A report of a new late toxic effect of lenvatinib

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To the Editor: Hepatocellular carcinoma (HCC) is the third most lethal malignancy globally.[1] Besides sorafenib, lenvatinib is currently the second approved targeted agent for the first-line treatment of HCC in 2018. Lenvatinib is an oral multikinase inhibitor that targets vascular endothelial growth factor (VEGF) receptors 1 to 3, fibroblast growth factor receptors 1 to 4, platelet-derived growth factor receptor α, RET, and KIT.[2] Patients who received lenvatinib experienced diarrhoea, and alopecia, and more instances of hypertension, proteinuria, and hypothyroidism. Here, we report two patients that developed irreversible pancreatic atrophy as a novel adverse event of lenvatinib.

The first patient received lenvatinib for 8 months at the recommended dose of 12 mg/day. Grade 1 diarrhea occurred 2 months post-treatment initiation of lenvatinib. Pancreatic exocrine insufficiency was diagnosed 3 months after the initiation of lenvatinib. Pancreatic-enzyme replacement was then performed to control diarrhea. We used volumetric measurement tools to calculate the pancreatic volume in a post-processing workstation (Advantage Workstation, version 4.6; GE Healthcare, Buc, France), revealing a 51% reduction in volume [Figure 1A and 1B]. A second patient received lenvatinib for 12 months at the recommended dose of 12 mg/day. To date, no diarrhea has occurred. Volumetric magnetic resonance imaging of the pancreas showed a 30% decrease in the volume [Figure 1C and 1D].[3] In summary, lenvatinib and sorafenib show the anti-angiogenic properties of anti-VEGF agents may reduce the microvasculature of normal tissues. Hescot *et al*[4] first reported on two patients who developed irreversible pancreatic atrophy after prolonged treatment with sorafenib. Li *et al*[5] also reported pancreatic atrophy could contribute to sorafenib-induced diarrhea. Patients frequently suffer from diarrhea, weight loss, anorexia, and nausea, considered common symptoms of exocrine pancreatic insufficiency. However, little is known about effects related to exposure to lenvatinib, and pancreatic atrophy amongst patients chronically treated with lenvatinib might be a predictive surrogate marker of therapeutic efficacy.

Declaration of patient consent

We certify that we have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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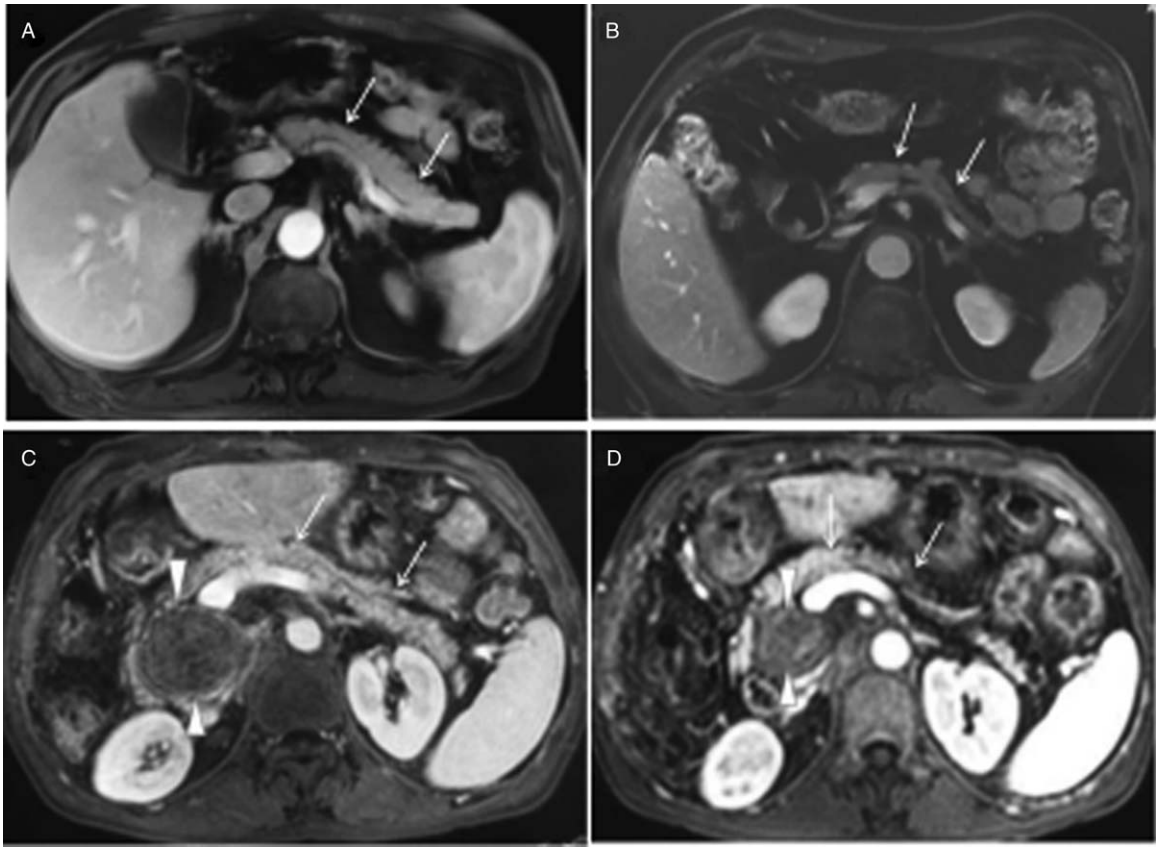

Figure 1: Two patients developed atrophy of the pancreas after prolonged treatment with lenvatinib. (A–B) The pancreatic volume loss of 51% after 3 months of treatment with lenvatinib (arrows); (C–D) pancreatic volume (arrows) loss of 30% and tumor (triangle) shrink significantly after 12 months of treatment with lenvatinib.

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