

HYPERPARATHYROIDISM IN A PATIENT WITH MAFFUCCI'S SYNDROME: A CASE REPORT

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Maffucci's syndrome is a nonhereditary mesodermal dysplasia which consists of multiple hemangioma of the soft tissue and multiple enchondromas.¹⁻³ Approximately 170 cases have been reported in the literature.³⁻⁵

We encountered a patient who suffered hyperparathyroidism by hyperplasia of the parathyroid gland with Maffucci's syndrome, adenomatous goiter, and adrenal mass.

Case Report

A 55-year-old woman was referred to our department for work-up of hypercalcemia. There was no family history of endocrine tumors or hypercalcemia. She had undergone surgery to treat multiple enchondromatosis of the fingers, toes, pelvis, and thorax at the age of 19 in 1957. Pain developed in the left foot in November 1992 and she was admitted to the department of orthopedics of our hospital in January 1993. The patient was diagnosed as having Maffucci's syndrome during this admission and underwent implant arthroplasty of the left ankle.

Physical examination revealed an enchondroma of the left ankle, and hemangiomas of the right ankle and left foot. The hemangiomas were softly palpable. A well-demarcated, hard, elastic mass (32 x 10 mm) with a smooth surface, and a hard elastic mass (15 x 15 mm) were palpable in the right and left lobes of the thyroid, respectively.

Laboratory data were as follows: serum calcium concentration 3.05 mmol/L (normal 2.25-2.75 mmol/L), inorganic phosphate concentration 2.3 mg/dL (normal 2.4-4.5 mg/dL), intact parathyroid hormone concentration (PTH) 330 pg/mL (normal 10-50 pg/mL), urinary calcium

93%). Thyroid function tests and the calcitonin concentration were normal, TSH 0.9 μ U/mL (normal 0.4-5.6 μ U/mL), free T₃ 3.1 pg/mL (normal 2.8-5.8 pg/mL), free T₄ 1.1 ng/mL (normal 0.8-1.4 ng/dL), thyroid-stimulating hormone receptor antibody (TRAb) negative (normal below 12%), but the thyroglobulin concentration was high: 245.5 pg/mL (normal 0-45 pg/mL). Other endocrine-related data were as follows: K 4.5 mmol/L (normal 3.5-4.8 mmol/L), renin 2.3 ng/mL/hr (normal 0.2-2.7 ng/mL/hr), aldosterone 11.9 ng/dL (normal 2-13.0 ng/dL), cortisol 14.8 μ g/dL (normal 6-15 μ g/dL), adrenaline 12 pg/mL (normal <120 pg/mL), noradrenaline 238 pg/mL (normal 50-400 pg/mL), urinary cortisol 15.5 μ g/day (normal 15-52 μ g/day), urinary metanephrine 0.05 mg/day (normal 0.05-0.23 mg/day), urinary normetanephrine 0.15 mg/day (normal 0.07-0.26 mg/day), urinary VMA 2.0 mg/day (normal 0.6-3.2 mg/day), urinary HVA 1.5 mg/day (normal 2.6-6.0 mg/day), urinary 17-KS 1.6 mg/day (normal 3-13 mg/day), urinary 17-OHCS 2.2 mg/day (normal 2.2-7.3 mg/day).

Radiographic examination revealed multiple enchondromas in the first to third fingers of the left hand. The radiographs of the left ankle showed a destructive lesion with phleboliths (Figure 1).

TABLE 1. Review of endocrine tumors with Maffucci's syndrome.

Authors	Lesion
Kuzuma and King ⁷	Pituitary adenoma suspected; ovarian tumor (teratoid tumor)
Strang and Rannie ⁸	Adrenal cortical adenoma; ovarian tumor (theca-cell tumor)
Baradnay et al. ⁹	Adrenal cortical adenoma; pituitary adenoma
Schnall and Genuth ¹⁰	Parathyroid adenoma; pituitary adenoma
Nemoto et al. ¹¹	Parathyroid adenoma; goiter
Miki et al. ¹²	Pituitary adenoma; goiter
Marymont et al. ¹³	Pituitary adenoma; breast cancer
Present case	Parathyroid hyperplasia; adenomatous goiter; adrenal tumor

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Accepted for publication 21 December 1996. Received 15 July 1996. excretion 436.8 mg/day (normal 100-300 mg/day), % TRP (tubular reabsorption of phosphate) 60% (normal 81%-

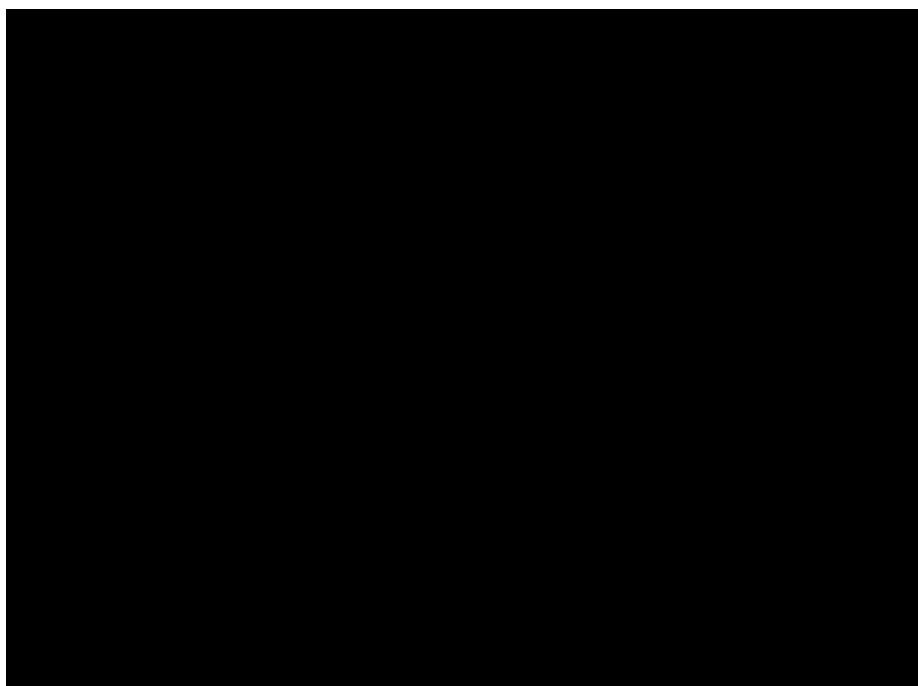


FIGURE 1. A roentgenogram of the first to third fingers of the left hand showed multiple enchondromas and that of the left ankle showed a destructive lesion with phleboliths.

Ultrasonography, CR and MRI showed multiple nodules in both thyroid lobes, which was compatible with adenomatous goiter of the thyroid. Two left parathyroid glands were tentatively identified by ultrasonography. Although the radiographic and sonographic findings demonstrated an adrenal tumor (2.0 x 1.0 cm, Figure 2), her blood pressure was normal (120/70 mm Hg) and did not rise during an induction test with primperan or glucagon. She had no history of attacks of sweating, palpitation or headache suggestive of pheochromochytoma. Therefore, we concluded that the adrenal mass was not functional.

An operation was performed in June 1993. Subtotal parathyroidectomy (three and a half glands resected) was performed. The upper left parathyroid gland was lobulated and enlarged, as was the lower left parathyroid gland. Both left parathyroid glands were excised. The parathyroid glands measured 33 x 30 mm and 25 x 12 mm (Figure 4). Both were diagnosed as hyperplastic based on histology. However, one of the right parathyroid glands resected was lymph node and another right one (half left in muscle tissue) was not atrophic. A total thyroidectomy was also performed, since the right lobe of the thyroid was grossly enlarged and many nodules were present in both lobes, and the fourth parathyroid gland could not be recognized. The histology of the thyroid showed a hyperplastic nodule composed of predominantly large follicles. Hemorrhage and an inflammatory infiltrate were also seen. The thyroid was then diagnosed as an adenomatous goiter. Intact PTH returned to normal after surgery. Moderately severe tetany-like contractions frequently occurred postoperatively, and resolved with the intravenous administration of calcium

gluconate. The postoperative course has been unremarkable, with administration of thyroxin and active vitamin D₃ orally. The patient's blood calcium concentration and thyroid hormone levels are normal under replacement therapy now.

Discussion

Maffucci's syndrome is characterized by multiple hemangiomas of the soft tissue and multiple enchondromas. As our case had multiple enchondromas (fingers, toes, pelvis, and thorax) and multiple hemangiomas (right ankle and left foot), her diagnosis was confirmed. Maffucci's syndrome is clinically similar to Ollier's disease, because skeletal lesions are the same. However, Ollier's disease has no hemangiomas. It is difficult to do differential diagnoses when hemangiomas are not apparent.

Maffucci's syndrome is known to be associated with malignant and benign tumors.³⁻⁵ Albrechts and Rapini reported in their review⁴ that malignant tumors with Maffucci's syndrome consist of chondrosarcoma, astrocytoma, ovarian tumors, pancreatic cancer, hemangiosarcoma and lymphangiosarcoma; and that benign tumors are pituitary adenoma, adrenal cortical adenoma, parathyroid adenoma, breast fibroadenoma, and

MEN-2 is well known to be induced by abnormality of RET oncogene.⁶ Maffucci's syndrome is nonhereditary and our patient had no family history of endocrine tumors or hypercalcemia.

Maffucci's syndrome is associated with malignant transformation of mesodermal tumors into chondrosarcoma, hemangiosarcoma and lymphangiosarcoma, with a frequency of 15% to 30%.³⁻⁵ The patient described in this report has not experienced any malignant changes, but she requires close follow-up.

References

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FIGURE 2. Abdominal CT of the patient. An arrow indicates the adrenal mass (2.0 x 1.0 cm). Density of CT showed that the adrenal mass was neither cyst nor lipoma.

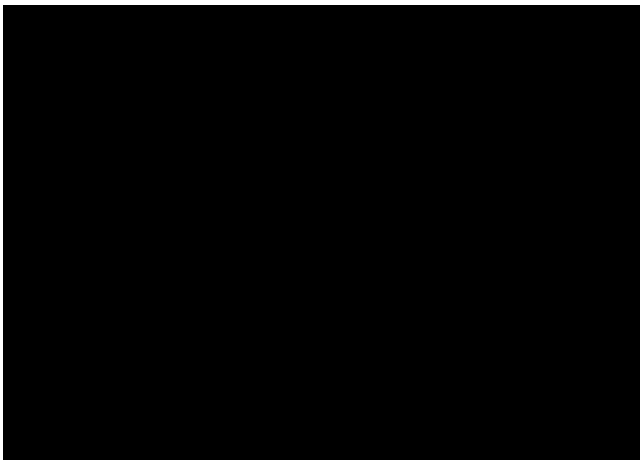


FIGURE 3. The upper left parathyroid gland was lobulated and measured 33 x 30 mm. The lower left parathyroid gland measured 25 x 12 mm.

thyroid adenomas.⁴ Most benign tumors with Maffucci's syndrome are endocrine tumors and there are often complications with more than one tumor. Cases of pituitary, adrenal parathyroid or thyroid tumor are listed in Table 1. Our patient was the third case with Maffucci's syndrome and hyperparathyroidism, and she was the first case of hyperplasia of the parathyroid gland. Moreover, she had three different endocrine tumors. This case is the first report of three different endocrine tumors with Maffucci's syndrome, which makes it worth reporting.

With regard to the patient's endocrine tumors, we cannot rule out double adenomas completely because histological differentiation between hyperplasia and adenoma of parathyroid is difficult, and in our case, the adenomatous goiter disturbed recognition of the fourth parathyroid gland. However, we found two large glands and one normal-sized gland (not atrophic) that were compatible with hyperplasia. Adenomatous goiter was confirmed histologically. The adrenal mass was nonfunctioning. The density of the abdominal CT showed that the adrenal mass was neither cyst nor lipoma.

Hyperplasia of parathyroidism is closely related to multiple endocrine neoplasia (MEN) and familial hyperparathyroidism, both of which are hereditary diseases.