Transarterial infusion chemotherapy for severe hepatic dysfunction and poor performance status in diffuse hepatic metastasis: A case report

XIAO-CHUN CHEN[1], XIAN-QIN LI[1], YI LIU[1], XU ZHANG[2], CHUAN LIN[1] and ZHI-PING YUAN[1]

[1]Department of Oncology, The First People's Hospital of Yibin, Yibin, Sichuan 644000, P.R. China;
[2]Department of Pathology, The First People's Hospital of Yibin, Yibin, Sichuan 644000, P.R. China

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Abstract. Severe hepatic dysfunction and high performance status (PS) scores in patients with cancer often indicate a poor prognosis, with an estimated survival time of <3 months, making them typically candidates for palliative care. The current study presents the case of a 66-year-old male patient with prostate neuroendocrine carcinoma and diffuse hepatic metastasis, accompanied by severe hepatic dysfunction (Child-Pugh C10) and poor PS (Eastern Cooperative Oncology Group PS3). The patient was treated with transarterial infusion chemotherapy (TAI) using a reduced-dose etoposide and cisplatin regimen. After six cycles, significant tumor regression occurred. According to Response Evaluation Criteria in Solid Tumors 1.1 criteria, the response was a partial response. The patient finally succumbed, achieving a progression-free survival time of 11.05 months and an overall survival time of 18.87 months. This case indicates that, for patients with sensitive and aggressive tumors (such as prostate neuroendocrine carcinoma) who have hepatic metastasis-induced severe hepatic dysfunction and poor PS, local reduced-dose TAI therapy may be a viable option to overcome traditional treatment contraindications.

Introduction

The liver is one of the most common sites for cancer metastasis. At initial diagnosis, solid tumors show an ~6.46% incidence of liver metastasis, accounting for 37.96% of all metastatic cases, with a median survival time of 4 months (1). According to the European Neuroendocrine Tumor Society guidelines (2), hepatic metastases are categorized into three types: Simple pattern, complex pattern and diffuse pattern. The diffuse pattern is characterized by widespread metastases occupying 60-70% of the liver.

Patients with a high hepatic metastasis burden often have poor performance and liver function scores (3,4). Studies show that Child-Pugh (5) class C patients receiving standard liver cirrhosis treatment have a mortality rate three times higher than class B patients (6). British Society of Gastroenterology guidelines recommend best supportive care for patients with Child-Pugh class C or Eastern Cooperative Oncology Group (ECOG) performance status (PS)>2 (7). In the present study, a patient with castration-resistant prostate cancer and diffuse hepatic metastasis, of ECOG PS3 score and with Child-Pugh class C liver function, was treated at the Department of Oncology, The First People's Hospital of Yibin (Yibin, China). After careful consideration, TAI was selected to explore its potential for prolonging survival and improving quality of life in this high-risk population.

Case report

Medical history. A 66-year-old man was diagnosed with acinar adenocarcinoma of the prostate at the Department of Urology, The First People's Hospital of Yibin, in June 2021. The patient was started on androgen-deprivation therapy in the Outpatient Clinic administered as 3.75 mg leuprorelin by subcutaneous injection every 4 weeks plus 50 mg bicalutamide orally once daily. After bone metastases were documented in January 2022, bicalutamide was replaced with 1,000 mg abiraterone orally once daily together with 5 mg prednisone twice daily. Progressive bone disease prompted palliative radiotherapy (30 Gy in 10 fractions over 2 weeks) administered at the Department of Oncology, Affiliated Hospital of Southwest Medical University, Luzhou, China) in August 2022. Widespread progression involving multiple liver and lung metastases was diagnosed in December 2022; 120 mg docetaxel was intravenously administered 3 days later (on day 1) and repeated 25 days later in January 2023, but the disease continued to advance.

In February 2023, the patient visited the Department of Oncology, The First People's Hospital of Yibin due to diffuse liver metastasis. Magnetic resonance imaging showed diffuse liver

Correspondence to: Professor Zhi-Ping Yuan, Department of Oncology, The First People's Hospital of Yibin, 65 Wenxing Street, Cuiping, Yibin, Sichuan 644000, P.R. China
E-mail: yuanzhip@126.com

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Table I. Primary antibodies used.

Antibody	Clone	Catalog no.	Dilution	Supplier
Pan-CK	AE1/AE3	CCM-0960	1:50	Celnovte Biotechnology Co., Ltd.
p504s	C7H4	CAM-0201	1:200	Celnovte Biotechnology Co., Ltd.
PSA	C2C12	CPM-0404	1:200	Celnovte Biotechnology Co., Ltd.
CgA	C1E8	CCM-0852	1:200	Celnovte Biotechnology Co., Ltd.
CD56	C5A2	CCM-0662	1:200	Celnovte Biotechnology Co., Ltd.
Syn	C9D11	CSM-0250	1:200	Celnovte Biotechnology Co., Ltd.
Hepatocyte	MX119	MAB-1034	Ready-to-use	Fuzhou Maixin Biotech Co., Ltd.
GS	C6E12	CGM-0191	Ready-to-use	Celnovte Biotechnology Co., Ltd.
Glypican-3	1C12	CCM-0200	Ready-to-use	Celnovte Biotechnology Co., Ltd.
Ki-67	ARC-5050-01	C1CR-0034	1:200	Celnovte Biotechnology Co., Ltd.

PSA, prostate-specific antigen; Pan-CK, pancytokeratin (AE1/AE3 cocktail); p504s, α-methylacyl-CoA racemase (AMACR); CgA, chromogranin A; CD56, neural cell adhesion molecule (NCAM); Syn, synaptophysin; Hepatocyte, hepatocyte paraffin 1 (Hep Par-1); GS, glutamine synthetase; Glypican-3, glypican-3 (GPC3); Ki-67, proliferation marker Ki-67.

metastasis (Fig. 1A) and retroperitoneal lymph node metastasis (Fig. 1B), and computed tomography showed lung metastasis (Fig. 1C). Tumor marker levels were elevated as follows: Neuron-specific enolase (NSE), 370 ng/ml (normal reference, ≤20.77 ng/ml); carcinoembryonic antigen (CEA), 458.62 ng/ml (normal reference, <5.0 ng/ml); carbohydrate antigen 19-9 (CA19-9), 394.09 U/ml (normal reference, <36 U/ml); total tPSA, 19.60 ng/ml (normal reference, <4 ng/ml); free PSA, 11.89 ng/ml (normal reference, <1 ng/ml). The α-fetoprotein level was 2.8 ng/ml (normal reference, <8.3 ng/ml) and the squamous-cell carcinoma antigen level was 1.1 ng/ml (reference, <1.5 ng/ml), which were within normal limits. Liver function assessment showed Child-Pugh class C10 with the following results: Total bilirubin, 49.3 μmol/l (normal reference, <21 μmol/l); albumin, 22.6 g/l (normal reference, <35 g/l); prothrombin time, 15.9 sec (normal reference, 10-14 sec); moderate ascites; and no hepatic encephalopathy. Liver biopsy showed diffuse small- to medium-sized tumor cells without definite glandular differentiation and significant fibrotic reaction (Fig. 1D). Immunohistochemistry was performed on 4-μm formalin-fixed, paraffin-embedded sections. Tissue blocks were fixed in 10% neutral-buffered formalin at room temperature for 24 h, processed through graded alcohols and xylene, and embedded in paraffin (Leica Paraplast Plus; Leica Biosystems). After dewaxing and rehydration, antigen retrieval was carried out in 0.01 M citrate buffer (pH 6.0) at 95˚C for 20 min. Endogenous peroxidase was quenched with 3% H_2O_2 for 10 min at room temperature, followed by blocking with 5% normal goat serum (cat. no. AR0009; Wuhan Boster Biological Technology, Ltd.) for 30 min at room temperature. Primary antibodies (Table I) were applied overnight at 4˚C. Sections were then incubated with HRP-conjugated secondary antibodies (goat anti-mouse/rabbit; cat. no. PV-6000; ready-to-use; Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.) for 30 min at room temperature. Color was developed with DAB (cat. no. ZLI-9018; Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.) and counterstained with hematoxylin at room temperature for 2-3 min. Slides were examined and images were captured with an Olympus BX53 light microscope (Olympus Corporation); representative images were acquired at x400 magnification. The results were as follows: Pan cytokeratin(+), p504s(weak+), PSA(-), chromogranin A (CgA)(-), CD56(-), synaptophysin (Syn)(-), hepatocytes(-), glutamine synthetase(-), glypican-3(-) and Ki-67(+, 50%) (data not shown; all results related to immunohistochemical findings described in this manuscript are based on official pathology reports, not retrievable image files). The pathological diagnosis was of a poorly differentiated carcinoma. A subsequent departmental multidisciplinary-team (MDT) review, integrating morphology, immunoprofile and treatment history, concluded that a diagnosis of treatment-related neuroendocrine prostate carcinoma with mixed adenocarcinoma-neuroendocrine features (2022 WHO Classification of Neuroendocrine Neoplasms) (8), pending RB transcriptional corepressor 1 (RB1)/tumor protein p53 (TP53) confirmation. The patient declined the collection of additional tissue for next-generation sequencing. In addition, the MDT recommended active therapy, given the recognized chemosensitivity of small-cell neuroendocrine carcinoma, absence of variceal bleeding or hepatic encephalopathy, and the patient's wish for treatment. Initial management consisted of 10 g human albumin (i.v.) once daily, 200 mg magnesium isoglycyrrhizinate (i.v.) once daily for hepatoprotection, 250 ml compound amino-acid injection (14AA-SF) (21.2 g) (i.v.) once daily combined with 1,000 ml 5% glucose (50 g) (i.v.) once daily for nutritional support; these measures failed to improve the patient's condition and repeat assessment confirmed a persistent Child-Pugh score of C10. Consequently, as the diffuse tumor burden rendered systemic intravenous chemotherapy likely to deliver sub-therapeutic hepatic drug concentrations and since the high risk of hepatic failure precluded both standard-dose systemic chemotherapy and transcatheter arterial chemoembolization (TACE), neither modality was offered. Accordingly, TAI was initiated on day 17 of admission (February 2023). The first cycle, delivered under local anaesthesia, comprised 120 mg etoposide plus 400 mg carboplatin on day 1 (80% of standard protocol), and five additional identical cycles were subsequently scheduled. On the night after surgery, the patient experienced hypoxemia

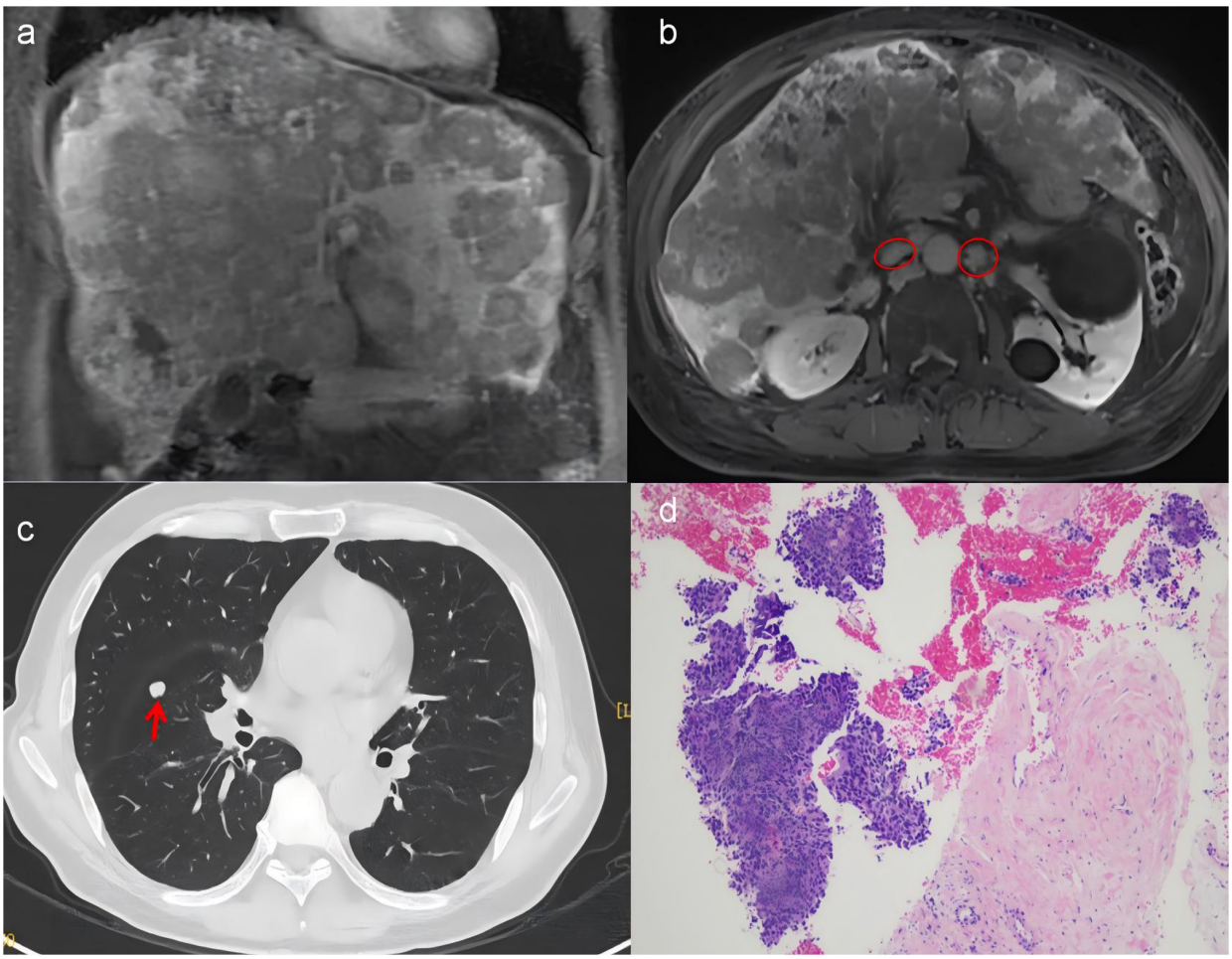

Figure 1. Diffuse hepatic metastasis in the patient, suggestive of prostate neuroendocrine carcinoma. (A) Coronal T1-weighted MR image showing diffuse nodular metastases in the liver. (B) Computed tomography pulmonary window image showing a metastatic lesion in the right middle lung (red arrow). (C) Axial T1-weighted MR image showing a tumor protruding from the liver surface, with retroperitoneal metastases in the red circle. (D) Hematoxylin and eosin-stained histopathological image (x40 magnification). MR, magnetic resonance.

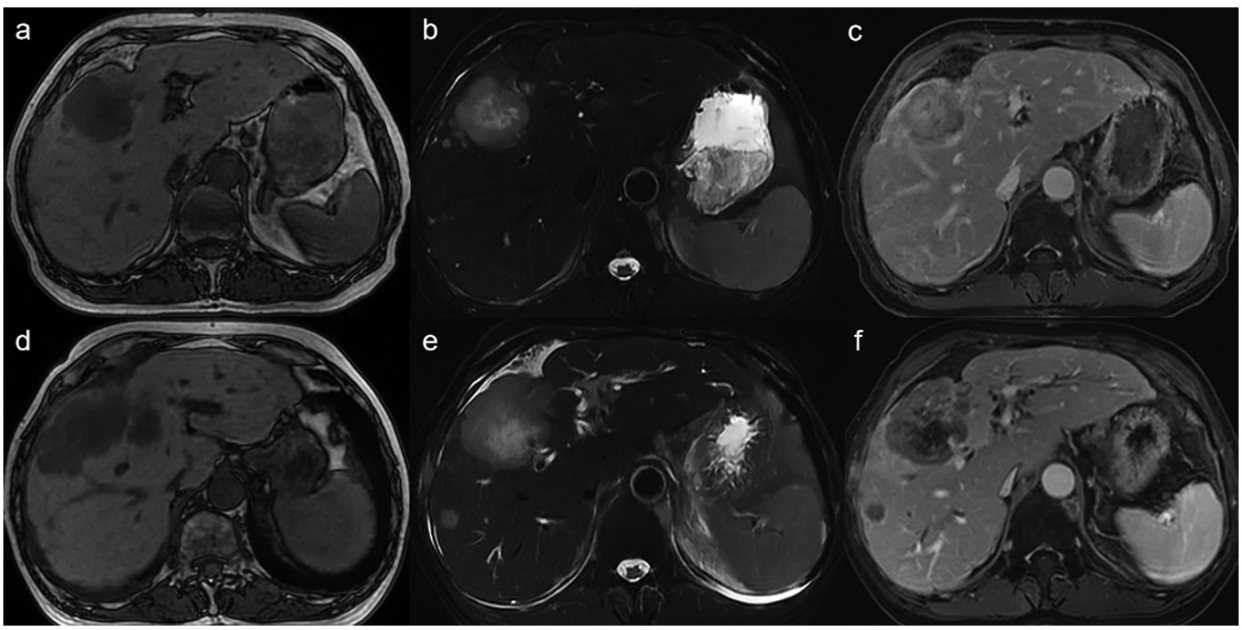

Figure 2. Comparison of efficacy in a patient with prostate neuroendocrine carcinoma and diffuse hepatic metastases. (A-C) Pretreatment: (A) Non-contrast T1-weighted, (B) non-contrast T2-weighted and (C) contrast-enhanced T1-weighted magnetic resonance images showing innumerable liver metastases. (D-F) Post-treatment: Corresponding (D) Non-contrast T1-weighted, (E) non-contrast T2-weighted and (F) contrast-enhanced T1-weighted sequences demonstrating >30% reduction in hepatic tumor burden consistent with a partial response.

(oxygen saturation of ~90%) and hypotension (86/54 mmHg); oxygen supplementation and intravenous saline promptly restored cardiopulmonary stability. On the second postoperative day, the patient experienced acute hepatic injury [total bilirubin, 70.3 μmol/l; aspartate aminotransferase, 206 U/l (reference range, 15-35 U/l)] that resolved after hepatoprotective therapy with 200 mg magnesium isoglycyrrhizinate (i.v.) once daily plus 465 mg polyene phosphatidylcholin (i.v.) once daily. The patient completed six cycles of the same TAI regimen and remained on anti-androgen maintenance consisting of 1,000 mg abiraterone orally once daily plus 3.75 mg leuprorelin subcutaneously every 4 weeks.

After treatment, efficacy was evaluated according to the Response Evaluation Criteria in Solid Tumors version 1.1. Baseline MRI had demonstrated innumerable T1-hypointense/T2-hyperintense hepatic nodules with peripheral rim enhancement on arterial-phase T1-weighted images (Fig. 2A-C). Post-therapy MRI showed >30% reduction in overall hepatic tumour burden, with smaller and less conspicuous nodules and markedly diminished contrast enhancement (Fig. 2D-F), consistent with a partial response. Concurrently, the ECOG PS score decreased to 1, liver function recovered to Child-Pugh A5 and the patient regained full self-care ability. Subsequently, after the tumor progressed again, with follow-up until September 2024, the patient died at home. The progression-free survival time from TAI was 11.05 months and the overall survival time was 18.87 months.

Discussion

The present study reports a case of castration-resistant prostate cancer with diffuse hepatic metastasis, severe hepatic dysfunction (Child-Pugh class C10) and poor PS (ECOG PS 3). The patient showed significant improvement after TAI with the EC regimen.

Hepatic metastasis in prostate cancer indicates a poor prognosis. A previous study showed that 20-30% of patients with metastatic castration-resistant prostate cancer develop hepatic metastasis during treatment, indicating high aggressiveness (9). Especially in patients with rapid progression and elevated NSE, neuroendocrine transformation should be suspected. Neuroendocrine prostate cancer (NEPC) has an incidence of 11-17% (10,11); it is characterized by decreased androgen receptor and PSA expression, and increased NSE, CEA and CA19-9 levels (12-14). Immunohistochemistry markers such as CgA, CD56 and Syn are usually positive (15). Mixed pathology is reported in 91.9% of cases (16). In the present case, immunohistochemistry showed negative expression of CgA, CD56, Syn and PSA, with diffuse small- to medium-sized cancer cells, and significantly elevated NSE, CEA and CA19-9 levels (17). The rapid progression and significant therapeutic response after NEPC-directed treatment were consistent with previous studies. Considering the concurrent PSA elevation, the presence of prostatic acinar adenocarcinoma components could not be ruled out. Although CgA, Syn and CD56 results were all negative, the composite evidence of i) treatment-emergent disease following prolonged androgen deprivation therapy and novel hormonal therapy, ii) rapid visceral spread, iii) loss of PSA expression accompanied by markedly elevated NSE, CEA and CA19-9 levels, iv) a Ki-67 index of 50%, and v) an unmistakable response to platinum-etoposide, strongly supports the diagnosis of treatment-related neuroendocrine prostate carcinoma with atypical marker expression or a mixed adenocarcinoma-neuroendocrine phenotype. The patient declined genetic testing, leaving the absence of RB1/TP53 evidence as an unresolved limitation.

Although Child-Pugh class C hepatic dysfunction and PS 3-4 are often considered treatment contraindications, some studies suggest that selective treatment can still be considered. One study showed that patients with Child-Pugh class C who received TACE had a median survival time of 7.1 months (18). Similarly, two studies on patients with small cell lung cancer and PS 3-4 showed that chemotherapy could significantly prolong survival time (19,20). These findings suggest that selective patients with poor PS time or severe hepatic dysfunction may still benefit from treatment and have their survival time extended.

In conclusion, for highly aggressive and treatment-sensitive tumors such as prostate neuroendocrine carcinoma, even in the presence of diffuse hepatic metastasis-induced poor PS and severe hepatic dysfunction, attempting low-dose local drug therapy can be a viable option. Otherwise, patients may succumb to rapid tumor progression, hepatic failure or other complications in a short period of time.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XCC was responsible for study conception, clinical data acquisition and interpretation, and drafting of the manuscript. XQL participated in follow-up data collection and analysis, literature review and manuscript revision. YL contributed to clinical data interpretation and critically revised the manuscript. XZ performed histopathological evaluation of biopsy specimens and revised the manuscript. CL performed all trans-arterial infusion procedures. ZPY analyzed and interpreted MRI/computed tomography images, and critically revised the manuscript. XCC and ZPY confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Ethics approval was granted from the Ethics Committee of the First People's Hospital of Yibin [approval no. 2025 (12)]. Informed written consent was obtained from the patient to participate in this study.

Patient consent for publication

Written informed consent for publication of this case report and any accompanying images was obtained from the patient after completion of trans-arterial infusion therapy. Following the patient's death, verbal confirmation of consent was obtained from the patient's son via telephone.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, AI tools were used to improve the readability and language of the manuscript or to generate images, and subsequently, the authors revised and edited the content produced by the AI tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

References

1. Wang S, Feng Y, Swinnen J, Oyen R, Li Y and Ni Y: Incidence and prognosis of liver metastasis at diagnosis: A pan-cancer population-based study. Am J Cancer Res 10: 1477-1517, 2020.
2. Pavel M, Baudin E, Couvelard A, Krenning E, Öberg K, Steinmüller T, Anlauf M, Wiedenmann B and Salazar R; Barcelona Consensus Conference participant: ENETS consensus guidelines for the management of patients with liver and other distant metastases from neuroendocrine neoplasms of foregut, midgut, hindgut, and unknown primary. Neuroendocrinology 95: 157-176, 2012.
3. Hsu CY, Lee YH, Hsia CY, Huang YH, Su CW, Lin HC, Lee RC, Chiou YY, Lee FY and Huo TI: Performance status in patients with hepatocellular carcinoma: Determinants, prognostic impact, and ability to improve the Barcelona clinic liver cancer system. Hepatology 57: 112-119, 2013.
4. Culine S, Kramar A, Saghatchian M, Bugat R, Lesimple T, Lortholary A, Merrouche Y, Laplanche A and Fizazi K; French Study Group on Carcinomas of Unknown Primary: Development and validation of a prognostic model to predict the length of survival in patients with carcinomas of an unknown primary site. J Clin Oncol 20: 4679-4683, 2002.
5. Pugh RNH, 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.
6. Conejo I, Guardascione MA, Tandon P, Cachero A, Castellote J, Abraldes JG, Amitrano L, Genescà J and Augustin S: Multicenter external validation of risk stratification criteria for patients with variceal bleeding. Clin Gastroenterol Hepatol 16: 132-139.e8, 2018.
7. Suddle A, Reeves H, Hubner R, Marshall A, Rowe I, Tiniakos D, Hubscher S, Callaway M, Sharma D, See TC, *et al*: British society of gastroenterology guidelines for the management of hepatocellular carcinoma in adults. Gut 73: 1235-1268, 2024.
8. Rindi G, Mete O, Uccella S, Basturk O, La Rosa S, Brosens LAA, Ezzat S, de Herder WW, Klimstra DS, Papotti M and Asa SL: Overview of the 2022 WHO classification of neuroendocrine neoplasms. Endocr Pathol 33: 115-154, 2022.
9. Ni X, Wei Y, Li X, Pan J, Fang B, Zhang T, Lu Y, Ye D and Zhu Y: From biology to the clinic-exploring liver metastasis in prostate cancer. Nat Rev Urol 21: 593-614, 2024.
10. Aggarwal R, Huang J, Alumkal JJ, Zhang L, Feng FY, Thomas GV, Weinstein AS, Friedl V, Zhang C, Witte ON, *et al*: Clinical and genomic characterization of treatment-emergent small-cell neuroendocrine prostate cancer: A multi-institutional prospective study. J Clin Oncol 36: 2492-2503, 2018.
11. Abida W, Cyrta J, Heller G, Prandi D, Armenia J, Coleman I, Cieslik M, Benelli M, Robinson D, Van Allen EM, *et al*: Genomic correlates of clinical outcome in advanced prostate cancer. Proc Natl Acad Sci USA 116: 11428-11436, 2019.
12. Yao JL, Madeb R, Bourne P, Lei J, Yang X, Tickoo S, Liu Z, Tan D, Cheng L, Hatem F, *et al*: Small cell carcinoma of the prostate: An immunohistochemical study. Am J Surg Pathol 30: 705-712, 2006.
13. Aparicio AM, Harzstark AL, Corn PG, Wen S, Araujo JC, Tu SM, Pagliaro LC, Kim J, Millikan RE, Ryan C, *et al*: Platinum-based chemotherapy for variant castrate-resistant prostate cancer. Clin Cancer Res 19: 3621-3630, 2013.
14. Szarvas T, Csizmarik A, Fazekas T, Hüttl A, Nyirády P, Hadaschik B, Grünwald V, Püllen L, Jurányi Z, Kocsis Z, *et al*: Comprehensive analysis of serum chromogranin A and neuron-specific enolase levels in localized and castration-resistant prostate cancer. BJU Int 127: 44-55, 2021.
15. Haffner MC, Morris MJ, Ding CKC, Sayar E, Mehra R, Robinson B, True LD, Gleave M, Lotan TL, Aggarwal R, *et al*: Framework for the pathology workup of metastatic castration-resistant prostate cancer biopsies. Clin Cancer Res 31: 466-4478, 2025.
16. Gagnon R, Kish EK, Cook S, Takemura K, Cheng BYC, Bressler K, Heng DYC, Alimohamed N, Ruether D, Lee-Ying RM, *et al*: Real-world clinical outcomes and prognostic factors in neuroendocrine prostate cancer. Clin Genitourin Cancer 23: 102274, 2025.
17. Liu S, Alabi BR, Yin Q and Stoyanova T: Molecular mechanisms underlying the development of neuroendocrine prostate cancer. Semin Cancer Biol 86: 57-68, 2022.
18. Choi TW, Kim HC, Lee JH, Yu SJ, Kang B, Hur S, Lee M, Jae HJ and Chung JW: The safety and clinical outcomes of chemoembolization in child-pugh class C patients with hepatocellular carcinomas. Korean J Radiol 16: 1283-1293, 2015.
19. Aida Y, Nakazawa K, Shiozawa T, Ogawa R, Kiwamoto T, Morishima Y, Sakamoto T, Sekine I and Hizawa N: Small-Cell lung cancer treatment of newly diagnosed patients with poor performance status. Case Rep Oncol 12: 613-620, 2019.
20. Bahij R, Jeppesen SS, Olsen KE, Halekoh U, Holmskov K and Hansen O: Outcome of treatment in patients with small cell lung cancer in poor performance status. Acta Oncol 58: 1612-1617, 2019.