**BRAF V600E Mutation Is not Always Present as Expected! A Case Report of Lung and Thyroid Carcinomas**

Nicolas Piton, MD, MPhil, Mathieu Salaün, MD, PhD, Florian Guisier, MD, MRes, Florent Marguet, MD, MRes, Emmanuel K. Touré, MD, Pierre Gémival, MD, Luc Thiberville, MD, PhD, Jean-Christophe Sabourin, MD, PhD

Department of Pathology, Rouen University Hospital, Rouen Cedex, France
Clinique Pneumologique, Rouen University Hospital, Rouen Cedex, France

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This 71-year-old man was a former smoker (30 pack-years) who had been professionally exposed to asbestos. He presented with mediastinal enlarged lymph nodes at stations 4R, 4L, 5, 6, and 7 that were discovered on a regularly scheduled computed tomography scan (Fig. 1A) along with an 18-mm thyroid lesion. No nodule was detected in the lungs, but pleural plaques were observed.

Transbronchial fine-needle aspiration of the mediastinal nodes revealed clusters of tumor cells positive for thyroid transcription factor 1 and negative for thyroglobulin, favoring diagnosis of a lung adenocarcinoma. Molecular analysis retrieved a c.1799T → A (p.Val600Glu) mutation of the BRAF gene, the so-called BRAF V600E mutation. Because no conspicuous lung lesion was visualized on the scan and given the thyroid lesion and this BRAF V600E mutation, a total thyroidectomy was performed with dissection of the bilateral mediastinal recurrent lymph nodes (at stations 1R, 1L, 2R, and 2L).

Microscopically, the 18-mm lesion was a vesicular adenoma, but two areas of papillary thyroid carcinoma measuring 3 mm in the right lobe and 2 mm in the left lobe, respectively, were observed. One node was infiltrated by both the thyroid papillary carcinoma and cells similar to those observed on transbronchial fine-needle aspiration (Fig. 2A). In accordance with genotyping, BRAF V600E protein expression was detected by immunohistochemistry in the latter but not in the papillary carcinoma cells (Fig. 2B).

The patient was initially treated with carboplatin-taxol, with ill-defined progression of the tumor in the right lower lobe associated with carcinomatous pleural effusion (Fig. 1B). Given the BRAF V600E mutation, it was decided to switch to an anti–BRAF V600E treatment (dabrafenib), which led to dramatic regression of the tumor (Fig. 1C). Given the worse prognosis of this metastatic lung adenocarcinoma compared with that of the rather localized thyroid carcinoma, no adjuvant treatment was given for the latter. BRAF V600E mutation is retrieved in slightly less than 50% of papillary thyroid carcinomas but in only 2% of lung adenocarcinomas. Two features of this observation are noteworthy: (1) the coexistence of two different carcinomas, one of the thyroid gland and one of the lung, with a so-called collision tumor in a lymph node, and (2) the fact that contrary to what might have been expected according to epidemiological data, the lung lesion harbored a BRAF V600E mutation whereas the thyroid carcinoma did not. Perhaps more importantly, this case report illustrates the importance of...
Figure 1. Computed tomography scans: mediastinal window (I), parenchymal window (II), initially (day 0) (A), and after treatment by carboplatin-taxol (day 170) (B). Mediastinal lymph nodes have increased in size (I), and an ill-defined lesion has appeared in the right lower lobe with right pleural effusion (II). (C) After second-line treatment with dabrafenib (day 483), mediastinal lymph nodes and the right lung lesion have dramatically regressed, with only a mild right pleural effusion remaining.

Figure 2. Photomicrographs of formalin-fixed paraffin-embedded tissue section of a cervical lymph node after staining by hematoxylin and eosin and by Safran (A) and immunostaining for BRAF V600E (B). This lymph node is infiltrated by both a papillary thyroid carcinoma for which the results of staining for BRAF V600E were negative (white star) and a BRAF V600E-positive adenocarcinoma (black star and arrow). Bar scales: 50 μm for (Ai), (Bi), (Aiii), and (Biii) and 200 μm for (Al) and (Blii).
genotyping lung adenocarcinoma, even when patients are current or former smokers.

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