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# BLOOD HYPEREOSINOPHILIA REVELING ADENOCARCINOMA WITH REARRAGEMENT ROS 1: A CASE REPORT

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## ABSTRACT

Lung cancer, like other solid tumors, is a rare cause of hypereosinophilia. We report a case of a young, non-smoking, 38-year-old woman presenting with a rare case of cancer "a pulmonary adenocarcinoma with ROS1 rearrangement associated with blood hyperosinophilia". Clinical presentation was marked by acute respiratory distress on right pleural effusion of great abundance. The diagnosis was obtained during a thoracoscopy. The evolution with crizotinib was spectacular with normalization of blood eosinophil level after five days of treatment. Lung cancer is one of the rare causes of blood eosinophilia.

**KEYWORDS:** Paraneoplastic hypereosinophilia, lung adenocarcinoma, ROS 1.

## INTRODUCTION

Bronchial cancer is a global public health problem. It is the 2nd cancer in men and 3rd in women in terms of frequency. It is the leading cause of cancer mortality. Non-small cell lung cancer with ROS1 rearrangement is rare, its prevalence is in arround 1 to 2%.[1-3] The ROS 1 rearrangement is essentially found in non-squamous cell cancer, which accounts for 65% of cases in France each year.[1] Paraneoplastic eosinophilia is found in 0.6 to 1.5% of cases.[4] In addition to haemopathies, the most frequently involved tumors are digestive and bronchial carcinomas. Our aim is to report an observation of a woman with eosinophilia on bronchial adenocarcinoma with ROS1 rearrangement.

## OBSERVATION

A 38-year-old non-smoking woman who was hospitalized for acute respiratory distress. She is pregnant of 10 weeks gestation. Symptomatology has occured for one month by chest pain associated with an impairment of general condition with loss of 3kg of weight. She had no other history except an appendectomy at 20 years of age. Clinical examination revealed a digital clubbing, a syndrome of right pleural effusion fluid which was confirmed by thoracic X-ray showed a white lung on the right with repression of the mediastinum towards the left side. There was no sign of systemic (articular, neurological, digestive, ENT or cutaneous). Index of performance status was at 2. Exploration of pleural fluid showed a hematic exudative fluid to 49 g of protein, lymphocytes to 70%, 16% of neutrophils and 12% of eosinophils. There were no malignant cells in cytopathological examination. Blood count showed major hyperleucocytosis at 77 Giga / L, of which predominantly eosinophilic with a value of 42 Giga / L or 55%. CRP was 89 mg/L. Immunological assessments for systemic diseases and parasitological records were negative. Tumor marker assay showed elevated NSE at 57 ng/mL, normal ACE, CYFRA 21.1 at 6.7ng/ml. The chest CT scan showed a septal right pleural effusion associated with thickening of entire pleura. The diagnosis was obtained after performing thoracoscopy with pleural biopsy that revealed a poorly differentiated carcinoma with a positive TTF1 and CK7 mark on histologic examination.

The search for cellular alteration was negative for the KRAS, BRAF, EGFR, HER2 genes but noted the existence of rearrangement of the ROS1 gene on 56% of the tumor cells. Extension assessment, in particular the PET and thoracoabdominal CT showed multiple hyper-metabolic mediastinal lymphadenopathies in the 1R, 2R, 4R and 7 loci, right hilar and left retro-clavicular, hepatic metastasis and multiple vertebral metastasis. Diagnosis was a

bronchial adenocarcinoma with ROS 1 rearrangement stage IV with pleural, ganglion, hepatic and bony (vertebral) secondary localization. After a multidisciplinary consultation meeting, the patient underwent pleural talcation, a medical interruption of pregnancy and oral tyrosine kinase inhibitor by CRIZOTINIB due to 250 mg twice a day. Therapeutic response was spectacular with clinical improvement after five days of treatment, especially in biological terms with the disappearance of blood eosinophilia. The tumor response was maintained for up to 3 months. After that, tumor progression was observed with increased right pleural thickening and onset of cerebral and retinal metastasis. The patient died after 18 months of the diagnosis in a major impairment chart.

## DISCUSSION

Bronchial cancer with ROS1 mutation is rare, found in 1-2% of adenocarcinoma.[2,3,5] This type of cancer is described to be susceptible and specific to adenocarcinoma.[5,6,7] ROS1 fusions are mainly observed in young female and/or nonsmoking patients[5,3,6,8] as our case.

Paraneoplastic syndrome is observed mainly in small cell lung cancer. The most classic forms are endocrine and neurological.[9] Paraneoplastic hypereosinophilia is rarely described. Hyperyosinophilia is defined as a blood eosinophil level greater than 1500 / mm3. It is a common manifestation that can reveal many diseases, the most common is of allergic or parasitic origin. Eryosinophilia classically directs clinicians to myeloproliferative pathologies, lymphoma, parasitosis, side effect of drugs or to a systemic disease. Severe eosinophils with eosinophil counts greater than 5000 / µl are mainly caused by myeloproliferative disorders, eosinophilic granulomatosis with polyanglyosis or tissue migration during parasitic infections.[10]

It can rarely reveal cancer. In 0.6 to 1.5% of cases, hyper eosinophilia corresponds to a paraneoplastic syndrome and intra-tumoral infiltration by eosinophilic polynuclear cells may be associated.[4] It can be found in many solid cancers: thyroid, breast, prostate, lungs, gastrointestinal, genitourinary. Mechanisms of occurrence of cases of neoplastic eosinophilia are still poorly understood. These would be soluble factors secreted by the tumor allowing activation of hematopoiesis and recruitment of eosinophils. The main cytokines involved are GM-CSF, interleukin 3 and interleukin 5.[11,12] Neoplastic origin of eosinophilia is retained after eliminating other causes and especially the disappearance with the tumor response to chemotherapy and reappearance during the progression of the disease. Authors have reported

cases of bronchial cancer whose eosinophilia disappears with tumor response to chemotherapy.[13-15]

## CONCLUSIONS

Paraneoplastic hypereosinophilia is rare. Its association with a bronchial adenocarcinoma with rearrangement ROS 1 is one of the peculiarities because this type of cancer is of rare prevalence. Often adenocarcinoma with ROS1 rearrangement has a poor prognosis. In the face of hypereosinophilia, the neoplastic origin should be sought.

## Conflict of interest

The author(s) declare(s) that there is no conflict of interest.

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