Anaplastic lymphoma kinase (ALK)-rearranged non-Small-cell lung cancer (NSCLC) is a distinct subtype with patients showing peculiar clinicopathological features and dramatic responses to the ALK tyrosine kinase inhibitor crizotinib. Patients with this cancer variant have a dismal prognosis and limited treatment options when it has progressed to intracranial metastases because of inadequate drug penetration into the central nervous system (CNS) [1)].

Anaplastic lymphoma kinase (ALK) gene rearrangement was reported in 3%-7% of primary non-small-cell lung cancer (NSCLC) and its presence is commonly associated with adenocarcinoma (AD) type and non-smoking history. ALK tyrosine kinase inhibitors (TKIs) such as crizotinib, alectinib and ceritinib showed efficiency in patients with primary NSCLC harboring ALK gene rearrangement. Moreover, response to ALK TKIs was observed in central nervous system (CNS) metastatic lesions of NSCLC. However, there are no reports concerning the frequency of ALK rearrangement in CNS metastases. We assessed the frequency of ALK abnormalities in 145 formalin fixed paraffin embedded (FFPE) tissue samples from CNS metastases of NSCLC using immunohistochemical (IHC) automated staining (BenchMark GX, Ventana, USA) and fluorescence in situ hybridization (FISH) technique (Abbot Molecular, USA). The studied group was heterogeneous in terms of histopathology and smoking status. ALK abnormalities were detected in 4.8% (7/145) of CNS metastases. ALK abnormalities were observed in six AD (7.5%; 6/80) and in single patients with adenosuqamous lung carcinoma. Analysis of clinical and demographic factors indicated that expression of abnormal ALK was significantly more frequently observed ($P = 0.0002$; $\chi 2 = 16.783$) in former-smokers. Comparison of IHC and FISH results showed some discrepancies, which were caused by unspecific staining of macrophages and glial/nerve cells, which constitute the background of CNS tissues. Their results indicate high frequency of ALK gene rearrangement in CNS metastatic sites of NSCLC that are in line with prior studies concerning evaluation of the presence of ALK abnormalities in such patients. However, they showed that assessment of ALK by IHC and FISH methods in CNS tissues require additional standardizations [2)].

see Anaplastic lymphoma kinase non-Small-cell lung cancer intracranial metastases.

1)
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2)
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