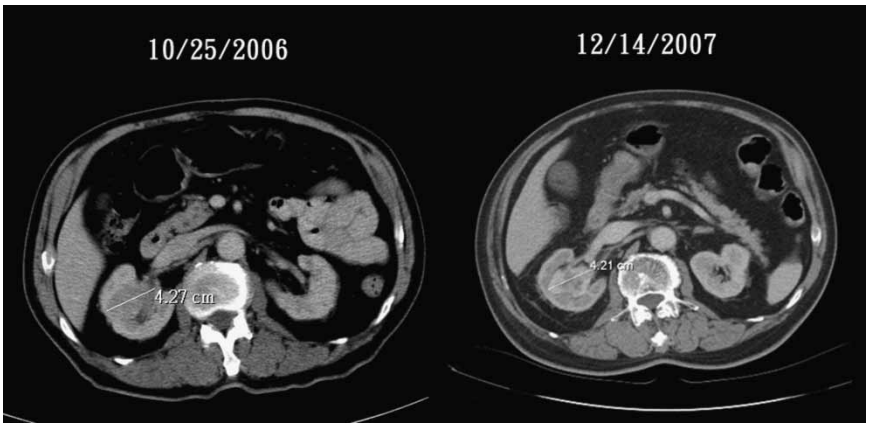

insisted on stopping the medication. Fifteen months later, we contacted him and he was healthy with an ECOG performance status of 0–1.

One of the main problems of using targeted therapy in metastatic cancer is whether the medication should be discontinued when the clinical status is stable or the patient is in remission. In most cases, patients are treated until disease progresses [3]. Therefore, it's difficult to determine when and whether to stop the medication. We also assumed that the addition of chemotherapy to these targeted medications might lead to better disease control and longer progression free intervals [4]. The cost of treatment is another problem. In metastatic RCC, the costs for sorafenib are around US$30 000–40 000. This usually prevents a patient from taking these medications without limit. Based on this case, we are particularly interested in the cost-effectiveness of treatment, an aspect which interests insurance authorities the most.

Presently, the eradication of metastatic RCC by available medications is still a long way off. Lower costs and longer survivals with better control remain the main goals of treatment.

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Persistent hiccups as an adverse event to FLAG-IDA regimen for leukemia

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To the Editor,

Hiccups are often unreported as an adverse reaction to cancer chemotherapy. Takiguchi et al. have reviewed database information from the corresponding pharmaceutical companies in Japan concerning hiccups related to the use of several specific chemotherapeutic agents, and reported an incidence of hiccups of 0.39% in chemotherapy treated patients, being higher in males than females [1]. We report the first case of persistent hiccups associated with the use of a fludarabine, cytarabine and idarubicin based regimen.

A 51-year-old man with acute myeloid leukaemia M6 to cytochemical FAB classification and at high risk for complex karyotype to WHO classification was refractory to a first remission induction regimen, containing standard dose cytarabine (100 mg/m^2, days+1 to+10), daunorubicin (50 mg/m^2 on days+1,+3 and 5) and etoposide (50 mg/m^2 on days+1 to+5) and was subjected to a salvage chemotherapeutic regimen (FLAG-IDA), consisting of high dose cytarabine (2 g/m^2 on days+1 to+5), fludarabine (30 mg/m^2 on days+1 to+3), idarubicin (8 mg/m^2, on days+1 to+3). On day+2, late in the evening, the patient developed persistent hiccups at a rate of 10 – 15 per minute. His past medical history included a previously diagnosed duodenal ulcer, 15 years before. Vital signs were stable. He was neurologically intact. A contrast-enhanced thoracic and abdominal computed tomography revealed neither mediastinal enlargement nor pericardial effusion, nor hepatic or pancreatic masses. Treatment with oral and intravenous metoclopramide and with chlopromazine was ineffective. On day+5, in the afternoon, after completion of cytarabine infusion, an esophago-gastro-duodenoscopy was performed, revealing neither signs of esophagitis nor of gastro-duodenitis. In the evening, hiccups cessated, but baclofen, 5 mg orally, three times daily, was however started. The patient remained entirely hiccup-free, for the following four weeks of observation.

The close temporal sequence and the absence of any alternative explanations make this adverse effect possibly related to the chemotherapy used, although a positive re-exposure relationship is lacking [2]. Of note, while complete and sudden cessation of hiccups is likely to be related to the completion of chemotherapy, we cannot exclude the effect of baclofen, which was, on the other hand, rapidly tapered, in few days. Moreover, persistence of hiccups until day+5, two days after the completion of either fludarabine or idarubicin administration, make high dose cytarabine the most plausible culprit among the three chemotherapeutic agents used. The hypothesis is raised that disturbance of the central nervous system or vagal and phrenic nerve, may be included among the neurotoxicity profiles of cytarabine, with or without fluadarabine, in patients with leukaemia [3]. The patient was receiving antibiotic prophylaxis with amoxicillin clavulanate and itraconzaole, but, although the former has been reported to cause hiccups, its role in this case is excluded by hiccup cessation, while maintaining the same prophylactic regimen.

In conclusion, we describe a previously unreported association between the administration of the FLAG-IDA regimen and the development of persistent hiccups. Awareness of such an adverse event is important for a prompt initiation of baclofen therapy.

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