Supernumerary parathyroid glands in hyperparathyroidism associated with multiple endocrine neoplasia type 1

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Summary

Objective: To evaluate frequency, anatomic presentation, and quantities of supernumerary parathyroids glands in patients with primary hyperparathyroidism (HPT1) associated with multiple endocrine neoplasia type 1 (MEN1), as well as the importance of thymectomy, and the benefits of localizing examinations for those glands. **Methods:** Forty-one patients with hyperparathyroidism associated with MEN1 who underwent parathyroidectomy between 1997 and 2007 were retrospectively studied. The location and number of supernumerary parathyroids were reviewed, as well as whether cervical ultrasound and parathyroid SESTAMIBI scan (MIBI) were useful diagnostic tools. **Results:** In five patients (12.2%) a supernumerary gland was identified. In three of these cases (40%), the glands were near the thyroid gland and were found during the procedure. None of the imaging examinations were able to detect supernumerary parathyroids. In one case, only the pathologic examination could find a microscopic fifth gland in the thymus. In the last case, the supernumerary gland was resected through a sternotomy after a recurrence of hyperparathyroidism, ten years after the initial four-gland parathyroidectomy without thymectomy. MIBI was capable of detecting this gland, but only in the recurrent setting. Cervical ultrasound did not detect any supernumerary glands. **Conclusion:** The frequency of supernumerary parathyroid gland in the HPT1/MEN1 patients studied (12.2%) was significant. Surgeons should be aware of the need to search for supernumerary glands during neck exploration, besides the thymus. Imaging examinations were not useful in the pre-surgical location of these glands, and one case presented a recurrence of hyperparathyroidism.

Keywords: Multiple endocrine neoplasia type 1; primary hyperparathyroidism; parathyroid glands; ultrasonography; parathyroidectomy.

Resumo

Paratireoides supranumerárias em hiperparatireoidismo primário associado a neoplasia endócrina múltipla tipo 1

Objetivo: Avaliação da frequência, da localização anatômica e do número de paratireoides extranumerárias em pacientes com hiperparatireoidismo primário (HPT1) associado a neoplasia endócrina múltipla tipo 1(NEM1), além da avaliação da importância da timectomia e da utilidade dos exames radiológicos para localização destes. **Métodos:** Foram avaliados de forma retrospectiva 41 pacientes portadores de NEM1 com HPT1 submetidos a paratireoidectomia entre 1997 e 2007. O número de glândulas supranumerárias encontradas e a sua localização foram revisados, assim como a utilidade do ultrassom cervical e do SESTAMIBI (MIBI) de paratireoide como ferramentas diagnósticas. **Resultados:** Em cinco pacientes (12,2%) foram identificadas glândulas supranumerárias. Em três destes (40%), as glândulas estavam próximas à glândula tireoide e foram encontradas durante a exploração cirúrgica. Os exames de imagem não foram úteis para a localização destas glândulas. Em um caso, apenas o exame anatomopatológico foi capaz de encontrar uma glândula extranumerária microscópica localizada no timo. No último caso, uma quinta glândula foi ressecada por meio de esternotomia após a recidiva do hiperparatireoidismo, cerca de 10 anos após a paratireoidectomia realizada sem timectomia na ocasião. Neste caso o MIBI detectou esta paratireoide apenas após a recidiva da doença. Em nenhum dos casos o ultrassom cervical foi capaz de detectar glândulas extranumerárias. **Conclusão:** A frequência de paratireoides supranumerárias em nossa casuística foi significativa (12,2%). Durante a exploração cervical, o cirurgião deve estar atento para localizar glândulas extranumerárias além do timo. Exames de imagem não foram úteis na localização pré-operatória dessas glândulas, e em um caso houve recidiva do hiperparatireoidismo.

Unitermos: Hiperparatireoidismo primário; paratireoidectomia; ultrassom; neoplasia endócrina múltipla tipo 1; glândulas paratireoides.

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Introduction

Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant disorder characterized by a germline mutation in the MEN1 gene that causes neoplastic changes in several endocrine glands, such as pituitary, pancreatic islet cells, and parathyroids[1,2]. Primary hyperparathyroidism (HPT1), an endocrine disturbance where an overproduction of parathyroid hormone (PTH) leads to elevated serum calcium, is usually the first manifestation of MEN1[1,3]. Most cases of HPT1 are sporadic (90%), but there are also some familial hereditary syndromes (10%), such as MEN1. Single parathyroid adenoma (85%) is the main cause of sporadic HPT1, while HPT1 with MEN1 generally presents an asymmetric parathyroid gland hyperplasia[3,4]. Parathyroidectomy is the treatment of the disease. Many authors recommend partial parathyroidectomy, in which part of or one small gland is left in the neck[5,6], and even selective parathyroidectomy of only abnormal macroscopic glands has been proposed[7]. Other authors prefer total parathyroidectomy with forearm autografting as the procedure of choice[8]. Irrespective to the type of parathyroidectomy, transcervical thymectomy seems to be advisable, due to the possibility of carcinoid thymic tumors, an extremely rare but aggressive neoplasm, which affects up to 8% of individuals with MEN1, being a cause of death in these patients with delayed diagnosis[3,4]. The second reason for this procedure is the embryological and anatomic relation between the inferior parathyroids and the thymus[9,10], which is a frequent site of ectopic parathyroid glands (up to 25% of cases) and possible supernumerary glands, when there are more than four parathyroids glands[11]. These supernumerary glands are an important cause of recurrent and persistent HPT1 after parathyroidectomy in MEN1 patients[11,12]. Thus, this study aimed to assess the frequency of supernumerary parathyroids in 41 Brazilian MEN1 patients with HPT1, their clinical importance, and the role of the diagnostic methods.

Methods

This retrospective study evaluates the frequency, anatomic presentation, and quantities of supernumerary parathyroids glands in 41 patients with HTP1 associated with MEN1 who underwent parathyroidectomy consecutively between 1997 and 2007 at the institution. These cases have been studied during the screening program for MEN1 that is being currently performed in this hospital[13,14]. They were diagnosed with MEN1 as they presented the proband with at least two of three tumors or with genetic tests in relatives of those patients, in accordance with international guidelines[15]. Whether the imaging examinations, namely cervical ultrasonography (USG) and parathyroid SESTAMIBI scan (MIBI), were effective to detect supernumary glands was reviewed. Whether prophylactic thymectomy could detect these glands was also studied.

Data collection on the patients' records searched the following parameters: age, gender, surgical procedure, and USG and MIBI reports. If available, these examinations images were compared with the macroscopic intra-operative findings, such as number, size, and location of the excised glands. The results of imaging were also analyzed when the glands were detected only in the routine histological examination of the thymus.

Results

Forty-one HTP1/MEN1 patients were operated. Nineteen were male and 22 were female. Their ages ranged from 19 to 73 years, with an average of 40.7 years.

In five patients (12.2%), a fifth parathyroid gland was found, and no patient presented more than five glands. Of these, only one patient was male and four patients were female. Their average age was 44 years (range: 32-59).

In the first case, a 32-year-old female, USG identified only one parathyroid gland, and MIBI found two hyperactive glands. Both findings were not correlated with the supernumerary parathyroid. The supernumerary gland was located between the upper right and lower right parathyroid glands, measuring 0.5 x 0.3 x 0.3 cm. In the second case, a female, 57 years old, USG identified only one parathyroid, and MIBI showed three hyperactive glands, but again none of the results was indicative of the supernumerary gland. The fifth gland was found medially between the left parathyroids, measuring 0.9 x 0.9 x 0.6 cm. In the third case, a female patient, 40 years old, had the same imaging parameters of case 2: only one parathyroid showed by USG and three hyperactive parathyroids in MIBI scan. Both examinations were not correspondent to the intraoperative finding of the supernumerary gland, which was just above the upper left parathyroid, measuring 0.6 x 0.4 x 0.3 cm. In these three cases the supernumerary parathyroids were found during the neck exploration, near the thyroid gland. In all these cases a clear separation of connective tissue was evident with the apparent topic parathyroids, which avoided the risk of the misdiagnosis of supernumerary gland by surgical splitting.

In the fourth case, a male patient of 59 years, none of the imaging studies or the neck exploration found a supernumerary gland, but the histological examination of the thymus revealed a microscopic supernumerary parathyroid.

The last patient, a 32 years old female, was submitted to a total parathyroidectomy with immediate autotransplantation in 1987. At that time, transcervical thymectomy was not a routine for these patients and USG was the only preoperative imaging available at the institution. Ten years after her first surgery (1997), she presented with recurrent HPT1. In the preoperative imaging examinations, MIBI scan suggested a mediastinal parathyroid gland, which was confirmed after resection requiring sternotomy. All cases are summarized in Table 1.