CASE REPORT

Adrenal gland non-Hodgkin's lymphoma in a patient with pulmonary adenocarcinoma

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SUMMARY

Although primary neoplasms of adrenal gland are uncommon, adrenal metastases are frequently encountered in patients with malignancy, and lung is the most common primary tumour site. Among primary tumours of the adrenal gland non-Hodgkin's lymphoma (NHL) is a very rare entity. We describe a case of a 79-year-old man with a previous diagnosis of adenocarcinoma of the lung who presented after 2 years with a unilateral adrenal gland mass. A solitary metastasis from pulmonary carcinoma was suspected and a laparoscopic adrenalectomy was performed. Histological examination revealed a diffuse large B-cell NHL. The patient was treated with CHOP regimen plus rituximab and a total remission was achieved. After an 8-month follow-up the patient was free of disease. This is the first reported case of a rare non-synchronous tumoral combination involving lung and adrenal gland, emphasising at the incidental discovery of the NHL during a procedure performed for a pulmonary adenocarcinoma.

BACKGROUND

The unilateral or bilateral adrenal masses always cause a significant problem of differential diagnosis especially in patients with a known history of primary malignancy in other sites. Primary lymphoma of the adrenal gland (PAL) is a rare origin of adrenal mass (1–6); in this case a correct preoperative diagnosis might spare unnecessary or aggressive surgical treatment. This report discusses of a case of a PAL in a patient with a previous history of lung carcinoma. We discuss the clinicopathological features and therapeutic issues with literature review.

CASE PRESENTATION

A 79-year-old man visited our hospital presenting with abdominal pain. He had left pneumonectomy for a pulmonary adenocarcinoma diagnosed 24 months ago (pT2G2pN0pM0) (figure 1; inset). Physical examination revealed that he had neither lymphadenopathy nor hepatosplenomegaly. Slight elevation of serum carcinoembryonic antigen level as well as anaemia were observed.

INVESTIGATIONS

The endocrinological examinations revealed that his adrenal function was normal. His serum adrenocorticotrophic hormone (ACTH) and cortisol levels at that time were 82.5 pg/ml and 10.5 µg/dl, respectively, indicating that his adrenal function was still normal. Laboratory tests revealed nothing of significance except for a considerable increase in lactate

dehydrogenase levels (LDH of 573 IU/l, normal range 135–250 IU/l). An abdominal CT showed the enlargement of the left adrenal gland (6.0 cm in maximum diameter) (figure 1), whereas his right adrenal gland was normal in size and shape. In the T1- and T2-weighted views in the MRI of his enlarged left adrenal gland showed a low-intensity and isointensity signals, respectively. To make a definite diagnosis, laparoscopic left adrenalectomy was performed. Grossly, the adrenal gland tumour was a well-circumscribed mass of 6 cm in maximum diameter with a solid homogeneous whitish cut surface. Histological examination demonstrated diffuse infiltration of atypical lymphocytes, with a large nuclei and prominent nucleoli that replaced normal adrenal structure (figure 2). Lymphoid cells infiltrated the adipose tissue of adrenal gland; no necrosis was present. Immunohistochemical staining demonstrated that most tumour cells were positive for B-cell markers such as CD20 (figure 3A), pax-5, bcl-2 (figure 3B) and multiple myeloma oncogene 1 (MUM1) (figure 3C), whereas those same tumour cells were negative for CD3, CD5, CD10, BCL-6. Ki-67 was 70% (figure 3D). Taking the findings together, a final diagnosis of diffuse B-cell non-Hodgkin's lymphoma, postgerminal centre subtype, was concluded. Then, a bone marrow biopsy revealed no lymphomatous infiltration.

DIFFERENTIAL DIAGNOSIS

Because the patient had a previous history of pulmonary carcinoma, a diagnosis of metastasis from the lung should be excluded.

Figure 1 inset: RX demonstrated the outcome of previous left pneumonectomy; Abdominal CT showed a circumscribed mass of left adrenal gland.

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Figure 2 Adrenal gland showed a diffuse infiltration of atypical lymphocytes, with large nuclei and prominent nucleoli that replaced normal adrenal architecture (H&E $\times 20$).

TREATMENT

As treatment, cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) therapy at a reduced dose was started due to advanced age and general status of the patient. We used 600 mg/m^2 of cyclophosphamide (80% of standard dose), 40 mg/m^2 of adriamycin (80% of standard dose), 1.12 mg/m^2 of vincristine (80% of standard dose) and 100 mg/body of prednisolone (standard full dose) for 5 days, combined with 375 mg/m^2 of rituximab on the first day, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP).

OUTCOME AND FOLLOW-UP

Positron emission tomography-CT scan performed after administration of six cycles of R-CHOP chemotherapy showed no signs of disease. So a complete remission of disease was obtained with a follow-up of 8 months.

DISCUSSION

In contrast with the high frequency of metastases and the most common adrenal neoplasms as adenoma, myelolipoma, pheochromocytoma and adrenocortical carcinoma, the primary lymphomas of adrenal gland are very rare with less than 70 cases reported in literature.^{1–7} Usually most often adrenal lymphomas present with bilateral tumours and symptoms of adrenal insufficiency.^{1–7} The aetiopathogenesis is still unknown, although frequent association with autoimmune diseases and immunodeficiency status is assessed.⁸ Diffuse large B-cell lymphoma (DLBCL) is the most common histological subtype.^{1–7} A high degree of suspicion is needed to obtain a quick diagnosis since prognosis is extremely poor.^{1–7} However, the increase in the use of ultrasound, CT and MRI has resulted in a large number of incidentally discovered adrenal masses.^{9–11} The diagnosis is initially directed by imaging approaches including adrenal ultrasound and CT scan used primarily to characterise the tumour.^{9–11} Generally, CT scan shows a homogeneous oval and well-circumscribed mass, slightly enhanced by the contrast agent. The primitive adrenal NHL involves differential diagnostic problems with other adrenal benign tumours such as pheochromocytoma, haematoma, infection and adenoma or malignant tumours such as adrenocortical carcinoma and metastases. Generally, a homogeneous morphology and small size indicate that a tumour is benign. Differentiation of benign from malignant adrenal masses and diagnosis of PAL during its early stages are of importance. Only pathological examination confirms the diagnosis of PAL. Moreover, in the event of suspected PAL, ultrasound- or CT-guided fine needle biopsy can obviate unnecessary surgery. In fact sonographically guided fine-needle aspiration biopsy (FNAB) is accurate and safe for evaluating enlarged adrenal glands.⁷ FNAB with adjuvant flow-cytometry is a useful technique for diagnosing and subtyping lymphomas. Only in a few cases core biopsy material is necessary for obtaining additional diagnostic and prognostic information that may

Figure 3 (A) Immunohistochemical staining demonstrated that most tumour cells were positive for B-cell markers such as CD20, (B) bcl-2 and (C) multiple myeloma oncogene 1; (D) tumour cells showed a high proliferative index with Ki-67 (immunoperoxidase).

not be easily derived from the FNAB. This allows optimal treatment planning in patients for whom surgical excision is contra-indicated. When the tumour is hormone-producing or if it is large, adrenalectomy is performed. Since PAL is a rare entity, therapeutic regimens have not been defined in detail, and most patients are treated with regimens similar to those used for other types of lymphoma.¹² Bilateral involvement of adrenal gland was considered as a single-site extranodal involvement, enabling more accurate predictions of survival, overall survival (OS) and pathology free survival (PFS) in primary adrenal DLBCL.¹² Among the treatment alternatives used are surgery, combination chemotherapy and radiation. PAL is usually lethal and early death may occur, even during chemotherapy. There have been a few cases of complete and partial remissions with a longer mean duration of survival.¹³ The case presented here received rituximab-CHOP chemotherapy, which were used to treat PAL by Kim *et al.*¹³ This case showed almost complete remission following the eight cycles. However, it seems that cases of unilateral adrenal lymphoma may have longer survival. Poor prognosis in case of bilateral adrenal lymphoma can be related to adrenal insufficiency. In conclusion, PAL should be kept in mind in the differential diagnosis of patients presenting with unilateral or bilateral huge adrenal malignant masses without nodal involvement in the absence of other malignancies. In addition, fine needle biopsy may help avoid unnecessary surgery. Surgeons should be cautious regarding adrenal insufficiency crisis, which is likely to arise during the follow-up period.

Learning points

- Primary adrenal gland lymphomas (PAL) are rare tumours.
- PAL should be kept in mind in the differential diagnosis of patients presenting with unilateral or bilateral huge adrenal malignant masses without nodal involvement in the absence of other malignancies.
- Fine needle biopsy may help diagnosis of lymphoma and to avoid unnecessary surgery.

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