Development of Mantle Cell Lymphoma in a Patient with Adrenocortical Carcinoma and an 18-year Survival after Complete Removal of the Primary Cancer and Resection of Local Recurrences

R. ORLANDO and F. LIRUSSI

Department of Medical and Surgical Sciences, University of Padua, Padua, Italy

Abstract. The case of a patient with a non-functional and poorly-differentiated adrenocortical carcinoma, who had an unexpected long-term survival after a right adrenalectomy and subsequent removal of 2 local recurrences, is reported. However, fifteen years after the complete resection of the primary neoplasm, the patient first developed an autoimmune thrombocytopenic purpura and later a mantle cell lymphoma located in the mediastinal lymph nodes. This case confirms the possible growth of a second tumour in patients with adrenocortical carcinomas, especially if presenting a long survival after resection of the primary malignancy, and emphasises the need for the close follow-up of these patients.

Case Report

In 2003, our case of a patient with a large non-functioning adrenocortical carcinoma, who had a 15-year survival after complete resection of the primary tumour and complete removal of two local recurrences, was reported (1). In March 2003, one year after resection, the patient was well and there was no clinical and/or radiological evidence of tumour progression.

However, in May 2003, the patient started complaining of non-productive cough while denying fatigue, anorexia, thoracic pain, night sweats, fever or weight loss. The physical examination was virtually normal, with no evidence of splenomegaly and/or lymph nodes in common stations. A computed tomography (CT) scan of the abdomen was negative, whereas a CT scan of the thorax showed multiple mediastinal pathological node enlargements in the laterotracheal dx station and in the lower subcarinal station. These adenopathies were not associated with pulmonary lesions and were considered compatible with a distant recurrence of the adrenocortical carcinoma, though distant metastases of this kind of tumour occur more frequently to the liver, lungs and bones (2-7). The patient, therefore, first underwent a transbronchial needle aspiration biopsy (TBNA), executed by means of bronchoscopy, which was negative, followed by a mediastinoscopic biopsy showing aspecific lymphadenitis.

In December 2003 and in June 2004, CT scans of the thorax showed an increase in the number and size of the mediastinal lymph nodes. In these instances, the plasma levels of ACTH, cortisol, 11-deoxycortisol, testosterone and aldosterone were normal. The 24-h urine-free cortisol, adrenaline and noradrenaline, 17-hydroxysteroid, 17-ketosteroids and vanillymandelic acid levels were within the normal range. Neoplastic markers were also negative. A skin test with tuberculin (5 TU) was negative and so was the sputum culture.

In October 2004, the CT scans of the thorax and the abdomen were unchanged. Laboratory analysis revealed a low platelet count (70,000/Ìl). The platelet-associated IgG was positive; anti-nuclear and anti-smooth muscle antibodies and cryoglobulin were negative; the bone marrow aspirate was normal. The patient was diagnosed as having autoimmune thrombocytopenic purpura (ATP) and was treated with steroids, but did not respond to therapy.

In March 2005, physical examination showed purpura on the upper and lower limbs; peripheral analysis showed a platelet count of 7,000/Ìl associated with a mild clone of B lymphocytes with a phenotype positive for CD20, CD5, and FM C7.

The CT scan of the abdomen was still negative, whereas that of the thorax demonstrated marked lymphadenopathy with aggregated fusion of the lymph nodes (with a maximum
Moreover, data in the literature did not support the later he developed a stage III disease (local invasion). In 1988 the patient had a stage II disease and that 15 years after a complete resection of the adrenocortical carcinoma. However, it should be noted that cancer, the initial diagnosis hinted at distant metastases of the additional tumour 15 years. Complete blood count, erythrocyte sedimentation rate, liver enzymes and kidney function tests were all normal.

In September 2005, the abdominal and thoracic CT scans were unchanged. Neither peripheral lymphadenopathy nor hepatosplenomegaly were detected on physical examination. The platelet count was 125,000/μl, haemoglobin was 13.1 g/dl and the white-cell count was 6,460/μl. However, because TBNA and mediastinoscopy had not allowed an accurate diagnosis, the patient underwent videothoracoscopy with biopsies of the paraesophageal lymph nodes. No intraoperative complications occurred. The histological examination revealed features of B cell non-Hodgkin’s lymphoma (mantle cell lymphoma; MCL). The cells were characterized as CD20+, CD22+ and CD79a+ with cyclin D1 overexpression on immunohistochemistry. The patient, therefore, started chemotheraphy with cyclophosphamide, vincristine, novantrone, prednisolone and monoclonal antibodies against CD20 (8).

Discussion

The case presented here concerns a patient with a non-functioning adrenocortical carcinoma who developed an additional tumour 15 years after a complete resection of the primary neoplasm and removal of 2 local recurrences. Looking at the patient’s 15-year history of his primary cancer, the initial diagnosis hinted at distant metastases of the adrenocortical carcinoma. However, it should be noted that in 1988 the patient had a stage II disease and that 15 years later he developed a stage III disease (local invasion). Moreover, data in the literature did not support the hypothesis of distant metastasis. For example, Luton et al. (3) and Schulich et al. (6) observed that adrenocortical carcinoma primarily metastasises into regional lymphatic tissue, whereas distant metastases are rare, occur at stage IV of the disease and are localised principally in the lungs and the liver, but not in the mediastinal lymph nodes. Other uncommon sites of metastatic disease include the omentum, the peritoneum, the bones, distal lymph node basins and the soft palate (6). Didolkar et al. (9), looking at the natural history of adrenocortical carcinoma, found that the most common metastatic sites were retroperitoneal lymph nodes (68%) and lungs (71%).

In a retrospective study of 54 patients with adrenocortical carcinoma, Grondal et al. (2) found that metastases were present in 25 patients (46%), of which 50% were located in regional lymph nodes, 48% in the lungs, 26% in the liver, 21% in the bones and 4% in the brain.

Crucitti et al. (4) reported 129 cases of adrenocortical carcinoma. Of these, 5 patients were excluded from both surgical and medical interventions because of the advanced stage of the disease and poor general condition. One hundred and twenty-four underwent surgery, which was curative in 91 cases and palliative in 33. Twenty-three patients (17.8%) had distant metastases at diagnosis: 13 in the liver, 5 in the lungs, 5 in the spleen. In the follow-up period, palliative surgery was followed by recurrent disease in 51% of cases whereas, after radical resection, local or distant metastases were observed in 23% of cases.

Bellantone et al. (5), in their study of patients with adrenocortical carcinoma collected in the Italian National Registry, reported that only 30 out of 188 patients had distant metastases (16%). Moreover, of the 179 patients with complete follow-up, 170 underwent surgery, which was radical in 140 and palliative in 30. In the 140 patients who had had radical surgery, recurrent disease was observed in 52 cases (37%) after a mean disease-free interval of 21.7 months. Local recurrence was observed in 27 cases, 14 of whom also presented distant metastases. Metastases alone were observed in 25 cases (12 in the lungs, 19 in the liver, 8 in the bones) (5).

In our case, the final histological diagnosis was mantle cell lymphoma, suggesting that another primary tumour may develop in patients with adrenocortical carcinoma. In fact, Didolkar et al. (9) conducted a clinicopathological study of 42 patients with adrenal cortical carcinoma and found that 22.4% of cases presented a second primary neoplasm, with breast cancer and lymphoma being the most common. Crucitti et al. (4) also reported the occurrence of a second tumour in 3/129 patients with adrenocortical carcinoma (2.3%).

In conclusion, our report: a) suggests that immune-related thrombocytopenia may represent an early expression of the lymphoproliferative disease, in keeping with the study by Numeroso et al. (10); b) confirms the possible development of an associated primary neoplasm in patients with adrenocortical carcinoma, especially when presenting a long survival after resection; c) emphasises the need for the strict follow-up of these patients and, finally; d) renders this rare tumour even more challenging for the physician and/or oncologist.

References


Received January 3, 2006
Accepted January 20, 2006