Malignant Non-Secreting Pheochromocytoma in a Patient Undergoing Surgery for a Pulmonary Adenocarcinoma

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Abstract

Pheochromocytoma is a neuroendocrine tumor derived from chromaffin cells of the adrenal medulla. Clinical presentation is not specific and depends on the type of hormone secreted. Evidence of secretion is sometimes challenging and misleading. Histology is still not helpful to diagnostic malignancy. Association to other neuroendocrine tumors has been reported before. We report the first case of a malignant pheochromocytoma associated to a pulmonary adenocarcinoma.

Keywords: Adrenal Tumor; Malignant; Pheochromocytoma; Pulmonary adenocarcinoma; Surgery

Introduction

Pheochromocytoma is a neuroendocrine tumor derived from chromaffin cells of the adrenal medulla. Association to other neuroendocrine tumors is well known and has been widely described. The association to a lung adenocarcinoma has never been reported before.

We report the case of a patient undergoing lung surgery for a pulmonary adenocarcinoma who had a malignant pheochromocytoma.

Case Presentation

A 72 years old patient has been admitted for left adrenal tumor discovered during investigation of a pulmonary adenocarcinoma.

He had a history of stroke and a peripheral arterial disease. He had hypertension discovered two weeks ago treated by captopril 50 milligrams twice a day and amlodipine 5 milligrams per day.

He had no complaints. Physical examination showed: Body mass index = 22 kg/m², Blood pressure = 135/88 mmHg, Heart rate = 65 beats per minute.

The thoraco-abdominal computed tomography showed a 22x19 millimeters posterior solid nodule of the left lung with irregular edges and heterogeneous enhancement associated with a solid nodule of the right lung and multiple metastatic micronodules; a 33x23 millimeters solid mass in the left adrenal area with heterogeneous enhancement.

Urinary tests showed normal metanephrines: 24 hours urinary normetanephrines: 360 nmol/24h (normal range: 44 - 213), 24 hours urinary metanephrines: 375 nmol/24h (normal range: 40 - 228), 24 hours urinary 3 ortho-methyl-dopamin: 137 nmol/24h (normal range: 88 - 320).

An adrenal transcutaneous biopsy was performed. The cytologic examination showed big cells with granular cytoplasm which were positive to chromogranin and synaptophysine in immunohistochemistry and concluded to a diagnostic of pheochromocytoma.

Hypertension was controlled with 10 milligrams of amlodipine and 2.5 milligrams of prazosine per day.

Left adrenalectomy was performed by lombotomy. Histology examination confirmed the diagnostic of a malignant pheochromocytoma. The Adrenal gland Scaled Score was 12.

Genetic screening by direct sequencing for SDHD gene and VHL gene didn't find any mutation.

Patient underwent an inferior left lung lobectomy one month after adrenalectomy. Histology examination confirmed the diagnostic of an invasive adenocarcinoma with endovascular tumor emboli scored T2aN0Mx.

After adrenalectomy, hypertension was controlled with captopril 50 milligrams per day. Two months after adrenal surgery, Metalodo-Benzyl-Guanidin scintigraphy didn't show any abnormal uptake.

Discussion

The originality of this case was the fortuitous discovery of a malignant non-secreting pheochromocytoma in a patient undergoing a surgery for a pulmonary adenocarcinoma. Malignant pheochromocytomas represent approximately 10 percent of pheochromocytoma [1].
The diagnosis of malignancy requires evidence of metastases at non-chromaffin sites [1]. Although there are no reliable methods to predict malignancy at the time of diagnosis, a histological score — Pheochromocytoma of the Adrenal gland Scaled Score— can identify potentially malignant tumors when it is more than 4. However, its sensitivity and specificity are 50% and 45% respectively [2,3].

Recent researches showed that at least 30% of malignant pheochromocytomas have a genetic origin [4]. Ten germ line mutations have been identified. The main mutations are RET, VHL, SDHB, SDHD, and NF1. The risk of malignancy is usually low, except for SDHB reaching 38% [5,6]. Our patient underwent genetic screening for SDHD and VHL which were negative.

Few years ago, three novel mutations were identified, exclusively found in malignant pheochromocytomas: MYCN, MYOSB and VCL [7]. An exhaustive genetic screening has had to be made. In all cases, especially in our patient, only a long term follow up could confirm metastasis which may occur even many years after the diagnosis [8].

Some biological markers can be helpful in the diagnosis of malignancy of pheochromocytoma. The neuroendocrine tumor can either produce adrenaline, noradrenaline or dopamine [9]. However, as the secretion is variable, repeating hormonal tests or referring to plasma free metanephrins can be an alternative [10]. Elevated urinary dopamine levels and elevated blood chromogranin A are predictive of malignancy [11,12]. In our patient all urinary metanephrine, even dopamine secretion were normal but chromogranin A has not been evaluated. Subclinical pheochromocytoma shouldn’t be considered safer as a sudden hypertensive crisis is possible in secreting ones [13]. For that, prazosine was prescribed before surgery in order to avoid this kind of events.

To our knowledge it’s the first case of association between a pheochromocytoma and a pulmonary adenocarcinoma. Lung carcinomas have a high propensity to metastasize to the liver, adrenal, bone or brain. In fact, patient with non-small cell lung cancer has adrenal metastasis in 17% of the cases [14]. This diagnosis was rejected as histology concluded to a pheochromocytoma. On the other hand, pheochromocytoma has been described to be associated with other neuroendocrine tumors such as pulmonary carcinoids [15]. It can also occur in Von Hippel Lindau (VHL) syndrome, von Recklinghausen disease and multiple endocrine neoplasia type 2. Our patient underwent genetic screening for VHL which was negative. Further genetic investigation should be made in order to make this point clear.

Conclusion

This is the first case of a malignant pheochromocytoma associated to a pulmonary adenocarcinoma. Association to other neuroendocrine tumors is well known. Malignant pheochromocytomas are less common. This exclusive association to an adenocarcinoma leads us to further genetic investigations.

References