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Letter to the Editor

Polymyalgia rheumatica occurrence under multikinase inhibitors (sorafenib and erlotinib) treatment

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Polymyalgia rheumatica (PMR) is a well-known inflammatory rheumatic disorder [1]. That may be isolated or associated with other condition, such as giant cell arteritis or cancer. The impact of kinase inhibitors on the development and the treatment of PMR is currently not known. The first case is a 72 years old man, treated for a hepatocellular carcinoma with sorafenib for one year. The treatment was effective with a stabilisation of the tumoral mass. He presented inflammatory arthromyalgia of the pelvic girdle for one month without triggering factor. The X-ray exams were normal with biological inflammatory syndrome (CRP: 98 mg/L) without auto antibodies. A PET-CT showed 18FDG uptakes of the shoulders, the hips, and ischiatic bursitis. No metastasis was found and the tumour size was unchanged as previously. A diagnosis of polymyalgia rheumatica meeting the ACR/EULAR criteria [4] was established. A treatment with an initial 0.3 mg/kg of prednisone was successfully started, with control of PMR symptoms, and a follow-up of 18 months; prednisone has been stopped after 12 months, while continuing sorafenib. The second case is a 72-year-old man treated for 3 months with erlotinib for a bronchial adenocarcinoma with good treatment efficacy. The patient presented suddenly inflammatory arthromyalgia of the limbs. There was a biological inflammatory syndrome without auto antibodies. A PET-CT confirmed the diagnosis of PMR, and showed the absence of metastasis and a decrease in tumour mass. Corticosteroid therapy at 0.3 mg/kg allowed a complete and sustained resolution of symptoms and biological inflammatory syndrome, with a follow-up of more than 6 months, while continuing erlotinib.

To our knowledge, these are the first descriptions of PMR occurring in patients treated with sorafenib and erlotinib, two multikinase inhibitors. To date, there is only one described case of PMR developed under treatment with PI3 kinase inhibitor [2]. Our two cases fulfil the current classification criteria for PMR [3], with suggestive 18F-FDG TEP-CT findings [4].

Sorafenib is a small molecule that inhibits tumour-cell proliferation and tumour angiogenesis [5]. It is an inhibitor of the serine–threonine kinases Raf-1 and B-Raf and of the receptor tyrosine kinase activity of vascular endothelial growth factor receptors (VEGFRs) 1, 2, and 3 and platelet-derived growth factor receptor β (PDGFR-β). Moreover, some studies showed that sorafenib inhibit the jak/STAT pathway [6]. Erlotinib is an Epidermal Growth Factor Receptor (EGFR) tyrosine kinase inhibitor that is involved in the activation of the JAK/STAT Our cases had two relevant informations.

First, although PMR is associated with increased plasmatic level of VEGF [7], the inhibition of its receptor with sorafenib did not avoid or prevent the occurrence of PMR. Second, the inhibition of the jak/STAT pathway by sorafenib and erlotinib was not effective to prevent and/or treat PMR. Sorafenib and erlotinib are multi-kinase inhibitors that can inhibit jak/STAT signal transduction, especially STAT1 and 5. Thus, the inhibition of the janus kinase pathway may not be a target of interest in the treatment of PMR. This point is of particular interest because connection between IL6, a major cytokine implied in the pathophysiology of PMR [8], and the jak/STAT signalling are close [9]. Thus, the role of IL6 in PMR is perhaps not only driven by the jak/STAT pathway. PMR occurrence has also been reported under immune check point inhibitors [10], another class of immunomodulators used in cancer treatment.

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Disclosure of interest

The authors declare that they have no competing interest.

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