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Contribution of intracranial vessel wall magnetic resonance imaging in nilotinib-associated vascular adverse effects diagnosis

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A 67-year-old man using nilotinib 300 mg twice a day to treat chronic myeloid leukemia for 3 years, with major molecular response, presented with sudden-onset left-sided paresis in the limbs, for 6 h. Brain magnetic resonance imaging (MRI) demonstrated acute ischemic lesions in the right frontal and parietal lobes, with restricted diffusion, hyperintense signal on fluid-attenuated inversion recovery, and reduced perfusion on mean transit time map, in the territory of the right middle cerebral artery. MR-angiography revealed an irregularity in the right middle cerebral artery flow signal. High-resolution intracranial vessel wall MRI showed a stenosis of the M1 segment of the right middle cerebral artery, with eccentric gadolinium-enhancement (Figure 1), suggestive of an unstable atherosclerotic plaque, responsible for the ischemic stroke. Despite the age, the patient had no other cardiovascular risk factors. The treatment was changed to imatinib as well as statin and anticoagulant were initiated due to ischemic attack.

Nilotinib is a second-generation tyrosine-kinase inhibitor, which can be used as a first-line drug to treat chronic myeloid leukemia. The arterial occlusive disease is a well-known nilotinib adverse effect [1]. Previous studies demonstrated nilotinib-related cerebrovascular disease associated with one or multiple intracranial arterial stenosis, causing ischemic strokes [2].

The pathophysiological mechanisms of nilotinib-associated vascular adverse effects are not fully known. However, nilotinib has a high affinity for discoidin domain receptor-1, which plays a role in atherosclerosis formation, and it is a major blocker of platelet-derived growth factor receptor and C-kit, which regulate various vascular and perivascular cells. Furthermore, nilotinib exerts direct pro-atherogenic and anti-angiogenic effects, due to altered endothelial cell function and increased expression of cytoadhesive molecules. In addition, nilotinib increases cholesterol and fast glucose [2].

Intracranial atherosclerotic plaques typically appear as eccentric vessel wall thickening, with outward remodeling of the arterial wall, with heterogeneous signal, involving the proximal intracranial branches or bifurcation points. Intraplaque hemorrhage and/or eccentric gadolinium enhancement are signs of vulnerability and increased risk of stroke. These findings are important in patients with more than one intracranial atherosclerotic plaque, to evaluate the most vulnerable plaque or the responsible for a stroke. Also, vasculitis, an important differential diagnosis of atherosclerosis, would typically demonstrate concentric parietal thickening and gadolinium enhancement in the vessel wall [3], instead of an eccentric enhancement, as our patient.

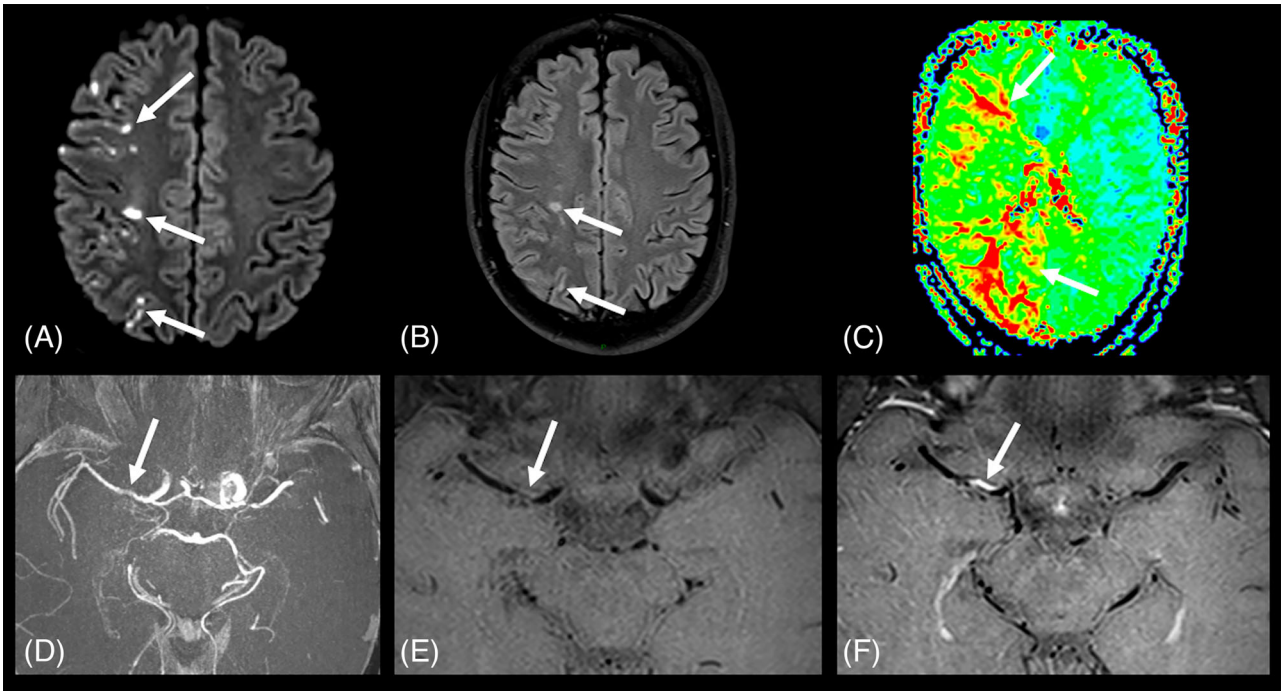

FIGURE 1 Nilotinib-associated acute stroke. Brain MRI demonstrated multiple foci of acute ischemic lesions in the right frontal and parietal lobes, with restricted diffusion (arrows in A), some with hyperintense signal on fluid-attenuated inversion recovery (FLAIR) (arrows in B), in the territory of the right middle cerebral artery. Mean transit time map demonstrated increased circulation time (arrows in C) in this territory. Magnetic resonance angiography revealed a slight irregularity in the flow signal of the middle cerebral artery (arrow in D). High resolution intracranial vessel wall imaging showed a stenosis of the M1 segment of the right middle cerebral artery (arrow in E), with eccentric gadolinium-enhancement (arrow in F), suggestive of an unstable atherosclerotic plaque.

Therefore, intracranial vessel wall imaging may aid in the evaluation of patients with nilotinib-associated vascular adverse effects and should be added to the brain MRI protocol.

AUTHOR CONTRIBUTIONS

Diogo Goulart Corrêa wrote the manuscript, assisted in taking original images, and produced the figure. Roberto Queiroz dos Santos assisted in taking original images, and provided valuable contributions to the manuscript. Luiz Celso Hygino da Cruz Jr. provided valuable contributions to the manuscript.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to disclose.

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DATA AVAILABILITY STATEMENT

Data from this manuscript will be shared upon request.

ETHICS STATEMENT

The information presented in this manuscript is deidentified, and there is no risk to the patient's privacy or confidentiality. IRB approval was not required by our institution for the preparation of this manuscript.

PATIENT CONSENT STATEMENT

Patient consent was obtained. No material from other sources is included in this manuscript.

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