Réponse radiologique complète après traitement par Sorafénib pour un carcinome hépato-cellulaire avancé

Complete radiological response after Sorafenib treatment for advanced hepato-cellular carcinoma.

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RÉSUMÉ

Introduction : Le sorafénib (Nexavar®), est une thérapie ciblée de type inhibiteur de la tyrosine kinase, ayant démontré un bénéfice en termes de survie dans le traitement palliatif du carcinome hépatocellulaire localement avancé. Cependant, les réponses partielles sont rares et les réponses complètes exceptionnelles.

Cas clinique : Nous rapportons le cas d'une patiente ayant une cirrhose post-hépatitique C compliquée d'un carcinome hépatocellulaire avancé non résécable qui a obtenu une réponse radiologique complète après traitement palliatif par sorafénib.

Conclusion : la connaissance des facteurs associés à une bonne réponse au sorafénib est nécessaire

Mots-clés
Carcinome hépatocellulaire - Sorafénib - traitement

SUMMARY

Introduction: Sorafenib, an oral multikinase inhibitor, has recently been shown to improve overall survival in patients with advanced hepatocellular carcinoma (HCC) but only a handful of reports of complete remission on sorafenib have been issued.

Case report: We report an intriguing case of advanced HCC complicating HCV infection with cirrhosis, in which the patient achieved complete remission by prolonged administration of sorafenib.

Conclusion: Identifying factors that could be associated with good response to this therapy are needed.

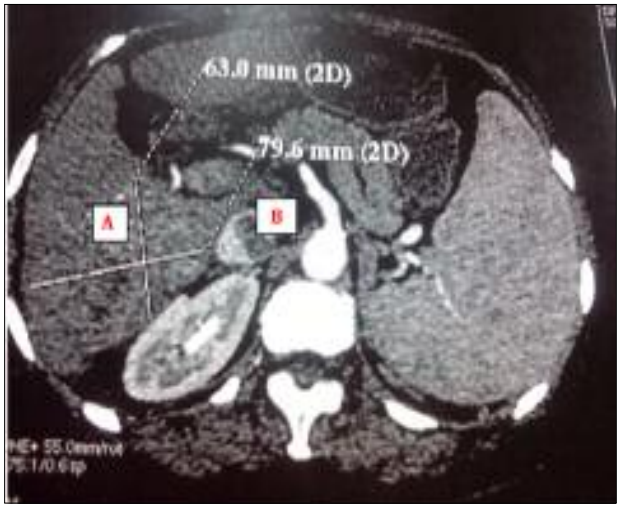
Key-words
Hepatocellular carcinoma - Sorafenib - treatment

Hepatocellular carcinoma (HCC) is the third most common cause of cancer related death worldwide. Early stage HCC can be effectively treated by resection, liver transplantation or percutaneous ablation whereas no effective treatment has been established for advanced HCC, especially when there is portal vein involvement. Sorafenib, an oral multikinase inhibitor, has recently been shown to improve overall survival in patients with advanced HCC in two randomized, double-blinded, placebo-controlled trials (the Sorafenib HCC Assessment Randomized Protocol: SHARP trial and the Asia-Pacific trial) [1,2]. This drug has been approved as the first-line therapy for advanced HCC patients. Treatment response to sorafenib in HCC manifests in different ways, but only a handful of reports of complete remission (CR) on sorafenib have been issued [3]. We report an intriguing case of advanced HCC in which the patient achieved CR by prolonged administration of sorafenib.

CASE PRESENTATION

A 67 year-old female had an HCV infection (genotype 2) since 2010. Her liver biopsy showed a moderate grade of necroinflammatory activity and a moderate intensity of fibrosis (Ishak grading 13, Ishak staging 3). She was started on antiviral treatment with Peg-interferon 180 µg/week and ribavirin 1000mg/day in 2011. Twenty-four weeks later, antiviral therapy was discontinued for virological failure. In April 2013, she was referred to our center with an abdomen computed tomography (CT) showing a large liver tumor of 8 cm in the posterior segment of the right lobe, which was enhanced in the arterial phase and washed out in the equilibrium phase, typical of HCC associated toan enhanced total thrombosis of the portal vein (Figure 1).

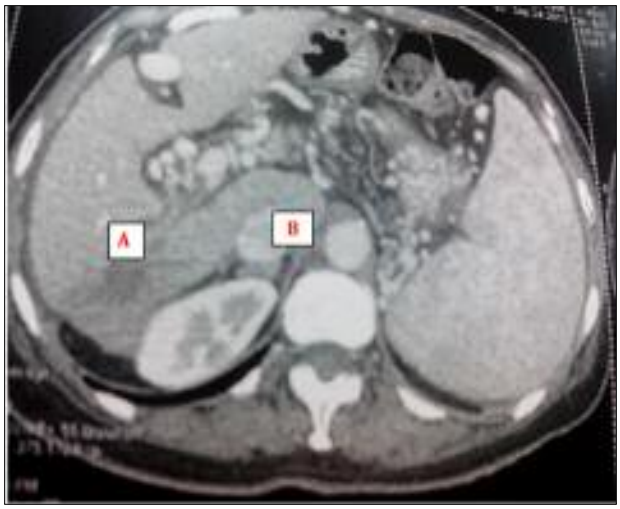
Figure 1 : Contrast-enhanced computed tomography scans before sorafenib treatment. (A) Arterial phase showed a large hypervascular lesion extending from to the posterior segment of the right lobe. (B) Portal vein thrombosis.



Extrahepatic metastasis was not observed. The patient was in good health, and his Eastern Cooperative Oncology Group performance status was 0. Elevation of alpha-fetoprotein (AFP) was observed at a level of 123 ng/ml (normal range < 10).

The diagnosis of cirrhosis was done according to clinical, laboratory and endoscopic finding showing signs of portal hypertension and liver failure. Her Child-Pugh score was A 6, and the tumor stage was Barcelona Clinic Liver Cancer stage C. According to the clinical practice guidelines for HCC, the patient was treated with sorafenib at 800 mg per day. No adverse effect was reported. After six months, follow-up CT showed that the tumor was hypodense in all phases and its size shrunk from 8 cm to 2 cm, the intense staining due to the portal vein thrombosis resolved.These findings were consistent with a partial response (PR) according to the revised Response Evaluation Criteria in Solid Tumors Guidelines (RECIST) and a CR according to modified RECIST (mRECIST) [4] (Figure 2).

Figure 2 : Abdomen computed tomography scan: Follow up. (A)The tumor was hypodense in all phases and its size shrunk from 8 cm to 2 cm. (B) The intense staining due to the portal vein thrombosis resolved



DISCUSSION

In this present case, a patient with cirrhosis and locally advanced HCC received sorafenib with palliative intent, allowing a CR. Sorafenib represents a breakthrough in the treatment of advanced HCC with a clinically meaningful improvement in overall survival, according to the results of two randomized, double-blind, placebo-controlled, multicenter, phase III trials (SHARP trial and the Asia-Pacific trial) [1,2]. In the SHARP trial, 602 patients with advanced HCC and cirrhosis were enrolled [1]. However, of the patients treated with sorafenib, only seven (2%) achieved PR assessed by RECIST and no CR was recorded [1]. Similarly, in the Asia-Pacific trial, no CR to sorafenib was observed among the 226 patients enrolled, despite a PR rate of 3.3% [2]. According to RECIST, CR correlate with the disappearance of all target lesions and PR with at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum longest diameter [4]. In our case, with RECIST evaluation, a decrease in greatest tumor dimension was noted, but this was not sufficient to reach the threshold for CR. Nevertheless, for HCC, evaluation of tumor hemodynamics is considered important for the

judgment of the anti-tumor therapeutic effect of sorafenib. Therefore, mRECIST may be more reliable than RECIST. These modified criteria increase the amplitude of the observed shrinkage and provides a more striking appraisal of the therapeutic effect. With mRECIST, CR is defined by the disappearance of any intratumoral arterial enhancement in all target lesion and partial response by at least a 30% decrease in the sum of diameters of viable (contrast enhancement in the arterial phase) target lesions, taking as reference the baseline sum of the diameters of target lesions [4].With mRECIST, we can judge that our patient achieved a CR. Patients with cirrhosis and HCC may develop either benign or malignant portal vein thrombosis (PVT). In this context, critical evaluation of PVT by imaging techniques and diagnostic criteria is mandatory to differentiate benign and malignant PVT [5,6]. According to RECIST and mRECIST evaluation, tumor portal vein thrombosis (TPVT) should be considered as a non-measurable lesion due to the difficulty in performing consistent measurements of the malignant thrombus during the course of the treatment [4]. Measurements of the extent of the malignant thrombus may be impaired by the possible presence of a bland component of the thrombosis. The clinical data of sorafenib in patients with HCC and PVT are rare and PVT revascularization after administering sorafenib has been reported in some cases [7,8]. Jeong SW and al showed that 10% of patients with advanced HCC and TPVT had remarkable outcomes with PR and TPVT revascularization, although the treatment results of this type of patients is extremely poor [9]. In the present case, we couldn't assert that portal vein thrombosis was tumoral. TPVT is caused by portal vein invasion by cancer cells, and vascular specific growth factors are important for this process [10]. Sorafenib reacts by blocking vascular endothelial growth factor receptor or platelet-derived growth factor receptor, and is believed to promote TPVT revascularization [11].

The discontinuation of medication subsequent to acquiring a CR in advanced HCC would be beneficial, as sorafenib is an expensive drug and has adverse effects. But, tumors may recur due to the discontinuation of treatment, and the appropriate timing of sorafenib discontinuation requires further investigation [12]. In our case, we maintained sorafenib.

CONCLUSION

The present report describes a case of advanced HCC that showed a CR after treatment with Sorafenib. In addition to produce significant improvement in survival, this targeted therapy raises the hope to achieve a CR in unresectable advanced HCC. Identifying factors that could be associated with good response to this therapy are needed.

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