathyroid scintigraphy demonstrated a focus of uptake inferior to the right submandibular gland, suspicious of an ectopic parathyroid adenoma or hyperplasia (Figure 1).

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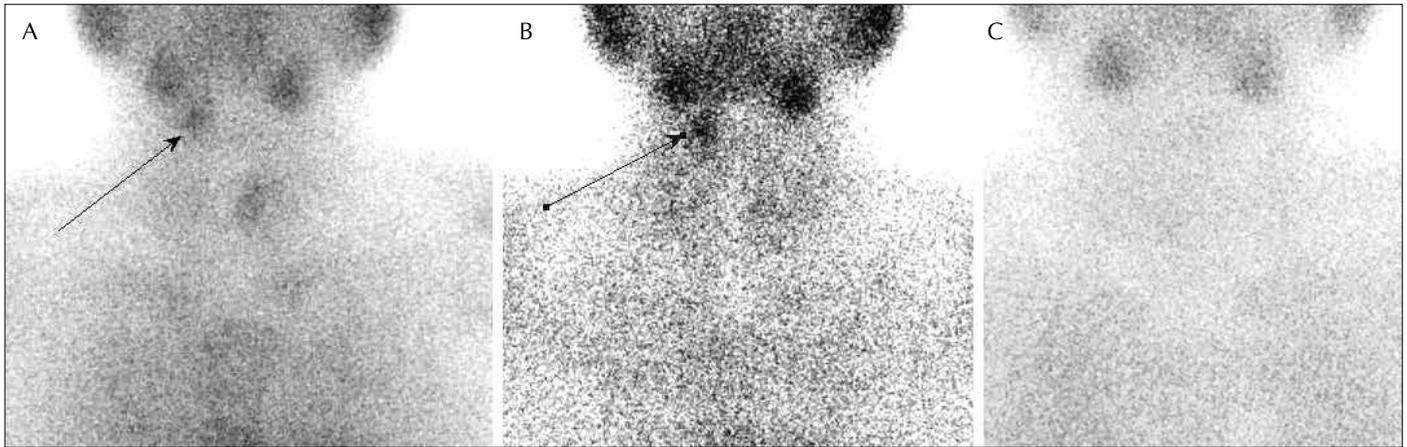


Figure 1. Dual phase Tc-99m sestamibi scintigraphy: 15th minutes (A) and 120th minutes (B) of Tc-99m sestamibi images showed an increased uptake in the inferomedial part of the right submandibular gland consistent with a right superior parathyroid gland. Image of Tc-99m sestamibi control scintigraphy (C) obtained after remote thyroid surgery did not show any focus in the same area

Surgical exploration was planned accompanied by gamma probe for the purpose of finding ectopic gland. The patient was then taken to the operating room after injection of 5 mCi of Tc-99m sestamibi for intraoperative localization. A gamma probe (Navigator, Gamma Positioning System) was placed on the neck with elevated counts in excess of 400 behind the right submandibular gland. This was excised with the ex vivo counts registering at 220, which was 140% of background. The excised tissue was thought to be the parathyroid gland based on the intraoperative gamma probe count. Histopathologic examination revealed nodular parathyroid hyperplasia showing a combination of chief and oxyphil cells in the fatty tissue (not shown). Postoperatively, parathyroid hormone levels were below detection level (6.7 pg/mL) and the patient required calcium supplementation for symptomatic hypocalcemia (5.5 mg/dL).

Because of the clinical manifestations of hyperparathyroidism and prolactinoma, the patient was diagnosed as MEN1 and whole body scanning performed to find the other endocrine and non-endocrine lesions. Abdominal computerized tomography (CT) revealed a unilocular, anechoic, thin-walled cystic lesion measured 5.5x3.5 cm in the right paraaortic region closer to the duodenum without signs of fistulisation infiltrating the surrounding structures (Figure 2). There were no enlarged lymph nodes or liquid collections intra-abdominally. Evidence of carcinoid tumor or paraganglioma, including increased urinary excretion of methanephine, normethanephine and 5-hydroxyindoleacetic acid (5-HIAA), were all absent. After standard preoperative preparation, the patient was operated under general anesthesia. Intraoperatively, the cyst was found to be intimately associated with his mesentery containing serous fluid. The cyst was successfully treated by total cystectomy.

Discussion

MEN1 is a rare autosomal dominant hereditary cancer syndrome presented mostly by tumours of the parathyroids, endocrine pancreas and anterior pituitary (1). Two different forms have been described: The sporadic form presents with two of the three principal MEN1-related endocrine tumours (parathyroid adenomas, GEP tumors and pituitary tumours) within a single patient. The familial form consists of a MEN1 case with at least one first degree relative showing one of the endocrine characterising tumours. MEN1

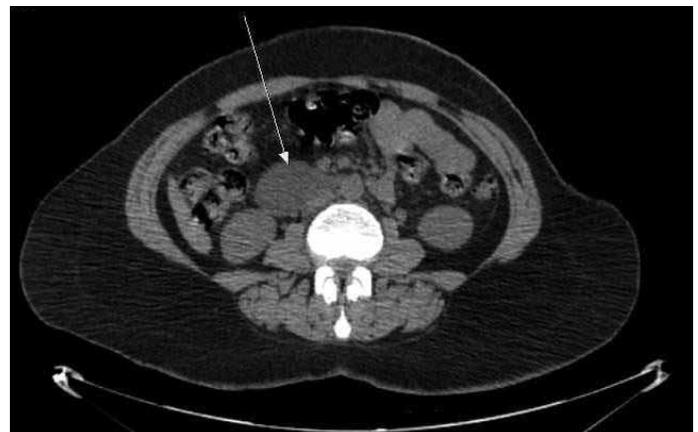


Figure 2. CT-scan of the abdomen presented a unilocular, anechoic, thin-walled cystic lesion in the right para-aortic region close to duodenum

clinical diagnosis is based on detection of MEN1-associated tumors and lesions and includes biochemical hormone evaluation, and endoscopic, nuclear medicine or other imaging studies. MEN1 germ line mutations are identified in most of patients with familial MEN1 syndrome (2). Associated with this syndrome, other endocrine and non-endocrine lesions, such as adrenal cortical tumours, carcinoids of the bronchi, gastrointestinal tract and thymus, meningiomas, lipomas, angiofibromas, collagenomas can also occur in varying combinations (3-6). However, to our knowledge, no case of mesenteric cyst related to MEN1 syndrome has been reported to date.

Our case had parathyroid gland hyperplasia, a pituitary adenoma and a mesenteric cyst. Imaging appearance of a cystic lesion is sometimes indistinguishable from that of solid tumors (7). Due to the difficulties in differentiation from other tumoral lesions like paragangliomas, and the uncertainty of their nature, the correct diagnosis might only be reached at laparotomy and after careful histological examination. Complete enucleation of cysts is considered to be the procedure of choice to prevent recurrence of benign tumors and possible malignant transformation (8). In our case, since all radiographic studies and subsequent biochemical analysis revealed no evidence of functional endocrine mass, this was deter-

mined to be a primary cystic lesion arising in the mesentery of the small bowel.

Parathyroid gland hyperplasias or adenomas are the most common clinical manifestation of MEN1, affecting more than 95% of all MEN1 patients (9). Accurate clinical and laboratory screening for parathyroid function promotes early biochemical diagnosis. However, imaging is usually used for the diagnosis of parathyroid adenomas or hyperplastic glands for successful surgery. These tumours may occur in the form of multiglandular hyperplasia and in ectopic location, accounting for 4% to 16% of patients with primary hyperparathyroidism (2). As ectopic parathyroid adenomas can be the cause of operative failure, preoperative localization of an ectopic gland is very important. Repeat surgery is associated with a dramatic reduction in the success rate and an increase in surgical complications (10). In these patients it is necessary to have all the information concerning the initial surgery, including the number and location of parathyroid glands that have been seen by the surgeon and the size and histology of the resected glands. Previously, surgery for primary hyperparathyroidism consisted of bilateral cervical exploration; however, preoperative imaging localization for parathyroid adenomas has enabled less invasive procedures since unilateral cervical exploration and minimally invasive techniques have become widely accepted procedures (11). These less invasive surgical techniques result in similar cure rates while shortening procedure times, hospital stay and avoiding the need for general anaesthesia. Sestamibi parathyroid scintigraphy is used to provide the surgeon with the best anatomical information, especially for an ectopic focus.

Although the most probable sites of an ectopic parathyroid gland are the intrathymic and tracheoesophageal groove, the undescended parathyroid gland, situated in the superior cervical regions, is often not considered among the potential sites for ectopic parathyroid tissue.

Matsuoka et al. (12) reported that the frequency of undescended parathyroid glands was 0.91%. In our case, both a previous neck operation history and abnormal foci uptake of Tc-99m sestamibi in the right submandibular region raising suspicion of an undescended gland made surgery more difficult. Radio-guided parathyroidectomy is especially recommended in re-operation for persistent or recurrent hyperparathyroidism and ectopic adenomas (13). Gamma probe-guided parathyroidectomy was performed successfully.

Conclusion

Superior cervical regions and submandibular areas may be alternative sites of parathyroid gland pathologies. These regions should be looked carefully for any uptake when evaluating patients with Technetium-99m MIBI scintigraphy for parathyroid diseases because of a potential conflict with salivary glands uptake of MIBI.

Furthermore, we can speculate that mesenteric cyst, like other GEP tumors, may be associated with MEN1 cases.

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Authors' contributions

Conceived and designed the experiments or case: ÜA, MK, AA, FT. Performed the experiments or case: ÜA, AA. Analyzed the data: ÜA, MK. Wrote the paper: ÜA. All authors read and approved the final manuscript.

Conflict of interest

No conflicts of interest were declared by the authors.

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