Delayed creatine kinase elevation after sonidegib therapy in a patient with decompensated cirrhosis and esophagogastric variceal hemorrhage: A case report

BOWU CHEN*, SHUTING ZHUANG*, YANXI ZHENG, BINYI SHANG and YUNHUI ZHUO

Department of Hepatology, Shuguang Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, P.R. China

Received June 21, 2026; Accepted October 13, 2026

DOI: 10.3892/etm.2026.13357

Abstract. Sonidegib, a hedgehog pathway inhibitor targeting the smoothened receptor, is widely used in advanced basal cell carcinoma (BCC). Creatine kinase (CK) elevation is a recognized adverse event following treatment with sonidegib, but its safety in patients with decompensated cirrhosis remains unclear. The present study reports the case of a 77-year-old man with chronic hepatitis B-related decompensated cirrhosis who developed CK elevation after sonidegib therapy for locally advanced BCC. The patient had received oral sonidegib at 200 mg/day for 35 days, which was discontinued due to worsening ascites. Shortly afterward, the patient experienced esophagogastric variceal hemorrhage and was admitted to the Department of Hepatology at Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine (Shanghai China). At 4 days post-admission (day 4) and 7 days after sonidegib discontinuation, CK was first found to be elevated to 3,291 U/l. The CK level peaked at 11,944 U/l on day 6, accompanied by elevated myoglobin, but without evidence of acute myocardial injury or renal impairment. Hypovolemia, electrolyte abnormality, critical disease-associated myopathy, occult infection and concomitant medication were assessed as alternative or contributing explanations. A Naranjo Adverse Drug Reaction Probability Scale score of 4 indicated a possible adverse drug reaction. The patient received intravenous fluid replacement, permanent withdrawal of sonidegib and close monitoring. The CK level returned to the reference range by day 21, and the myoglobin level normalized by day 57; both remained normal during the 3 months of follow-up. This case is notable for the delayed severe CK elevation after sonidegib discontinuation in the combined setting of decompensated cirrhosis and acute variceal bleeding, and highlights the importance and need for close and extended CK monitoring, careful assessment of hepatic function, and individualized treatment decisions in patients with cirrhosis receiving sonidegib.

Introduction

Basal cell carcinoma (BCC) is one of the most common types of skin cancer worldwide (1,2). Globally, the annual number of new BCC cases has increased over recent decades, reaching ~4.4 million in 2021, partly reflecting population ageing and cumulative sun exposure (3,4). Although most cases are curable through surgical excision, a subset of patients with locally advanced BCC (laBCC), metastatic BCC or nodal BCC require systemic therapy (1). Hedgehog pathway inhibitors, including vismodegib and sonidegib, have improved the management of laBCC by targeting the smoothened (SMO) receptor and suppressing the activated Hedgehog signaling pathway that drives tumor growth (5,6).

Sonidegib is a second-generation SMO receptor that has demonstrated efficacy and tolerability in patients with laBCC (7-9). However, its use may be limited by adverse muscular events, particularly elevated serum creatine kinase (CK) levels, which have been reported in 61% of patients receiving sonidegib (200 mg) and may be related to mitochondrial dysfunction within muscle cells (5,10,11). Regular CK monitoring is therefore recommended during treatment to identify muscle injury early and prevent progression to rhabdomyolysis or renal injury. Sonidegib is metabolized mainly in the liver through oxidation and amide hydrolysis mediated by the cytochrome P450 3A4. Although pharmacokinetic studies have suggested that dose adjustment may not be required for mild hepatic impairment, evidence remains limited for patients with moderate or severe hepatic dysfunction (12-14). Decompensated cirrhosis may reduce hepatic capacity and drug clearance. Hypoalbuminemia may decrease plasma protein binding and increase the unbound fraction of albumin-bound drugs, while ascites may increase the volume

Correspondence to: Professor Yunhui Zhuo, Department of Hepatology, Shuguang Hospital, Shanghai University of Traditional Chinese Medicine, 528 Zhangheng Road, Pudong New Area, Shanghai 201203, P.R. China
E-mail: huihuiz1688@icloud.com

*Contributed equally

Abbreviations: BCC, basal cell carcinoma; CK, creatine kinase; CK-MB, creatine kinase-myocardial band; laBCC, locally advanced BCC; SMO, smoothened

Key words: sonidegib, creatine kinase elevation, decompensated cirrhosis, basal cell carcinoma, case report

of distribution of hydrophilic drugs, thereby increasing the risk and severity of adverse events (15).

To the best of our knowledge, delayed CK elevation after sonidegib discontinuation has not been reported in patients with decompensated cirrhosis. The present study describes a case of a 77-year-old man with chronic hepatitis B-related decompensated cirrhosis who developed CK elevation after receiving sonidegib for locally advanced BCC, reporting the temporal association, causality and competing explanations in order to emphasize the importance of careful monitoring and individualized dosing strategies. The reporting of this study conforms to Case Report guidelines (16).

Case report

In April 2025, a 77-year-old man with a history of chronic hepatitis B virus infection for >40 years and hepatitis B-related cirrhosis diagnosed >30 years earlier, was admitted to the Department of Hepatology at Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine (Shanghai, China) after two episodes of hematemesis totaling ~500 ml. Long-term antiviral therapy had been received in the form of 25 mg/day tenofovir alafenamide fumarate and 0.5 mg/day entecavir.

A total of 6 months before admission, a lesion below the left canthus, ~1 cm in diameter and without clinical evidence of nodal or distant metastasis, was clinically diagnosed as BCC. Surgery was not considered due to the high-risk periocular location, limited tolerance to surgery and anesthesia due to decompensated cirrhosis, and the patient's preference for non-surgical therapy. Sonidegib at 200 mg/day was initiated 35 days before admission for BCC treatment.

The patient developed fatigue, abdominal distention and a poor appetite 3 days before admission. Abdominal ultrasonography revealed cirrhosis and moderate ascites with a maximum depth of 93 mm (Fig. 1A), leading to the discontinuation of sonidegib in April 2025. The patient then developed two episodes of hematemesis and was admitted to hospital as an emergency. Emergent gastroscopy confirmed an esophagogastric variceal hemorrhage (Fig. 1B). The lowest blood pressure during bleeding was 109/75 mmHg (reference range: 90/60-140/90 mmHg) without vasopressor use. The patient reported no recent trauma, strenuous exercise, seizures, prolonged compression of muscles or use of statins or any other medications known to cause CK elevation. The patient also exhibited no muscle weakness, myalgia or exercise intolerance.

On admission, the vital signs of the patient were stable, with a body temperature of 36.7˚C (reference range: 36.0-37.0˚C), a blood pressure of 122/71 mmHg (reference range: 90/60-140/90 mmHg), a heart rate of 78 beats/min (reference range: 60-100 beats/min) and a respiratory rate of 16 breaths/min (reference rage: 12-20 breaths/min). The patient weighed 55 kg and was 168 cm tall (body mass index of 19.5 kg/m^2). A physical examination revealed abdominal distension with positive shifting dullness without jaundice. A neuromuscular examination showed normal muscle tone and muscle strength, full range of motion in all extremities and no muscle tenderness. The patient was not admitted to an Intensive Care Unit, mechanically ventilated or treated with neuromuscular blocking agents. Based on clinical and laboratory measurements at admission, the patient was classified as Child-Pugh class B (17), with a model for end-stage liver disease score of 11 (18).

Initial laboratory testing on day 1 post-admission showed a normal CK level of 150 U/l (reference range, 50-310 U/l), although the serum myoglobin level was elevated at 525 ng/ml (reference value, <70 ng/ml). However, on day 4, which was the fourth day after hematemesis and the seventh day after discontinuation of sonidegib, CK elevation was first detected at 3,291 U/l in the morning and increased to 6,002 U/l later that day. The CK value further increased to 8,766 U/l on day 5 and peaked at 11,944 U/l on day 6. The myoglobin level reached its peak of 7,633.7 ng/ml on day 4. CK-myocardial band (CK-MB) level also increased from 5.68 ng/ml on day 4 to 17.26 ng/ml on day 6 (reference value, <5 ng/ml). However, serum cardiac troponin I remained within the reference range, and an electrocardiogram showed low limb-lead voltage and a slightly negative P-wave terminal force in lead V1 below 0.04 mm/sec, providing no evidence of acute myocardial injury (Fig. 1C). Aspartate aminotransferase values (reference range: 15-40 U/l) increased in parallel with CK and peaked at 508 U/l on day 6, while alanine aminotransferase values (reference range: 9-50 U/l) reached the peak of 122 U/l on day 11. Other liver-related laboratory measurements, including total bilirubin, alkaline phosphatase and γ-glutamine transpeptidase levels, remained unchanged. Renal function tests, including creatinine and blood urea nitrogen, remained within the normal range, and urinalysis showed clear urine with 5-7 red blood cells per high-power field (reference range: 0-3 red blood cells per high-power field). There was no progressive decrease in hemoglobin level and red blood cell count throughout hospitalization. All available relevant laboratory results are presented in Table I and Fig. 2.

The preliminary potential diagnoses were sonidegib-associated CK elevation, hepatitis B-related decompensated cirrhosis (Child-Pugh stage B), esophagogastric variceal hemorrhage in the recovery phase and BCC. A Naranjo Adverse Drug Reaction Probability Scale assessment (19) yielded 4 points, including points for previous reports (+1), onset after exposure (+2), improvement after withdrawal (+1), plausible alternative causes (-1) and objective laboratory confirmation (+1), with all other items scoring zero, corresponding to a possible adverse drug reaction (Table II).

The variceal hemorrhage was treated with octreotide acetate (0.3 mg administered by intravenous infusion every 12 h), lansoprazole (30 mg administered by intravenous infusion once daily) and fluid resuscitation of ~2,000 ml/day. After CK elevation was identified, the patient received immediate intravenous fluid replacement at ~3,000 ml/day to maintain a urine output of >100 ml/h, promoting myoglobin clearance and preventing renal injury. Sonidegib was permanently withdrawn and all potentially myotoxic medications were avoided.

Following treatment, the CK level gradually declined to 246 U/l by day 21 and remained within the reference range thereafter without renal impairment. Myoglobin remained elevated through day 30 and normalized to 59 ng/ml by day 57. No recurrence of liver function elevation, muscle enzyme elevation or other adverse events were observed. The patient underwent regular monthly outpatient follow-up, supplemented

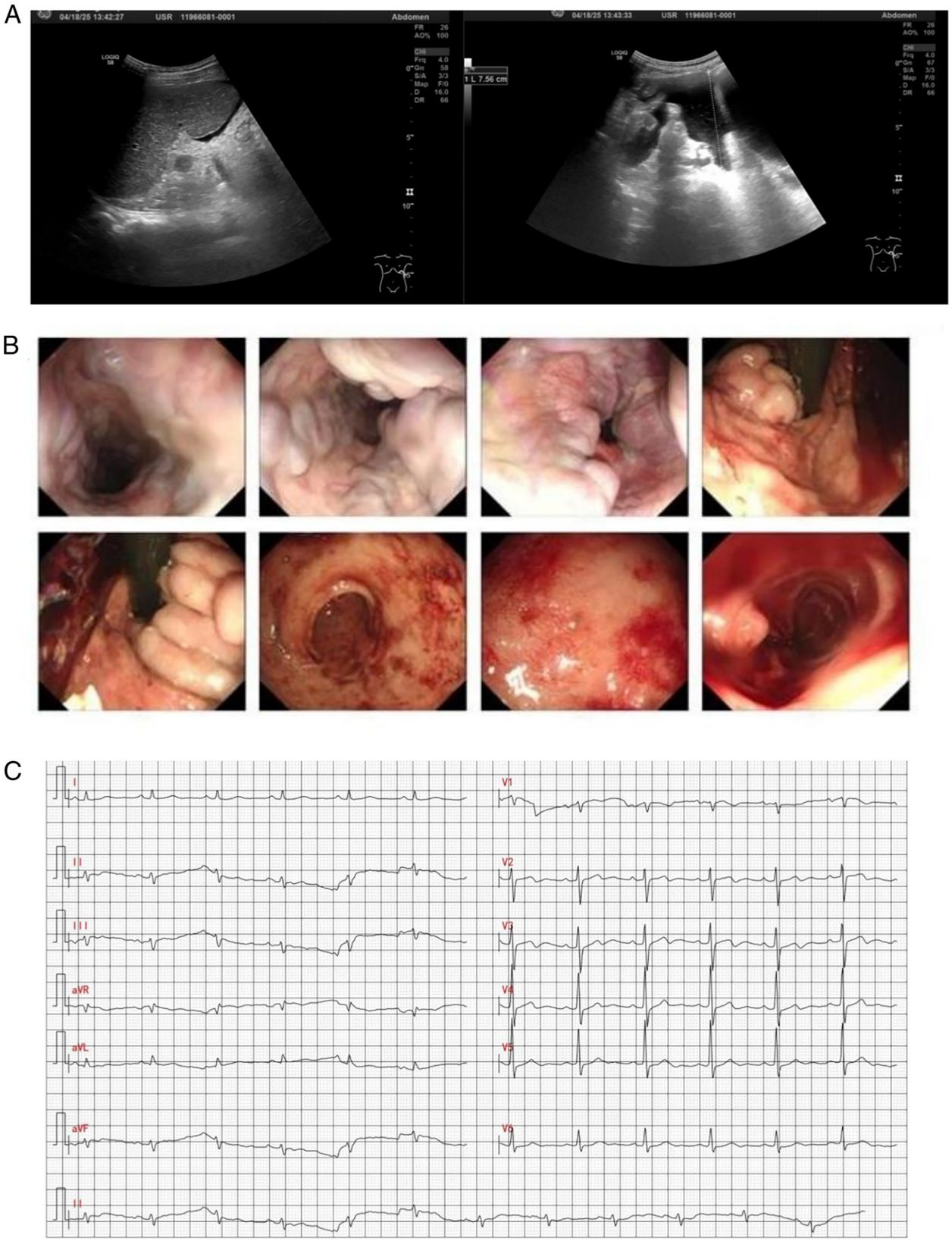


Figure 1. Ultrasonographic, gastroscopic and electrocardiographic findings. (A) Abdominal ultrasonography performed at Shuguang Hospital after admission, showing ascites with a depth of 75 mm. (B) Gastroscopic images showing esophagogastric varices and evidence of bleeding. (C) Electrocardiogram recorded during the period of CK elevation. aVR, augmented right arm lead; aVL, augmented left arm lead; aVF, augmented left leg lead.

by intermittent telephone contacts. Follow-up included assessment of muscle symptoms, review of available laboratory results including liver and renal function and CK, treatment and monitoring of decompensated cirrhosis and updates of the subsequent management of the periocular BCC. No recurrent CK elevation or further episodes of hepatic decompensation

Table I. Serial laboratory results during CK elevation and follow-up.

Day	CK, U/l	CK-MB, ng/ml	Myoglobin, ng/ml	ALT, U/l	AST, U/l	TBIL, μmol/l	ALB, g/l	Creatinine, μmol/l	BUN, mmol/l	K, mmol/l	Ca, mmol/l	Na, mmol/l
Day 1	150	21	525	20	33	27.7	29.7	75	10.4	3.71	1.93	143
Day 4 AM	3,291	2	1,029	53	227	25.3	37.9	82	9.5	3.59	2.12	142
Day 4 PM	6,002	5.68	7,634	NA	NA	NA	NA	NA	NA	NA	NA	NA
Day 5	8,766	6.72	4,199	NA	NA	NA	36.0	69	8.6	3.77	1.91	138
Day 6	11,944	17.26	3,628	100	508	22.6	37.0	68	9.07	NA	NA	NA
Day 8	1,573	29	1,073	120	346	22.7	36.9	80	8.1	3.56	2.18	139
Day 11	2,137	12	1,006	122	257	22.5	36.6	77	6.7	3.47	2.20	140
Day 15	532	24	1,097	87	103	16.2	33.1	75	7.6	2.37	2.07	143
Day 21	246	3	610	65	58	20.5	33.9	73	7.7	2.84	2.17	147
Day 30	305	3	626	52	62	22.6	NA	74	NA	4.84	2.30	141
Day 44	65	17.93	NA	30	42	25.4	40.0	71	6.37	4.41	2.27	144
Day 50	42	7	85	14	26	17.1	35.4	84	9.8	3.33	2.19	141
Day 57	20	1	59	14	23	16.2	39.2	84	12	3.89	2.36	139
Day 63	16	1	56	9	18	14.1	39.4	91	12.1	4.06	2.41	140
Day 70	17	1	55	10	22	13.5	38.1	89	13.5	4.21	2.33	138
Day 77	17	1	55	23	32	9.6	38.1	86	12.4	4.29	2.27	139
Day 86	20	12	59	32	41	16.0	43.6	89	10.3	3.79	2.40	137

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Ca, calcium; CK-MB, CK-myocardial band; K, potassium; Na, sodium; NA, not available; TBIL, total bilirubin.

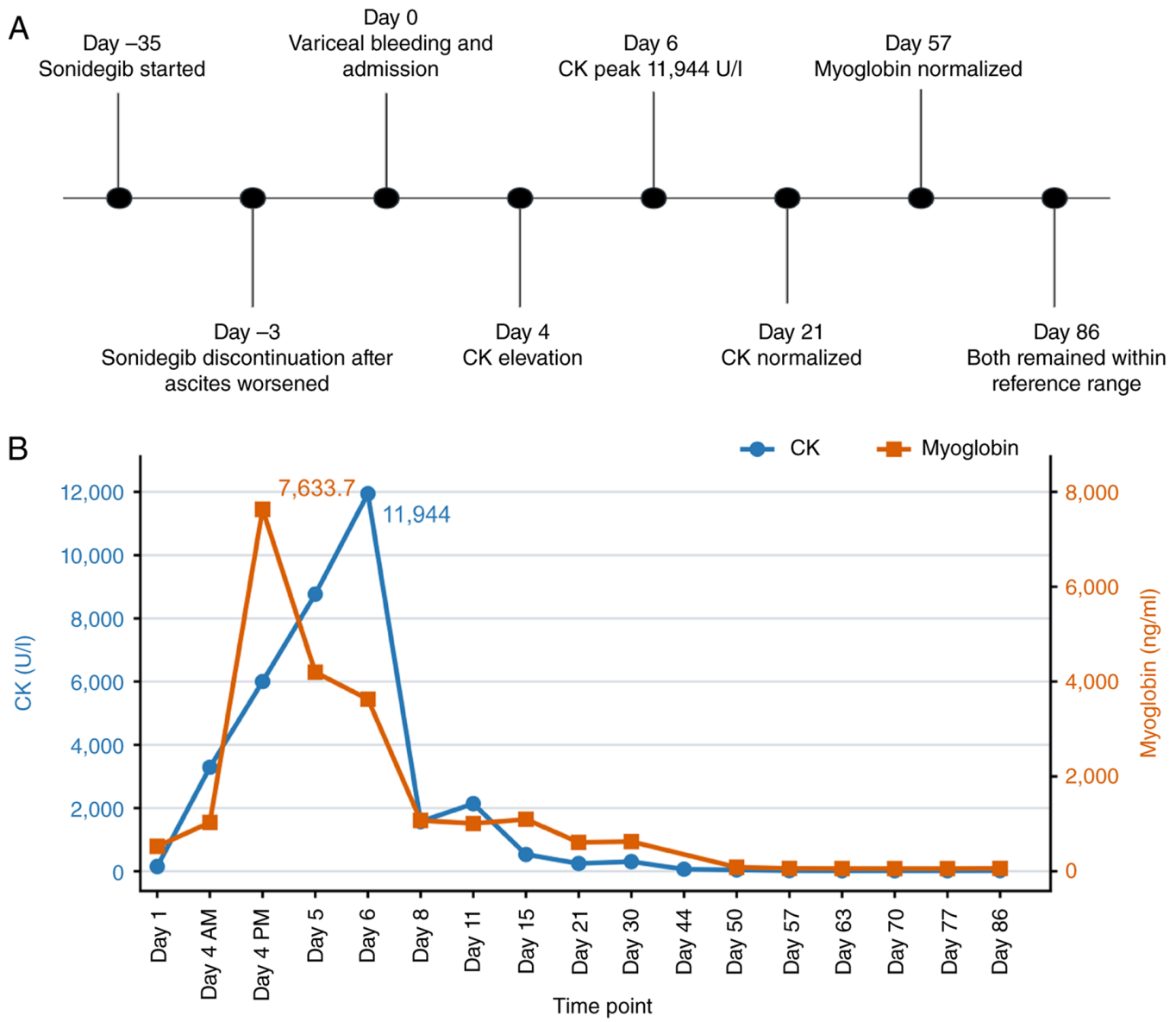


Figure 2. (A) Clinical timeline and (B) serial CK and myoglobin measurements. CK, creatinine kinase.

were reported during follow-up. After liver function was stabilized, the patient underwent excision of the periocular lesion in July 2026, at Shanghai Ninth People's Hospital affiliated to Shanghai JiaoTong University School of Medicine (Shanghai, China). The formal histopathological report, obtained and reviewed by the authors, confirmed nodular BCC measuring 1.0x0.8x0.4 cm, with invasion into the reticular dermis but no perineural or vascular invasion.

Written informed consent for treatment and publication was obtained from the patient, and all patient details were de-identified to protect anonymity.

Discussion

The present study describes a case of delayed CK elevation detected after sonidegib discontinuation in an elderly patient with decompensated cirrhosis and esophagogastric variceal hemorrhage. Sonidegib-associated CK elevation is a well-known adverse event (7,9), therefore, the novelty of the present study is the post-discontinuation timing and the coexistence of advanced liver disease and acute bleeding, which is rare in clinical trials. The Naranjo score of 4 supported the possible association between sonidegib and CK elevation in this case.

Sonidegib is a widely used systemic treatment medication for laBCC, with recent guidelines and studies having supported the role of hedgehog pathway inhibitors when local curative treatment is not applicable for the disease (20-22). However, the safety of sonidegib remains a major concern, as muscular adverse events and CK elevation are its common toxicities. In a phase I trial of sonidegib in patients with advanced solid tumors, including BCC, dose-limiting toxicities mainly included grade 3/4 CK elevation in 18% of patients at doses of ≥400 mg/day, indicating that CK elevation may be exposure-dependent (23). CK elevation was also observed in a dose-escalation study of sonidegib in Asian patients, contributing to the determination of the maximum tolerated dose and recommended safe dose (24). Pharmacovigilance studies

Table II. Assessment of potential causes and contributing factors for creatine kinase elevation.

Potential cause or contributing factor	Relevant findings in this patient	Assessment
Sonidegib-related muscle toxicity	The Naranjo assessment yielded a total score of 4: previous reports of sonidegib-associated muscle toxicity (+1); occurrence of CK elevation after drug exposure (+2); improvement after drug withdrawal (+1); no rechallenge (0); alternative causes that could not be completely excluded (-1); no placebo challenge (0); no measurement of serum sonidegib concentrations (0); no evaluable dose-response relationship (0); no documented previous similar reaction to sonidegib or a related drug (0); and objective confirmation by CK and myoglobin elevations (+1).	Temporally compatible and biologically plausible, while the Naranjo score indicated a possible adverse drug reaction.
Acute bleeding and transient hypoperfusion	Acute variceal bleeding occurred before admission. The lowest blood pressure was 109/75 mmHg, no vasopressor was used and lactate level was 1.20 mmol/l on day 4 after fluid resuscitation.	A plausible contributing factor. Transient hypoperfusion before admission could not be excluded, although the available data did not support sustained shock or severe muscle injury.
Critical disease-associated myopathy	The patient was not mechanically ventilated, did not receive neuromuscular blocking agents and had preserved muscle strength without tenderness.	Less likely.
Electrolyte abnormality	Mild hypocalcemia was present on days 1 and 4. Potassium was normal when CK elevation was detected, while hypokalemia developed on days 15 and 21 after the CK peak.	Electrolyte abnormality might influence susceptibility or recovery, but the timing did not support it as the initiating cause.
Occult infection	No fever, leukocytosis or focal infection was found. C-reactive protein and serum amyloid A levels were elevated early and subsequently normalized, and no definite infectious focus was identified.	No clinical evidence of infection was found, although an occult infectious process could not be completely excluded.
Myocardial injury	Serial troponin I levels remained within the reference range and electrocardiography showed no acute ischemic changes despite CK-MB elevation.	Acute myocardial injury was not supported.
Trauma, exertion, seizure or muscle compression	The patient denied trauma and strenuous exercise, and no seizure or prolonged immobilization was found.	Unlikely based on the available history.
Cirrhosis and possible sarcopenia	The patient was elderly and had decompensated cirrhosis with a body mass index of 19.5 kg/m^2; however, no formal assessment of muscle mass, muscle strength or physical performance was performed.	A potential susceptibility factor.
Concomitant medications and drug interactions	Tenofovir alafenamide and entecavir had been used long term. No statin or other myotoxic medication was identified. Acute bleeding treatment included octreotide and lansoprazole.	No clear alternative drug trigger or cytochrome P450 3A4 interaction was identified, although residual confounding remained possible.

CK-MB, CK-myocardial band.

have further supported the association between sonidegib and CK elevation (25,26), and a systematic review reported a pooled CK elevation rate of ~19% among sonidegib-treated patients (27). The mechanism of sonidegib-associated CK elevation has not been fully understood and is likely associated with muscle contraction and muscle fiber twitching in human skeletal muscle cells by inducing changes in normal calcium influx caused by SMO inhibitors (28). Although the safety of sonidegib treatment in patients with decompensated cirrhosis remains poorly characterized, a recent review on hedgehog inhibitors for advanced BCC underscored the need for regular laboratory monitoring, including analysis of muscle enzymes, especially in patients with comorbidities or impaired drug metabolism (29).

Several factors may contribute to the delayed CK elevation in the present patient. Sonidegib has an ~28-day terminal half-life, meaning that exposure may persist for weeks after discontinuation (30). However, pharmacokinetic information did not identify a clinically meaningful increase in sonidegib exposure in subjects with mild, moderate or severe hepatic impairment compared with subjects with normal hepatic function (31). As serum sonidegib concentration was not measured in the present patient, drug overexposure could not be determined. Therefore, decompensated cirrhosis and acute bleeding could not solely be assumed to have caused drug accumulation. Decompensated cirrhosis and acute bleeding may have contributed to altered pharmacokinetics or increased susceptibility to toxicity; however, direct evidence is unavailable. Alternative causes of muscle injury, including acute blood loss and transient hypovolemia, were also considered. Factors against a sustained shock as the explanation for CK elevation, were the fact that the lowest blood pressure was 109/75 mmHg, no vasopressor was used and the lactate level was 1.20 mmol/l after fluid resuscitation; however, an earlier transient perfusion deficit could not be excluded. Critical disease-associated myopathy was less likely as the patient was not ventilated or treated with neuromuscular blockers and retained normal strength. No fever, leukocytosis or focal infection was documented, although elevated inflammatory markers meant an occult infection could not be fully excluded. An older age and decompensated cirrhosis might have increased the vulnerability of the patient. The use of chronic antiviral therapy and treatment for acute bleeding were reviewed, but no alternative myotoxic drug or strong cytochrome P450 3A4 interaction was found. These assessments are summarized in Table II.

The present case has several clinical implications. First, for patients with hepatic impairment receiving sonidegib, a practical risk assessment should include analysis of baseline CK levels, renal function, electrolytes, muscle-related symptoms and concomitant myotoxic drugs. CK level and renal function should be monitored closely during treatment and after drug discontinuation when muscle symptoms, acute bleeding, infection, hemodynamic instability or electrolyte disturbances occur. Second, physicians may consider fractionating CK into its isoenzymes, such as CK-MB, creatine kinase-muscle type and creatine kinase-brain type when applicable, which can help distinguish between cardiac, skeletal muscle and brain-derived CK elevations, and provide more precise information on the source of muscle injury. Third, clinicians should individualize treatment decisions in patients with decompensated cirrhosis, considering closer surveillance, temporary interruption or alternative therapy in high-risk patients. Limitations of the present report included it being a single case, the absence of serum sonidegib measurement, the lack of muscle biopsy and CK isoenzyme fractionation, the lack of an assessment of sarcopenia, and the inability to completely exclude alternative causes, including transient hypoperfusion and occult inflammation. The initial BCC diagnosis lacked histopathology reports, formal pathological staging and a standardized response assessment.

In conclusion, a possible association was observed between sonidegib exposure and delayed CK elevation after drug discontinuation in a patient with decompensated cirrhosis and acute variceal hemorrhage. Prolonged drug half-life, impaired hepatic metabolic reserve and acute hypovolemia after gastrointestinal bleeding may contribute to sustained systemic exposure and delayed toxicity, but drug accumulation was not demonstrated and competing contributors remain. CK level, renal function, electrolytes, muscle symptoms and interacting medications should be monitored during and after sonidegib therapy in patients at high risk.

Acknowledgements

Not applicable.

Funding

The present study was supported in part by the Training Program for High-caliber Talents of Clinical Research at Affiliated Hospitals of SHUTCM (grant no. 2025LCRC01), the Traditional Chinese Medicine Research Project of the Shanghai Municipal Health Commission (grant no. 2024QN006) and the National Administration of Traditional Chinese Medicine (grant no. zyyzdxk-2023060).

Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

BC, BS and YHZ designed the present study. BC and YXZ performed the data collection and analysis. BS and YHZ advised on patient treatment. BC drafted the manuscript. SZ compiled and verified all available serial laboratory and follow-up data, contributed to the analysis of additional data, and revised the manuscript. BC and SZ confirm the authenticity of all the raw data. BS and YZ revised the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The reporting of this study conforms to Case Report guidelines and the principles of the Declaration of Helsinki.

Patient consent for publication

Written informed consent for treatment and publication was obtained from the patient, and all patient details were de-identified to protect anonymity.

Competing interests

The authors declare that they have no competing interests.

References

1. Schmults CD, Blitzblau R, Aasi SZ, Alam M, Amini A, Bibee K, Bordeaux J, Chen PL, Contreras CM, DiMaio D, *et al*: Basal cell skin cancer, version 2.2024, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 21: 1181-1203, 2023.
2. Rogers HW, Weinstock MA, Feldman SR and Coldiron BM: Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the U.S. Population, 2012. JAMA Dermatol 151: 1081-1086, 2015.
3. Hu W, Fang L, Ni R, Zhang H and Pan G: Changing trends in the disease burden of non-melanoma skin cancer globally from 1990 to 2019 and its predicted level in 25 years. BMC Cancer 22: 836, 2022.
4. Zhou L, Zhong Y, Han L, Xie Y and Wan M: Global, regional, and national trends in the burden of melanoma and non-melanoma skin cancer: Insights from the global burden of disease study 1990-2021. Sci Rep 15: 5996, 2025.
5. Patel S, Armbruster H, Pardo G, Archambeau B, Kim NH, Jeter J, Wu R, Kendra K, Contreras CM, Spaccarelli N, *et al*: Hedgehog pathway inhibitors for locally advanced and metastatic basal cell carcinoma: A real-world single-center retrospective review. PLoS One 19: e0297531, 2024.
6. Villani A, Fabbrocini G, Costa C and Scalvenzi M: Sonidegib: Safety and efficacy in treatment of advanced basal cell carcinoma. Dermatol Ther (Heidelb) 10: 401-412, 2020.
7. Migden MR, Guminski A, Gutzmer R, Dirix L, Lewis KD, Combemale P, Herd RM, Kudchadkar R, Trefzer U, Gogov S, *et al*: Treatment with two different doses of sonidegib in patients with locally advanced or metastatic basal cell carcinoma (BOLT): A multicentre, randomised, double-blind phase 2 trial. Lancet Oncol 16: 716-728, 2015.
8. Dummer R, Lear JT, Guminski A, Leow LJ, Squittieri N and Migden M: Efficacy of sonidegib in histologic subtypes of advanced basal cell carcinoma: Results from the final analysis of the randomized phase 2 basal cell carcinoma outcomes with LDE225 treatment (BOLT) trial at 42 months. J Am Acad Dermatol 84: 1162-1164, 2021.
9. Dummer R, Guminksi A, Gutzmer R, Lear JT, Lewis KD, Chang ALS, Combemale P, Dirix L, Kaatz M, Kudchadkar R, *et al*: Long-term efficacy and safety of sonidegib in patients with advanced basal cell carcinoma: 42-month analysis of the phase II randomized, double-blind BOLT study. Br J Dermatol 182: 1369-1378, 2020.
10. Villani A, Fabbrocini G, Micali G, Fornaro L, Potestio L and Scalvenzi M: The efficacy of sonidegib in treating locally advanced basal cell carcinoma involving the periocular area. Dermatol Ther (Heidelb) 13: 2121-2126, 2023.
11. Nguyen NM and Cho J: Hedgehog pathway inhibitors as targeted cancer therapy and strategies to overcome drug resistance. Int J Mol Sci 23: 1733, 2022.
12. European Medicines Agency: Odomzo 200 mg hard capsules: Summary of product characteristics. https://ec.europa.eu/health/documents/community-register/2015/20150814132561/anx_132561_en.pdf.
13. Burness CB and Scott LJ: Sonidegib: A review in locally advanced basal cell carcinoma. Target Oncol 11: 239-246, 2016.
14. Teschke R and Danan G: Drug-induced liver injury: Is chronic liver disease a risk factor and a clinical issue? Expert Opin Drug Metab Toxicol 13: 425-438, 2017.
15. Thomson MJ, Lok ASF and Tapper EB: Appropriate and potentially inappropriate medication use in decompensated cirrhosis. Hepatology 73: 2429-2440, 2021.
16. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H and Riley D; CARE Group: The CARE guidelines: Consensus-based clinical case reporting guideline development. Headache 53: 1541-1547, 2013.
17. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC and Williams R: Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 60: 646-649, 1973.
18. Kim WR, Mannalithara A, Heimbach JK, Kamath PS, Asrani SK, Biggins SW, Wood NL, Gentry SE and Kwong AJ: MELD 3.0: The model for end-stage liver disease updated for the modern era. Gastroenterology 161: 1887-1895.e4, 2021.
19. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C and Greenblatt DJ: A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 30: 239-245, 1981.
20. Massella Patsea AAL, Verkouteren BJA and Mosterd K: Transforming outcomes in advanced basal cell carcinoma: The evolving role of systemic therapy. Am J Clin Dermatol 27: 765-777, 2026.
21. Peris K, Fargnoli MC, Kaufmann R, Arenberger P, Bastholt L, Seguin NB, Bataille V, Brochez L, Del Marmol V, Dummer R, *et al*: European consensus-based interdisciplinary guideline for diagnosis and treatment of basal cell carcinoma-update 2023. Eur J Cancer 192: 113254, 2023.
22. Moreno-Arrones OM, Béa-Ardebol S, Mayo-Martinez F, Pérez-Pastor G, Torres-Navarro I, Bonfill-Ortí M, Deza G, Ruiz-Salas V, Masferrer E, Feal C, *et al*: Sonidegib as a locally advanced basal cell carcinoma therapy in real-life clinical setting: A national multicentre study. Actas Dermosifiliogr 114: 565-571, 2023 (In English, Spanish).
23. Rodon J, Tawbi HA, Thomas AL, Stoller RG, Turtschi CP, Baselga J, Sarantopoulos J, Mahalingam D, Shou Y, Moles MA, *et al*: A phase I, multicenter, open-label, first-in-human, dose-escalation study of the oral smoothened inhibitor sonidegib (LDE225) in patients with advanced solid tumors. Clin Cancer Res 20: 1900-1909, 2014.
24. Minami H, Ando Y, Ma BBY, Hsiang Lee J, Momota H, Fujiwara Y, Li L, Fukino K, Ito K, Tajima T, *et al*: Phase I, multicenter, open-label, dose-escalation study of sonidegib in Asian patients with advanced solid tumors. Cancer Sci 107: 1477-1483, 2016.
25. Zhao K, Li Q, Qin M, Xiao S, Li J and Liu J: Real-world safety profile of sonidegib: A disproportionality analysis based on the FDA adverse event reporting system. Front Oncol 15: 1642867, 2025.
26. Qiu ZQ, Ye SY, Zhang RD, Cao M and Wang Y: Clinical prioritization of adverse events associated with hedgehog pathway inhibitors in basal cell carcinoma patients: Insights from the FDA adverse event reporting (FAERS) system. J Cutan Med Surg: 12034754261427496, 2026 (Epub ahead of print).
27. Nguyen A, Xie P, Litvinov IV and Lefrancois P: Efficacy and safety of sonic hedgehog inhibitors in basal cell carcinomas: An updated systematic review and meta-analysis (2009-2022). Am J Clin Dermatol 24: 359-374, 2023.
28. Casey D, Demko S, Shord S, Zhao H, Chen H, He K, Putman A, Helms W, Keegan P and Pazdur R: FDA approval summary: sonidegib for locally advanced basal cell carcinoma. Clin Cancer Res 23: 2377-2381, 2017.
29. Burshtein J, Shah M, Zakria D, Dinehart S, Lewin J, Monks G, Mortazie M, Trotter S, Schlesinger T, Lebwohl M and Rigel D: Efficacy and safety of hedgehog inhibitors for advanced basal cell carcinoma: An expert consensus panel. J Drugs Dermatol 24: 465-471, 2025.
30. Brancaccio G, Pea F, Moscarella E and Argenziano G: Sonidegib for the treatment of advanced basal cell carcinoma. Front Oncol 10: 582866, 2020.
31. Horsmans Y, Zhou J, Liudmila M, Golor G, Shibolet O, Quinlan M, Emotte C, Boss H, Castro H, Sellami D and Preston RA: Effects of mild to severe hepatic impairment on the pharmacokinetics of sonidegib: A multicenter, open-label, parallel-group study. Clin Pharmacokinet 57: 345-354, 2018.