Spontaneous Complete Remission of a Non-small Cell Lung Cancer Associated with Anti-Hu Antibody Syndrome

Jean-Louis Pujol, MD,* Anne-Laure Godard, MD,† William Jacot, MD,* and Pierre Labauge, MD, PhD†

Abstract: Anti-Hu antibodies are directed against lung cancer cell antigens. The anti-tumor effect of anti-Hu antibodies has been suggested by several studies demonstrating that patients presenting with anti-Hu antibodies have a longer survival. In this case report, we suggest that the immunology of HuAb paraneoplastic syndrome by itself could induce tumor response.

Key Words: Lung cancer, Anti-Hu paraneoplastic syndrome.

CASE REPORT

Anti-Hu antibodies are responsible for lung cancer associated cerebellar ataxia and peripheral neuropathy. We herein report the case of a woman presenting with anti-Hu antibodies (HuAb)-related neuronopathy and non-small cell lung cancer. Spontaneous disappearance of hilar tumor involvement with concomitant impairment of neurological symptoms suggests a putative efficacy of patient’s immunity against non-small cell lung cancer.

A 75-year-old woman with a long history of type I diabetes and tobacco consumption was admitted in December 2004 to the neurological department of the Nîmes Academic Hospital (France) because of a subacute ataxia. Initial examination showed generalized areflexia and massive proprioceptive ataxia with pseudo-choreic arm movements. Electromyography demonstrated lack of nerve sensory action potential and significant decrease in motor potentials. Conduction velocity examinations were normal. Cerebrospinal fluid study was normal. Serum and cerebrospinal fluid HuAb detection confirmed the paraneoplastic origin of the symptoms. A tumor involving the right hilum was demonstrated by means of a computed tomography scan (Figure 1A), and high fluorine-18 deoxyglucose uptake as shown on positron emission tomography scan (Figure 2A) precipitated the performance of a fine-needle transbronchial biopsy. The procedure demonstrated a non-small cell lung cancer of the squamous cell histological subtype. Brain computed tomography scan and magnetic resonance imaging were normal; particularly, neither metastasis nor cerebellum atrophy was found. The patient was denied surgery because her poor physiological condition was thought to be incompatible with pulmonary resection. Neither radiotherapy nor chemotherapy was initiated because of the patient’s poor performance status of 3 and a 12% body mass weight loss. A joint follow-up by neurology and thoracic oncology units was proposed. In December 2005, the clinical examination detected a worsening of the ataxia. HuAb was still detected in the serum, and the patient was referred for plasmapheresis. Nevertheless, a new computed tomography scan (Figure 1B) of the chest, abdomen, and brain did not show any evidence of disease, and complete remission of formerly histologically proven gross tumor involvement was observed. A new positron emission tomography scan performed in March 2006 did not demonstrate significant uptake of fluorine-18 deoxyglucose (Figure 2B). In May 2006, 18 months after HuAb paraneoplastic syndrome associated with non-small cell lung cancer had been diagnosed, a new computed tomography of the chest confirmed a complete remission. Despite therapy using plasmapheresis, begun in January 2006, the patient remains severely disabled with persistent and continuous weight loss.

DISCUSSION

The HuAb is directed against RNA-associated neuronal proteins and is known to cause paraneoplastic encephalomyelitis/sensory neuronopathy syndrome, mostly when associated with small cell lung cancer.1 Anti-Hu paraneoplastic syndromes, such as cerebellar ataxia or peripheral neuropathy, might be the first clinical manifestation of human malignancies.2 This presentation has been observed in small cell lung cancer and non-small cell lung cancer,3 cancer of the breast and uterus, and both non-Hodgkin’s and Hodgkin’s lymphomas.4,5 In some case reports, determining which malignant disease was responsible for these paraneoplastic syndromes has been difficult or impossible. In addition, the disease might be so difficult to detect that patient could die of neurological complications, whereas small cell lung cancer remains nearly undetectable at minimal tumor burden.2 One can hypothesize that patients with anti-Hu antibodies without demonstrable lung cancer are those for whom immunity against the disease may have reduced the tumor to an undetectable level. Our case report could be considered to favor this hypothesis.
Several studies have been undertaken to determine whether patients with small cell lung cancer with detectable serum HuAb at the time of diagnosis have a particular prognosis compared with patients without this immunological feature. It has been suggested that patients with paraneoplastic encephalomyelitis have a higher probability of survival at 30 months compared with similar patients without that clinical feature. In a prospective study, patients with small cell lung cancer were tested for the serum HuAb determined by immunoblot of purified Hu antigen; up to 16% of patients had a detectable level of anti-Hu antibodies. HuAb was associated with limited disease stage (59.3% versus 38.6%; \( p = 0.047 \)), complete response to therapy (55.6% versus 19.6%; \( p < 0.001 \)), and longer survival (14.9 versus 10.2 months; \( p = 0.018 \)). In a logistic regression analysis, HuAb status was an independent predictor of complete response induction. Our case report suggests that the immunology of HuAb paraneoplastic syndrome itself could partially explained the better response rate usually associated with treatment of patients with lung cancer who present with a high serum HuAb level. The probability of achieving a complete response was more than five times greater for HuAb-positive versus HuAb-negative patients (95% odds ratio, 5.4). In contrast with small cell lung cancer, complete remission among patients with non-small cell lung cancer is a rare event, particularly long-term remission, which reinforces the peculiarity of this case report.

Most patients with lung cancer and HuAb-associated paraneoplastic encephalomyelitis die of neurological complications rather than tumor progression. Fortunately, the patient presented in this report is still alive without evidence of lung cancer 18 month after the diagnosis of an otherwise untreated lung cancer. However, the vital prognosis remains poor because of the slow and ineluctable progression of neurological symptoms.

REFERENCES


