To the Editor,

Targeted anticancer therapy with tyrosine kinase inhibitors (TKIs) has shown remarkable efficacy in selected malignancies. With increased use of these new agents, the knowledge about their adverse effects will grow, even more when combinations of TKIs are used. Erlotinib (Tarceva®, Roche) has been approved for the treatment of advanced or metastatic non-small-cell lung cancer (NSCLC) after the failure of prior chemotherapy [1]. Sunitinib (Sutent®, Pfizer) has been approved for the treatment of metastatic renal cell carcinoma [2], and has been investigated in a single arm phase II trial in NSCLC [3]. Often reported side effects are for erlotinib rash and diarrhea, for sunitinib diarrhea, nausea, mucositis and rash. We report a patient who developed necrotizing pancreatitis during combination treatment with erlotinib and sunitinib.

The patient is a 46-year-old female with NSCLC (adenocarcinoma). One year before she had received sequential chemo-radiation for locally advanced disease. By now, she presented with clear distant metastases (not histologically or cytologically proven) and participated in a phase 3 multicenter clinical trial on the efficacy and safety of sunitinib in patients with NSCLC treated with erlotinib (Pfizer, Protocol A6181087), and received oral erlotinib 150 mg once daily and oral sunitinib 37.5 mg once daily, both continuously. She experienced mild diarrhea but no oral erlotinib and sunitinib. Since there were no classic risk factors for pancreatitis, it was most probably related to the medication she used.

At admission, all medication was stopped. The patient was rehydrated, received intravenous calcium and magnesium supplementation, and parenteral nutrition. The clinical situation however deteriorated. She developed high fever, and a second CT scan was suitable to necrotizing pancreatitis. Despite maximal supportive care, the patient died 4 weeks after admission. Obduction confirmed the diagnosis of necrotizing pancreatitis with extended peripancreatic fat necrosis (Fig. 1). Vital tumour was not found anywhere in the body, suggesting that the therapy was responsible. Laboratory examination revealed a good tumour response after 12 weeks of treatment.

Asymptomatic elevations in serum amylase and serum lipase have been reported in about 5% of patients being treated with sunitinib [2,4]. Lareb, the Dutch registration centre for adverse events, has confirmed that other cases of pancreatitis and hypocalcaemia in patients treated with erlotinib or sunitinib have been reported, but so far there have been no publications on fatal pancreatitis during this therapy.

In conclusion: we report a patient with fatal necrotizing pancreatitis with extended peripancreatic fat necrosis (Fig. 1). Vital tumour was not found anywhere in the body, suggesting that the therapy revealed a good tumour response after 12 weeks of treatment.

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In conclusion: we report a patient with fatal necrotizing pancreatitis, with at presentation an extreme low serum calcium, and since elevated serum amylase and pancreatitis is being observed during treatment with sunitinib or erlotinib, it is probable...
that this combination therapy is responsible for this fatal pancreatitis.

Conflicts of interest

The authors indicate no potential conflicts of interest.

References


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