Brown tumor involving the sellar-parasellar region mimicking pituitary adenoma as the top of the iceberg of generalized primary hyperparathyroidism

Joanna Malicka,1 Maria Kurowska,1 Robert Kaczmarsczyk,2 Marek Sawicki,3 Beata Chrapko,4 Agnieszka Zwalok1,5 Andrzej Nowakowski1
1Department of Endocrinology, 2Department of Neurosurgery and Pediatric Neurosurgery, 3Department of Thoracic Surgery, 4Department of Nuclear Medicine, 5Department of Internal Medicine in Nursing, Medical University, Lublin, Poland

Abstract

The authors present a case study of a 40-year-old man with advanced, previously undiagnosed primary hyperparathyroidism (PHPT), which first manifestation directing to correct diagnosis was sellar-parasellar brown tumor. Further studies disclosed PHPT. The patient presented many of the classic signs of the disease, including renal stones, duodenal ulcer, muscle weakness and bone pains, but suspicion of PHPT was made on the basis of a post-operative histological examination of the sellar-parasellar tumor. Laboratory investigations showed hypercalcemia, hypophosphatemia, elevated levels of parathyroid hormone and alkaline phosphatase. A skeletal survey showed generalized decreased density of bones and multiple brown tumors. The problems of diagnosis and localization of parathyroid glands have been discussed. The literature has been reviewed and the importance of early diagnosis and treatment has been stressed.

Case Report

A 40-year-old man was first ophthalmologically and then neurologically diagnosed because of one-week history of diplopia, headache and periodic numbness of left limbs which disabled him to drive a car.

He had a three-year history of recurring duodenal peptic ulcers and dyspepsia and four-month of nephrolithiasis with left renal colic. He was complaining of ostealgia, polyuria, polydipsia and loss of about 6 kg weight within the last several weeks. Thirteen years earlier the patient underwent subtotal thyroidectomy propter multinodular goiter. Postoperatively he remained euthyroid.

Computed tomography (CT) (Figure 1) and magnetic resonance imaging (MRI) (Figure 2) showed a tumor 30×30×25 mm in diameter with calcifications and high contrast enhancement, localized in the sellar region, spreading through the supra sellar region, clivus and sphenoid sinus with the expansion to the right cavernous sinus. The pituitary gland was elevated and the optic chiasm was not compressed. Pituitary function has not been examined before surgical treatment.

The patient underwent transsphenoidal resection for suspected meningioma or pituitary expansive adenoma. Postoperatively the patient’s vision and neurologic symptoms improved and the pituitary function remained normal. Histopathological examination of the excised sellar-parasellar lesion revealed two possibilities: a brown tumor or giant cell tumor. The nature of the disease was elucidated by histological finding of a brown tumor or osteoclastoma.

The patient was referred to the Department of Endocrinology for further differential diagnosis with the suspicion of primary hyperparathyroidism.

Correspondence: Joanna Malicka, Department of Endocrinology, Medical University, Lublin, Poland.
E-mail: jdmaliccy@poczta.onet.pl

Key words: primary hyperparathyroidism, brown tumor, sella turcica.

Received for publication: 17 September 2011. Revision received: 6 November 2011. Accepted for publication: 16 November 2011.

This work is licensed under a Creative Commons Attribution Non-Commercial 3.0 License (CC BY-NC 3.0)

©Copyright J. Malicka et al., 2012
License PAGEPress srl, Italy
Endocrinology Studies 2012; 2:e3
We confirmed the diagnosis of PHPT with abnormal biochemical tests showing elevated serum parathyroid hormone level=1090 pg/mL (normal range: 14-72 pg/mL), total serum calcium levels=12.0-14.26 mg/dL (normal range: 8.48-10.48 mg/dL), Ca2+=1.89 mmol/L (normal range: 1.15-1.32), alkaline phosphatase concentration=511 U/L (normal range: 15-117 U/L) and low serum phosphorus levels=1.47-2.17 mg/dL (normal range: 2.6-4.5 mg/dL). Renal biochemical functional tests showed: blood urea level of 14.9 mg/dL (normal range: 10-50 mg/dL), creatinine level of 0.8 mg/dL (normal range: 0.8-1.2 mg/dL), uric acid level of 5.3 mg/dL (normal range: 3.6-8.2 mg/dL) and potassium level of 4.5 mmol/L (normal range: 3.7-4.9 mmol/L). Calcium excretion in urine was 298.0 mg/24 h (normal range: 100-300 mg/24h) and phosphorus=319.8 mg/24h (normal range 0.4-1.3 mg/24h). Other hormone levels were within their normal ranges.

His bone mineral density (T-score) of the hip was minus 3.52 and of the lumbar spine was minus 3.57. Skeletal scintigraphy (Figure 3) revealed multiple spots with increased radiotracer (MDP99mTc) uptake in skull, ribs, fourth lumbar vertebra, pelvis and lower and upper limbs. The largest ones were localized in the right hip and the proximal portion of the right tibia.

There were also multiply local destructive lesions or cysts in phalanges of the fingers found during an X-ray examination. Based on these results, the presumptive diagnosis of sphenoid-parasellar tumor was the brown tumor caused by primary hyperparathyroidism.

Further diagnostic imaging techniques, including neck ultrasound and technetium Tc-99m sestamibi (Tc-99m MIBI) parathyroid scintigraphy with the dual-tracer subtraction, carried out in search of pathological parathyroid glands, were difficult to interpretation because of previous thyroidectomy. They suggested the localization of parathyroid adenoma above the upper part of thyroid isthmus.

Surgical treatment was undertaken with total thyroidectomy and parathyroidectomy; however normalization of PTH and calcium concentration after surgery was not noticed and the levels of these parameters were respectively: PTH=809 pg/mL, Ca=11.5 mg/dL. Moreover, after surgery, histopathological examination revealed nodular goiter with fragment of parathyroid gland only.

The next parathyroid Tc-99m MIBI scans, performed by use of single-photon emission computed tomography (SPECT) technique together with CT of the neck (Figure 4) showed increased radiopharmaceutical uptake in the right, lower part of the neck.

The patient has been reoperated ten days later. The parathyroid gland localized behind the trachea was visualized and removed by the use of the hand-held gamma probe after 99mTc-MIBI administration before surgery. Histopathological examination of the removed 2.5 cm in diameter parathyroid gland revealed hyperplasia.

Parathyroidectomy invariably resulted in PTH normalization (PTH=41 pg/mL) and then in developing hungry bone syndrome with severe hypocalcaemia (Ca=7.53 mg/dL) demanding long-term calcium and vitamin D analog treatment. Unfortunately postoperative hypothyroidism and vocal cord palsy ensued.

At his four-year postoperative follow-up examination the patient shows a remarkable improvement in his clinical condition and partial regression of bone lesions. The levels of plasma parathyroid hormone are 38.46 pg/mL and calcium levels range from 9.8 mg/dL to 10.3 mg/dL. His T-score of the lumbar spine was -2.7 six months after surgery and -1.86 one year after surgery.

**Discussion**

Nowadays primary hyperparathyroidism is characterized by higher prevalence and incidence than previously and it is recognized usually before obvious clinical manifestations develop.1,2,3,7-26,31 It is estimated that overt PHPT occurs in only 20% of cases.3,4 On the base of these data it is evident that advanced stages of PHPT are not frequent at the moment in clinical practice. Also the sporadic form of this disease in young people is thought to be extremely rare.3,26

We report a case of a young man with advanced PHPT being an illustration of accumulation of multiply uncommon and serious clinical symptoms. We also discuss the difficulties in parathyroid localization during the surgery, despite of great progress in imaging techniques.

Actually, as a result of earlier diagnosis, brown tumors are very rare clinical phenomenon.1,4,10,11,28 A brown tumor located in sellar space, parasellar region and sphenoid sinus with subsequent pituitary compression and simulating expansive pituitary adenoma was the first symptom directing to proper diagnosis in our patient.

Involvement of the sellar-parasellar region by brown tumor is extremely rare and usually occurs in primary hyperparathyroidism. Only seven cases of brown tumors around the sellar region and skull base have been reported since 1986 in English literature.21,22 There were four patients with primary[1,24,26 and three patients with secondary hyperparathyroidism among them.22,23,27 In three patients the tumor mass was located within the sellar space,21,22,24 In another three it filled the sphenoid sinus22,26,27 and in the remaining one - ethmoid sinus.25
Similarly as presented by Yilmazlar et al., our patient had a generalized stadium of PHPT with a brown tumor located in the sella turcica, spreading through the suprasellar region, clivus, and sphenoid sinus, compressing neighboring bone structures and elevating pituitary gland. On initial examination he exhibited vision and neurological disturbances. To our knowledge this is the eighth reported case of a brown tumor localized around the sellar-parasellar region, the fifth with primary hyperparathyroidism and the fourth with a brown tumor located within the sellar space. The coexistence of thyroid and parathyroid gland diseases is not rare. Thyroid disease accompanying PHPT can aggravate the clinical decisions, procedures of visualization and surgery treatment. Thyroid nodules are the most common cause of false-positive or negative preoperative parathyroid localization. Parathyroidectomy performed after thyroidectomy makes a great challenge to the surgeon and should be conducted with the same care and concern that he reserves for a reoperative parathyroid operation. The problems associated with parathyroidectomy after prior thyroidectomy arise from scarring and fibrosis, from the inability to estimate the number of viable, normal parathyroid glands left after previous operations and from the requirement of additional thyroid resection.

The application of Tc-99m MIBI scintigraphy in early 1990s significantly changed parathyroid surgery. Now it is based on accurate, pre-operative and intraoperative localization of pathologic glands. However its sensitivity decreases in multiglandular disease, small parathyroid adenomas and in the coexistence of nodular goiter.

On the field of surgical treatment of PHPT, the success rate from referral centers exceeds 95%, but some patients experience operative failure. Surgeon’s inexperience and incomplete exploration are major components of initial treatment failure. Patients with persistent hyperparathyroidism frequently have a history of thyroidectomy or previous parathyroidectomy and are less likely to have correct findings in sestamibi or ultrasonographic localizing studies. On the field of surgical treatment of PHPT, the success rate from referral centers exceeds 95%, but some patients experience operative failure. Surgeon’s inexperience and incomplete exploration are major components of initial treatment failure. Patients with persistent hyperparathyroidism frequently have a history of thyroidectomy or previous parathyroidectomy and are less likely to have correct findings in sestamibi or ultrasonographic localizing studies.

Our patient underwent subtotal thyroidectomy propter multinodular goiter thirteen years earlier and this fact could influence the results of his neck ultrasound and 99mTc-MIBI scintigraphy conducted before the first parathyroidectomy. These imaging studies suggested the possibility of parathyroid adenoma localized above the upper part of thyroid isthmus. However midline is an exceptional place of parathyroid adenoma localization, previous surgery performed in our patient could cause such an atypical location. Surgical treatment was undertaken with total thyroidectomy and suspected parathyroidectomy, but there was no normalization of plasma PTH and calcium level after surgery.

Many authors suggest, that there is a correlation between preoperative serum PTH and calcium levels with adenoma’s weight or volume in PHPT. According to other researchers, biochemical parameters do not accurately predict the size of a parathyroid adenoma. In our patient, whose PTH level was above 1000 pg/mL and calcium level exceeded 14 mg/dL, we could expect a big parathyroid adenoma, but histopathological examination revealed nodular goiter with fragment of parathyroid gland only. The possible reason of such a surgical failure was previous thyroidectomy. The surgeon removed the scar in one block with the rest of the thyroid and parathyroid glands and intraoperative separation and estimation of parathyroid adenoma size was impossible. Unfortunately, intraoperative iPTH assay was not available on the day of the surgery. The patient needed further neck exploration with the removal of 2.5 cm in diameter parathyroid gland with hyperplasia.

Although an operative failure can issue from
a multiple parathyroid disease or the ectopic location of the glands, less experienced surgeons are more likely to miss an abnormal parathyroid in its physiologic anatomic location.46 The knowledge of the anatomy and embryology of the parathyroid glands is essential for their identification and surgical success. The superior and the inferior parathyroid glands originate from the 4th and the 3rd branchial pouches respectively and migrate caudally during fetal development to occupy their normal positions. Any aneuropy during this descent may lead to ectopic locations of these glands. When enlarged, they may fall downwards as a result of gravity. They may be located in posterior or anterior mediastinum, within the thymus, in the trachea-esophageal groove or within the thyroid gland.5,53 Silberfein et al.54 evaluated and categorized the locations of missed parathyroid glands found during reoperative parathyroidectomy. They determined several factors associated with these locations and concluded that in spite of all, missed parathyroid glands can be found in standard locations in most cases.

Taking into account data mentioned above we assume that previous thyroidectomy and cationization contributed to the parathyroid displacement in our patient, but missed parathyroid gland, multiple gland disease and ectopic localization were also considered.

Many authors55-57 strongly support the utility of MIBI SPECT application in exploration of parathyroid adenomas located deep in the neck and in ectopic sites. Intraoperative use of a hand-held scintillation gamma probe makes the detection easier and helps in recognition especially small parathyroid adenomas. Besides this method minimizes the surgical trauma in patients who underwent previous thyroid or parathyroid surgery.

Repeated parathyroid exploration is associated with more complications and worse effect compared with the initial surgery and should be undertaken by an experienced surgeon in a referral center that can provide accurate preoperative localization and adjunctive intraoperative tools, as ultrasound and scintillation probe and intraoperative serum PTH level measurement.5,56,58 Such operations should be performed during 3-4 days following the initial parathyroid surgery or after 2-3 months. For any reoperative neck surgery, the benefits and risks of the surgical procedure must be reevaluated because the potential for morbidity, including recurrent laryngeal nerve injury, is significantly increased.5

The next sestamibi scanning together with CT performed in our patient after first operation showed an increased isotope accumulation in the right, lower part of the neck. The parathyroid localized behind the trachea was visualized and removed using the hand-held gamma probe after previous MIBI administration. The localization of parathyroid adenoma within the upper posterior mediastinum is a typical site for superior parathyroid adenoma in secondary ectopic position, due to displacement downwards as a result of gravity. In such a case, the adenoma is located deep in the neck behind the inferior normal parathyroid gland and it is covered by the recurrent nerve. Surgeons can overlook such a lesion or they can injure the recurrent nerve during the dissection in a scary field. Unfortunately, the second parathyroidectomy undertaken in our patient 10 days after the initial surgery, in spite of usage of intraoperative nerve monitoring, was complicated by stable vocal cord palsy. It should be performed earlier, but further imaging studies and waiting for histopathological examination generated a delay. On the other hand, taking into account serious clinical symptoms of advanced stage of PHPT in our patient with very high calcium levels and his own opinion, the surgeon decided not to wait longer with the parathyroid reoperation.

Cure criterion of PHPT is defined as normocalcaemia 6 months after surgery irrespective of the parathormone level.4 In our patient the second parathyroidectomy resulted in PTH normalization with the development of hungry bone syndrome and severe hypocalcemia. At his four-year postoperative follow-up examination he shows a remarkable improvement in his clinical condition and partial regression of the bone lesions. The symptoms suggesting MEN diagnosis (family form of primary hyperparathyroidism) are absent as yet. This observation, in concordance with definition of cure cited above, empower us to find our patient as cured from sporadic PHPT.

Conclusions

We present an example of rare manifestation of PHPT — advanced clinical stage with multiple brown tumors and the unusual localization of one of them - in sella turcica and sphenoid sinus region. Delayed diagnosis, despite of multiple classical clinical symptoms, proves the lack of the knowledge of the disease. The report also shows the difficulties in parathyroid imaging and proves the usefulness of pre- and intra-operative radionuclide techniques, especially the usage of the scintillation gamma probe.

References