

Clinical features, therapeutic strategies and survival outcomes in primary hepatic neuroendocrine neoplasms

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Research Article

Keywords: primary hepatic neuroendocrine neoplasms, diagnosis, therapy, surgical resection, TACE, prognosis

Posted Date: September 25th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10830144/v1>

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Additional Declarations: No competing interests reported.

Abstract

Introduction:

Primary hepatic neuroendocrine neoplasms (PHNENs) are extremely rare liver tumors with fewer than 200 cases reported worldwide. Diagnosis is challenging due to vague symptoms and atypical imaging that often mimics hepatocellular carcinoma or cholangiocarcinoma. We reviewed our institutional experience with PHNENs, focusing on clinical features, treatment, and prognostic factors.

Methods

We retrospectively analyzed 20 PHNENs patients treated at West China Hospital (2015–2025). Demographic, clinical, radiological, pathological, and survival data were collected. Disease-free survival (DFS) was estimated using Kaplan–Meier analysis.

Results

Median age was 54 years (range, 22–72), with slight female predominance ($n = 11$). Most patients ($n = 14$) were asymptomatic. Elevated CA 19 – 9 was noted in 10 patients, and 8 had blood type B. Preoperative imaging frequently led to misdiagnosis. Pathologically, 14 tumors were G2 and 4 were G1. Among 19 followed patients, median DFS was 44 months (range, 10–74), with 12 remaining recurrence-free. One unresectable patient received TACE, enabling subsequent curative resection with 61-month DFS. G3/NEC ($p = 0.004$) and blood type B ($p = 0.01$) predicted worse DFS.

Conclusion

PHNEN is a rare disease. PHNENs are characterized as middle-aged population and rarely exhibit classic carcinoid syndrome. Preoperative imaging is atypical and curative surgery is still the mainstream treatment option to prolong the long-term outcome. TACE may result in tumor cytoreduction and some inoperable tumors may become resectable. Re-resection or radiofrequency ablation is also an alternative method for local intrahepatic metastasis.

Introduction

Neuroendocrine neoplasms (NENs) are relatively rare tumors that derived from neuroendocrine cells of multiple organs¹. Recent study shows that the incidence of NEN is steadily arising over the past 20 years². NENs display a carcinoma-like imaging feature but behave in a more indolent fashion; prolonged survival is often seen even in those with advanced disease^{3–5}. NENs tend to secrete biogenic amines and peptide hormones, causing carcinoid syndrome with the characteristic of flushing and diarrhea^{1, 2, 6}.

Gastrointestinal tract is the most common primary site for these tumors, accounting for 1%-2% of all the gastrointestinal malignancies and 67% of all the NENs, followed by the bronchopulmonary system^{2, 7, 8}. Within the gastrointestinal tract, NENs are mostly found in the small intestines, followed by rectum, colon, pancreas, appendix and the stomach, respectively^{7, 9}.

Among all the hepatic NENs, approximately 80% of the cases are found to be metastatic^{10, 11}. Primary hepatic neuroendocrine neoplasms (PHNENs) are extremely rare, with no more than 200 cases reported in the current English literature^{11–23}. When NENs are found in the liver, thoracoabdominal computed tomography (CT) and gastrointestinal endoscopes are needed to exclude the extrahepatic metastatic disease. Since few neuroendocrine cells are found in the liver, the exact derivation of PHNENs continues to be a mystery, with three hypothesis exist. The first hypothesis indicates PHNENs arise from liver malignant stem cells with neuroendocrine differentiation; the second suggests they are differentiated from heterotopic pancreatic or adrenal tissues situated in the liver; the third hypothesis affirms they are transformed from neuroendocrine cells located in the epithelium of the intrahepatic bile duct^{2, 24}. Different from NENs originated from other site, PHNENs seem to be endocrinologically silent and only 6.8% of PHNENs present with the classic carcinoid syndrome²⁵. As most PHNENs are slow-growing and asymptomatic with non-specific imaging features, preoperative diagnosis may be difficult^{23, 25}.

Due to the rarity features of PHNENs, only few reports have summarized the clinicopathological characters, imaging features, staging and prognosis traits of PHNENs. Thus, we aimed to present a single-center experience in diagnosis and treatment of PHNENs so as to analyze the preoperative features, treatment options and prognosis of patients with PHNENs.

Methods

Twenty patients with PHNENs were diagnosed and treated at West China Hospital of Sichuan University between November 2015 and November 2025. The diagnosis of hepatic NENs was made and confirmed by the histopathologic examination of surgically resected specimen or the biopsy specimen. Gastrointestinal endoscopy, computed tomography (CT) of the chest and abdomen, magnetic resonance imaging (MRI) and PET-CT were performed after the pathologically diagnosis of the hepatic NENs so as to rule out any extra-hepatic neuroendocrine tumors and the metastatic hepatic NENs. Institutional review board approval was obtained prior to the start of the investigation.

Initially, all patients underwent CT or MRI to determine the location, size, number, vascular involvement and resectability of the hepatic lesions. The demographic, clinical, imaging, laboratory and pathological data were retrieved from the medical records. PHNENs were classified as G1, G2 and G3 NET and NEC tumors according to mitotic rate or the Ki-67 index using the World Health Organization (WHO) classification of the digestive system tumors in 2019^{26, 27}.

Patients were monitored with abdominal ultrasound or CT scans every 2–3 months for the first two years and every 4–6 months thereafter. A postoperative follow-up was updated to March 2026 via the

medical records or making phone calls. Disease-free survival (DFS) and overall survival (OS) were calculated.

Statistical analyses were performed using SPSS version 22. Patient characteristics were reported using frequency and descriptive analysis. Continuous factors were expressed as means $\pm$ standard deviation and categorical variables were presented as percentages. Median DFS or OS survival was calculated by the Kaplan–Meier method. Factors associated with survival were evaluated. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Among 132 hepatic NENs, after careful screening, 20 were identified as PHNENs with no extrahepatic primary origin. Nine patients were male while 11 were female, with a median age of 54 years (range, 22–72 years). Most of the patients were found incidentally ($n = 14$), 4 patients were presented with an abdominal pain; another two patients were presented with jaundice and diarrhea, respectively. Only 2 patients had a hepatitis B virus (HBV) infection, no patient was noted to have hepatitis C virus (HCV) infection. For the liver function test, the median TB value of the entire cohort was 10.5 $\mu\text{mol/L}$ (range, 5.1–156.0 $\mu\text{mol/L}$); the median ALT level was 21.0 IU/L (range, 12.0–90.0 IU/L), the median AST level was 25.0 IU/L (range, 15.0–127.0 IU/L), the median ALB level was 44.1 g/L (range, 30.6–48.1 g/L). For the tumor markers (Table 1), ten patients (50%) had elevated CA 19 – 9 levels (normal range, $< 37 \text{ U/ml}$), Elevated CA 125 levels were noted in 2 patients (normal range, $< 35 \text{ U/ml}$). Two patients (10%) were with an AFP level larger than the normal range (normal range, $< 8 \text{ ng/ml}$). Three patients (15%) had increased CEA levels (normal range, $< 3.4 \text{ ng/ml}$). Of note, 8 patients (40%) had blood type B while only 1 patient (5%) had blood type AB (Table 1).

Table 1

Demographic and Clinical features of patients with primary hepatic neuroendocrine neoplasm

Case 1	Age (years)	Sex	Presentation	HBV/HCV	CA 19 – 9 U/ml	CEA ng/ml	AFP ng/ml	CA125 U/ml	Blood Type
	64	F	Incidental finding	-	11.3	0.9	5.3	13.3	O
Case 2	34	F	Incidental finding	HBV (+)	33.3	0.7	1.9	25.3	A
Case 3	53	F	Incidental finding	HBV (+)	66.9	2.6	2.4	16.5	B
Case 4	41	F	Incidental finding	-	5.4	1.4	2.0	49.5	O
Case 5	44	F	Incidental finding	-	14.6	1.8	2.0	8.2	A
Case 6	52	M	Abdominal pain	-	19.2	3.2	5.2	29.2	B
Case 7	57	F	Jaundice	-	160.8	1.5	2.1	19.3	A
Case 8	51	M	Incidental finding	-	27.3	3.6	8.1	11.5	B
Case 9	30	M	Abdominal pain	-	45.9	1.8	3.9	4.3	B
Case 10	59	F	Incidental finding	-	24.5	1.4	2.1	13.1	B
Case 11	59	M	Incidental finding	-	105.3	3.2	16.7	21.1	A
Case 12	63	M	Incidental finding	-	843.7	4.5	4.1	18.4	O
Case 13	67	M	Incidental finding	-	8.7	1.4	2.4	22.3	B
Case 14	55	F	Abdominal pain	-	11.9	4.7	0.7	44.2	O
Case 15	49	M	Incidental finding	-	1.01	3.1	6.5	6.4	B
Case 16	29	M	Incidental finding	-	342.9	0.9	2.7	32.2	A

Case 1	Age (years)	Sex	Presentation	HBV/HCV	CA 19 – 9 U/ml	CEA ng/ml	AFP ng/ml	CA125 U/ml	Blood Type
	64	F	Incidental finding	-	11.3	0.9	5.3	13.3	O
Case 17	22	F	Diarrhea	-	54.9	1.0	4.3	31.4	AB
Case 18	53	M	Incidental finding	-	5.85	9.42	3.56	11.64	B
Case 19	72	M	Incidental finding	-	62.5	1.9	4.5	21.9	O
Case 20	63	F	Incidental finding	-	48.9	4.7	3.5	11.6	A

As for the lesions, 11 patients were with single lesions. Six patients had lesions on the left lobe of the liver, five were localized at the right lobe, 4 patients had single lesions in between the left and right lobe; the rest 5 patients had multiple lesions on the both sides of the lobe. The maximal tumor size of each patient was calculated, with a median size of 6.7 cm (range, 2-17.4 cm). Case 1 patient was suspected as cystadenoma on the CT imaging (Fig. 1), case 8 was suspected as parasitic infection; others were mainly suspected as hepatocellular carcinoma (HCC) with or without intrahepatic metastasis and cholangiocarcinoma (CCA). En bloc resection was made on 18 patients with hemihepatectomy (n = 4), extended hemihepatectomy (n = 3), mesohepatectomy (n = 6), irregular hepatectomy (n = 5). Two patients were found to have unresectable tumors and underwent biopsy. Case 7 was previously found to be unresectable and did transarterial chemoembolization (TACE) twice and percutaneous transhepaticcholangial drainage; he then underwent extended right hemihepatectomy resection (Table 2).

Table 2
 clinicopathological features and survival outcomes of patients with primary hepatic neuroendocrine neoplasm

Case 1	Max size (cm)	Location	Tumor number	Imaging features	Treatment	Tumor Grade	Follow-up	Status
	5.1	L	Multiple	solid-cystic	Resection	G2	51	AWOD
Case 2	2.0	L	Multiple	Solid	Resection	G2	17	AWOD
Case 3	7.5	In between	Single	Solid	Resection	G2/G3	30	AWD
Case 4	12.0	R	Single	Solid	Resection	G1	24	AWOD
Case 5	3.0	R	Multiple	Solid	Resection	G2	65	AWOD
Case 6	6.7	Bi-lobar	Multiple	Solid	Resection	G2	14	AWD
Case 7	8.8	In between	Single	Solid	Resection	G2	61	AWOD
Case 8	6.7	R	Multiple	solid-cystic	Resection	G2	49	AWD
Case 9	7.6	L	Single	Solid	Resection	G1	42	AWD
Case 10	6.1	Bi-lobar	Multiple	Solid	Resection	G2	29	AWOD
Case 11	5.5	Bi-lobar	Multiple	Solid	Resection	G2	19	AWD
Case 12	6.0	R	Single	Solid	Resection	G3	10	AWOD
Case 13	11.6	Bi-lobar	Multiple	solid-cystic	Biopsy	G2	Lost	-
Case 14	17.4	L	Single	Solid	Biopsy	G2	13	DOD
Case 15	6.8	L	Single	Solid	Resection	G2	33	AWOD
Case 16	14.2	L	Single	Solid	Resection	G2	17	AWOD

Case 1	Max size (cm)	Location	Tumor number	Imaging features	Treatment	Tumor Grade	Follow- up	Status
	5.1	L	Multiple	solid- cystic	Resection	G2	51	AWOD
Case 17	2.5	R	Single	Solid	Resection	G1	12	AWOD
Case 18	5.9	R	Single	Solid	Resection	G3	3	AWOD
Case 19	8.8	In between	Single	Solid	Resection	G2	74	AWOD
Case 20	3.9	In between	Single	Solid	Resection	G1	26	AWOD

Grossly, most of the tumors were grayish-white (n = 14), followed by pinky-grey (n = 4) and taupe (n = 2). Most of the tumors were solid, medium (n = 14) and medium-to-firm (n = 3) in texture, followed by solid-cystic (n = 3). According to the WHO NENs classification, 4 patients were labeled as G1, 14 patients were classified as G2; the remaining 2 patients were sorted as G3 NET and NEC respectively. Microscopically, the tumor cells were round to oval, arranged in a glandular or cord shape, obvious nuclear atypia was noted (Fig. 2). The immunohistochemical staining showed the tumor was positive for CgA (18/20, 90%), Syn (Fig. 2, 20/20, 100%) and CD56 (13/16, 81.2%). Most of the patients were having a Ki-67 index between 3–20% (Fig. 2, Table 3).

Table 3
Histological and immunohistochemical features
of patients with primary hepatic neuroendocrine
neoplasm

Case 1	CgA	Syn	CD56	ki-67 index
	+	+	+	10%
Case 2	+	+	+	3%
Case 3	+	+	-	10%
Case 4	+	+	-	1–2%
Case 5	+	+		10%
Case 6	+	+	+	10%
Case 7	+	+	+	5–10%
Case 8	+	+		5–15%
Case 9	+	+		2%
Case 10	+	+	+	15%
Case 11	+	+	-	12%
Case 12	+	+	+	60%
Case 13	+	+		5–10%
Case 14	+	+	+	5–10%
Case 15	+	+	+	8%
Case 16	+	+	+	5%
Case 17	+	+	+	1%
Case 18	+	+	+	35%
Case 19	+	+	+	8%
Case 20	-	+	+	< 2%

Nineteen patients were well followed-up with a median follow-up time of 26 months (range, 4–74 months). One biopsy patient was lost with unknown follow-up information. Most of the patients (n = 12) were alive without recurrence (Fig. 3A). Five patients were alive with disease recurrence, 4 of them were with intrahepatic recurrence, one patient underwent chemotherapy of sunitinib, and was followed up for 5 months with stable disease; one patient underwent secondary surgery and was free from recurrence 14 months after the second surgery. Two patients found disease recurrence recently and underwent radiofrequency ablation. Another patient with disease recurrence was found to have bone metastasis 14

months later after the primary surgery, palliative treatment combined with Chinese traditional medicine was adopted. The median disease-free survival was 44 months (range, 10–74 months), while the median OS was not reached (Fig. 3B). Literature reviews comparing the survival differences among major studies about PHNENs are presented in Table 4.

Table 4
Comparison of major studies including patients with primary hepatic neuroendocrine neoplasms

Author/Year	Country	Cases	Age median	M/F ratio	R0 resection	S/M	OS	DFS
Hwang 2008	Korea	8	50 (37–64)	4:4	6	8:0	34 (3–121)	NR
Huang 2010	China	11	49.5 (34–59)	7:4	11	3:8	39 (12–107)	25 (1–98)
Park 2012	Korea	12	66.5 (37–80)	7:5	3	2:10	17 (0.7–41)	19.7 (6–36)
Yalav 2012	Turkey	5	42 (34–50)	3:2	5	5:0	NR	NR
Wang 2014	China	10	43.7 (25–62)	5:5	8	5:5	38 (13–74)	NR
Chen 2014	China	9	46 (24–66)	6:3	0	1:8	NR	NR
Shen 2014	China	15	55.5* (38–79)	9:6	15	14:1	35%**	30%**
Li 2016	China	10	45 (27–72)	6:4	NR	6:4	NR	NR
Yang 2017	China	11	54* (37–71)	4:7	1	1:10	NR	NR
Qiu 2018	China	13	54 (34–76)	8:5	4	10:3	9	NR
Li 2019	China	12	55.9 ± 13.0*	7:5	6	NR	25.4 ± 6.7	NR
Shah 2019	India	8	55 (35–69)	5:3	4:4	4:4	NR	NR
Parray 2020	India	13	50 (14–65)	9:4	8	9:4	41 (6–108)	20 (5–72)
Bari 2021	Pakistan	2	64 (50–64)	1:1	2	2:0	NR	19
Liu 2022	China	4	56 (40–73)	0:4	NR	0:4	(11–81)	NR
Kadi 2022	China	19	47	8:11	14	NR	42.2	NR
* mean age; ** 5-year survival rate								

Author/Year	Country	Cases	Age median	M/F ratio	R0 resection	S/M	OS	DFS
Li 2023	China	15	46.1 ± 18.2*	NR	NR	8:7	NR	NR
Cao 2023	China	1	72	1:0	0	0:1	NR	NR
Ghattas 2024	Lebanon	1	55	1:0	1	1:0	NR	NR
Jiang 2025	China	10	63	8:2	10	NR	NR(10–73)	NR
Luo 2025	China	1	22	0:1	1	1:0	6	NR
Zhang 2026	China	7	54(53–64)	4:3	6	6:1	11(3–102)	NR(8–96)*
* mean age; ** 5-year survival rate								

We further analyzed potential prognostic factors (age, sex, tumor markers, liver functions, white blood cells, blood type, tumor size, tumor number, tumor grading) of DFS in patients with resection, we found patients with blood type B seemed to have inferior DFS when compared with non-B type (Fig. 3C, $p = 0.01$). Tumor grading was also an important factor; patients with G3 NET and NEC had poor survival outcomes when compared with G1/G2 (Fig. 3D, $p = 0.004$). The tumor number was reaching statistical difference as a prognostic factor ($p = 0.083$).

Discussion

The diagnosis of PHNENs requires a consecutive procedure initiating from preoperative suspect to precise postoperative pathological evidence and long-term follow-up to exclude any potential extrahepatic primary origin²⁵. Thus, the ultimate diagnosis of PHNENs can only be clinically issued until long-term follow-up to preclude the metastasis disease from extrahepatic organs by digestive tract endoscopy, thoracoabdominal CT or PET-CT examination. In our current study, after long-term screening, we identified 20 patients with PHNENs. In literature, unlike some extrahepatic NENs, only few PHNENs show classic carcinoid syndromes, such as flushing, diarrhea, Zollinger–Ellison syndrome, bronchial spasm^{25, 28}. Consistent with previous studies, most of the patients in our study were asymptomatic and found incidentally.

HBV or HCV infection is an important risk factor for HCC or CCA. More than half of HCC patients are with HBV or HCV infection, a Meta-Analysis also revealed a pooled HBV infection rate of 31% in CCA patients^{29, 30}. In the 20 patients with PHNENs in the present study, only two were found to be with HBV infection. Park et al³¹ reported a low HBV or HCV infection rate (8.3%) in 12 patients with PHNENs. Several previous studies also showed PHNENs were not commonly with HBV or HCV infection or even

zero HBV/HCV infection rate^{20, 28}. Taken together, these data suggest HBV/HCV infection may not be a risk factor for PHNENs.

Most previous studies including ours found the median age of PHNEN patients was in the 4th or 5th decades, which is one of the clinical characters of PHNENs³. Studies have shown that serum tumor markers such as AFP, CEA, CA 125 and CA19-9 are not regularly elevated in PHNENs and have little diagnostic significance^{15, 32}. In the current study, 13 patients had elevated serum tumor marker levels, including 10 with elevated CA 19 – 9 levels. CA 19 – 9 is an important diagnostic and prognostic factor for patients with pancreatic cancer or CCA^{33–35}. A recent study by Han et al also showed almost half of the PHNENs patients had increased CA 19 – 9 levels³, which raises questions about true diagnostic value of CA 19 – 9 in PHNENs.

Preoperative radiological imaging of PHNENs can always be misdiagnosed as other hepatic neoplasms². PHNENs lack specific imaging manifestations and sometimes exhibit the classic HCC or CCA features; as some PHNENs display central cystic degeneration traits, it can also be misdiagnosed as cystadenoma or parasitic infection^{20, 28}. However, some PHNENs also exhibit specific features including nonenhancing cystic areas with hemorrhagic part and enhanced solid areas. Octreotide scintigraphy (OctreoScan) can achieve a higher diagnostic sensitivity in NENs, ranging from 85% to 90%²⁰. It also has the ability to forecast the response to the treatment of octreotide analogue.

Until now, surgical resection is the mainstream treatment option for PHNENs². TACE or liver transplantation is also an effective method for those with unresectable lesions confined to the liver parenchyma. Since NENs are rich of blood supply and are more susceptible to ischemia, TACE also seems to be a proper alternative treatment. In the current study, one patient was deemed as unresectable tumor when admitted and underwent TACE twice, an obvious tumor shrinking and cytoreduction was noted, then, curative resection was adopted, and the patient was still tumor-free with a follow-up time of 61 months. For those with local intrahepatic metastasis, radiofrequency ablation is also an effective method, two patients with intrahepatic metastasis in the current study underwent radiofrequency ablation were still free from tumor recurrence.

Due to the biology characters of PHNENs, the prognosis is optimistic with a mean overall survival of 148 months and 5-year survival of 80%³⁶. In the current study, we reported a median DFS of 44 months, while the OS was not yet reached since only one patient with G3 stage tumors died after the curative surgery. These data indicate that PHNENs exhibit a relatively benign course when compared with HCC or CCA³⁴. Further study focused on the prognostic factors for predicting DFS. We found blood type B and tumor grading were significant factors, while tumor number (single or multiple) was approaching statistical difference. Higher cellular proliferation tumors tend to have inferior survival outcome, it provides a convenient method to assess the potential of tumor malignancy degree and predict the survival outcome^{9, 37, 38}. However, there were also survival differences among different individuals within each

stage; meanwhile, no TNM staging system for hepatic NENs has been proposed so far. Therefore, more accurate staging systems based on the preoperative, pathological indicators are required.

Interestingly, we found blood type was a prognostic factor. Blood type O and A are the main blood types (accounting for more than 60%) for humans; in our current study, nearly half of the patients were with blood type B. Patients with blood type B were more likely to have inferior DFS when compared with non-B patients (mean survival, 28.9 vs 66.0 months; $p = 0.01$). ABO blood system is an established prognostic marker for patients with pancreatic cancer, hepatocellular carcinoma or bladder urothelial carcinoma^{39, 40}. Given the notion above, attentions should be paid on the blood type status of PHNENs, as blood type B patients seem to have detrimental survival outcome.

Our current study had some limitations; the retrospective nature and the small sampling size owing to rarity of this kind of disease made the conclusions less representative. As the slow-growing and low potential malignancy nature of PHNENs, most patients have not reached their endpoints. The current staging system was mainly for extrahepatic NENs, thus, whether this grading system is appropriate for PHNENs merits further verification.

In conclusion, given the single center experience and literature review, the incidence of PHNENs is increasing. PHNENs are characterized as middle-aged population with non-specific clinical manifestations and rarely exhibit classic carcinoid syndrome. Preoperative imaging is atypical and may be misdiagnosed as cystadenoma, some infectious disease, hepatocellular carcinoma or cholangiocarcinoma. Curative surgery is still the mainstream treatment option to prolong the survival outcome of PHNENs. TACE may result in tumor cytoreduction and some unresectable diseases may become resectable. For those with local intrahepatic metastasis, re-resection or radiofrequency ablation is also an alternative method. Patients with high tumor grade and blood type B tend to have inferior survival outcome.

Figure 1 Image examination of primary hepatic neuroendocrine carcinomas. (A) Case 1, contrast-enhanced CT revealed cystic areas and enhanced solid areas in the left lobe of the liver, the lesion was suspected as cystadenoma; (B) Case 16, contrast-enhanced CT showed a solid mass with irregular enhancement and colliquative necrosis in the center, the lesion was suspected as hepatocellular carcinoma; (C) Case 9, several solid masses with obvious enhancement in the right lobe of the liver, the lesion was suspected as hepatocellular carcinoma with intrahepatic metastasis; (D) Case 17, MRI scanning revealed a nonuniform high signal in the right lobe of the liver, with the proximal bile duct dilation, the lesion was suspected as cholangiocarcinoma; (E), Case 4, MRI scanning showed an irregular high density soft-tissue mass with colliquative necrosis in the center, the lesion was suspected as hepatocellular carcinoma.

Figure 3 (A) Disease-free survival of patients with primary hepatic neuroendocrine; (B) Overall survival of patients with primary hepatic neuroendocrine; (C) Kaplan–Meier curves comparing disease-free survival status based on blood type B and type non-B in patients with primary hepatic neuroendocrine

carcinomas ($P = 0.01$); (D) Kaplan–Meier curves comparing disease-free survival status based on G1/G2 and G3/NEC in patients with primary hepatic neuroendocrine carcinomas ($P = 0.004$).

Declarations

Consent to publish

Not applicable. This manuscript does not contain any individual person's identifiable data in any form.

Alternative if the journal requires consent for the anonymized clinical images:

Written informed consent for publication of anonymized clinical images and data was obtained from all patients.

Ethics approval and consent to participate:

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Biomedical Research Ethics Committee of West China Hospital, Sichuan University. The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study.

Informed Consent:

The requirement for informed consent was waived by the Biomedical Research Ethics Committee of West China Hospital, Sichuan University due to the retrospective nature of the study.

Declaration of Interest:

The authors declare no conflicts of interest.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Declaration of Interest

Informed consent was obtained from all patients for this study, which adhered to the Declaration of Helsinki.

Human Ethics declaration

Not applicable

Clinical trial number

Not applicable

Funding

Supported by 1.3.5 project for disciplines of excellence-Clinical Research Incubation Project, West China Hospital, Sichuan University (2021HXFH001); National Natural Science Foundation of China for Young Scientists Fund (82303669); Sichuan Natural Science Foundation (2024NSFSC1896, 2026NSFSC1935); Sichuan Science and Technology Program (2024YFFK0384); Sichuan Medical Science and Technology Innovation Research Association Special Research Project (2025YCZD194, 2025YCZD155, YCH-KY-YCZD2024-300); “Qimingxing” Research Fund for Young Talents (HXQMX0020, HXQMX0177, HXQMX0152); Sichuan Provincial Health Commission Youth Nursery Project (24QNMP031); Research Project of Sichuan Rehabilitation Medicine Association (SCKFKY20250101); Sichuan Provincial Health Science and Technology Project (ZH2026-101); Cancer Prevention and Treatment Research “Huai er” Special Fund (2025 – 107). (Qilu) Clinical Research of Sichuan Anticancer Association (XH2023-032; XH2023-502).

Author Contribution

Rabia Zahid Bukhari and Dong Cai contributed equally to the data acquisition, statistical analysis, drafted the manuscript, and shared the first authorship. Zou Rui Qi and Liu Fei were involved in editing and reviewing the manuscript. Haijie Hu and Fuyu Li contributed to the study design and revision of the manuscript. All authors reviewed the results and approved the final version of the manuscript.

Data Availability

Supported by 1.3.5 project for disciplines of excellence-Clinical Research Incubation Project, West China Hospital, Sichuan University (2021HXFH001); National Natural Science Foundation of China for Young Scientists Fund (82303669); Sichuan Natural Science Foundation (2024NSFSC1896, 2026NSFSC1935); Sichuan Science and Technology Program (2024YFFK0384); Sichuan Medical Science and Technology Innovation Research Association Special Research Project (2025YCZD194, 2025YCZD155, YCH-KY-YCZD2024-300) ; “Qimingxing” Research Fund for Young Talents (HXQMX0020, HXQMX0177, HXQMX0152); Sichuan Provincial Health Commission Youth Nursery Project (24QNMP031); Research Project of Sichuan Rehabilitation Medicine Association (SCKFKY20250101); Sichuan Provincial Health Science and Technology Project (ZH2026-101); Cancer Prevention and Treatment Research “Huai er”

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Figures

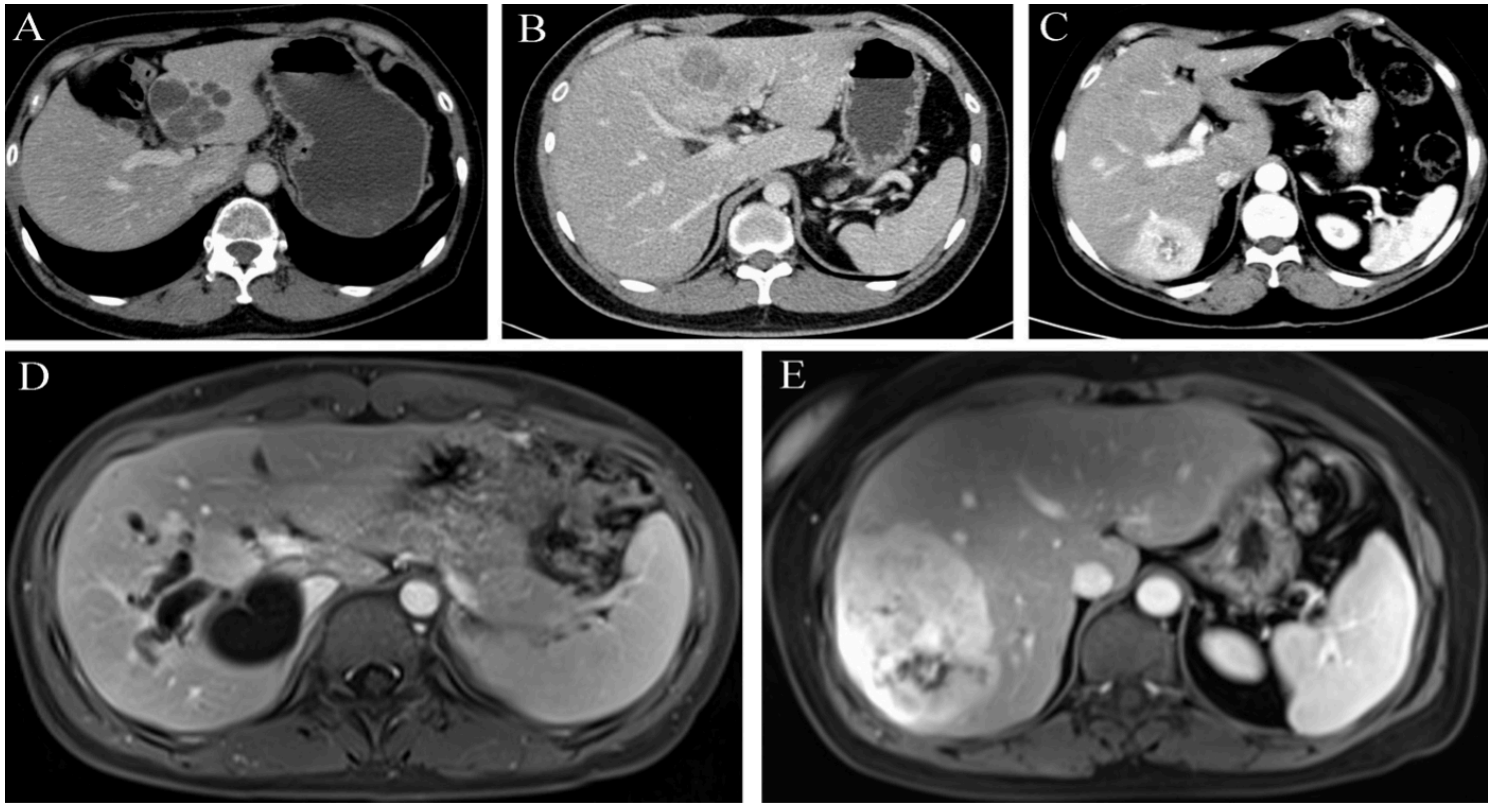


Figure 1

Image examination of primary hepatic neuroendocrine carcinomas. (A) Case 1, contrast-enhanced CT revealed cystic areas and enhanced solid areas in the left lobe of the liver, the lesion was suspected as cystadenoma; (B) Case 16, contrast-enhanced CT showed a solid mass with irregular enhancement and colliquative necrosis in the center, the lesion was suspected as hepatocellular carcinoma; (C) Case 9, several solid masses with obvious enhancement in the right lobe of the liver, the lesion was suspected as hepatocellular carcinoma with intrahepatic metastasis; (D) Case 17, MRI scanning revealed a nonuniform high signal in the right lobe of the liver, with the proximal bile duct dilation, the lesion was suspected as cholangiocarcinoma; (E), Case 4, MRI scanning showed an irregular high density soft-tissue mass with colliquative necrosis in the center, the lesion was suspected as hepatocellular carcinoma.

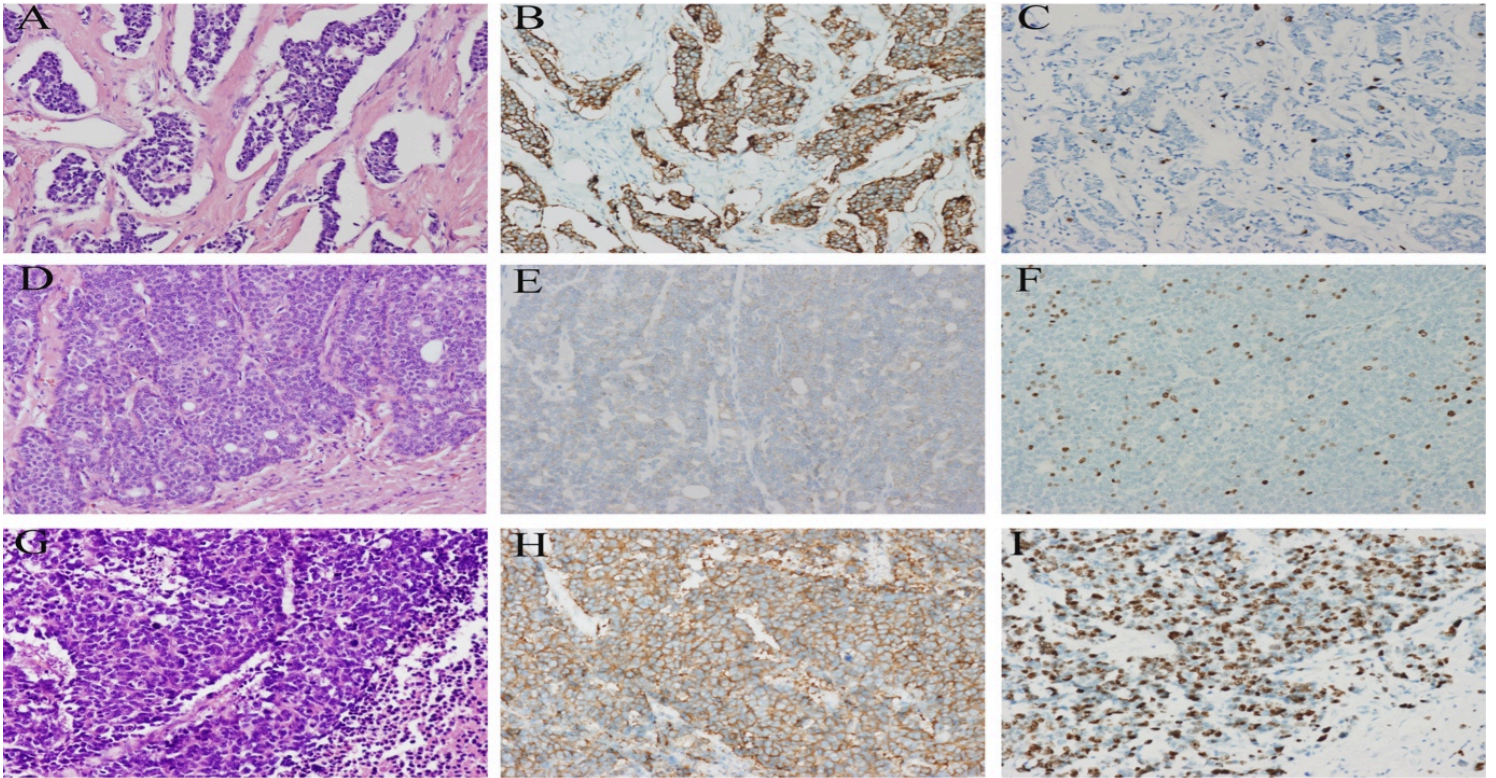


Figure 2

Pathological features of primary hepatic neuroendocrine carcinomas. A-C Case 17, G1, (A) HE staining demonstrated tumor cells were round to oval, with a nest or trabecular feature, surrounded by the proliferous fibrous tissues. The chromatin was granular and nucleus is not obvious; (B) Immunohistochemistry revealed that the tumor cells were positive for synaptophysin; (C) The Ki-67 index was approximately 1%. D-F Case 16, G2, (D) HE staining showed tumor cells were round to oval, arranged in an organoid or nest-like shape, with pseudoadenoid structure inside. The chromatin was granular and nucleus is not obvious, pathological nuclear division was scarce; (E) Immunohistochemistry revealed that the tumor cells were positive for synaptophysin; (F) The Ki-67 index was approximately 5%. G-I Case 12, G3, (G) HE staining revealed the tumor cells were arranged in a nest-like or Homer-Wright structure. Necrosis and mitoses were abundant, the chromatin was granular and cytoplasm is sparse, the pathological nuclear division was obvious; (H) Immunohistochemistry revealed that the tumor cells were positive for synaptophysin; (I) The Ki-67 index was approximately 60%.

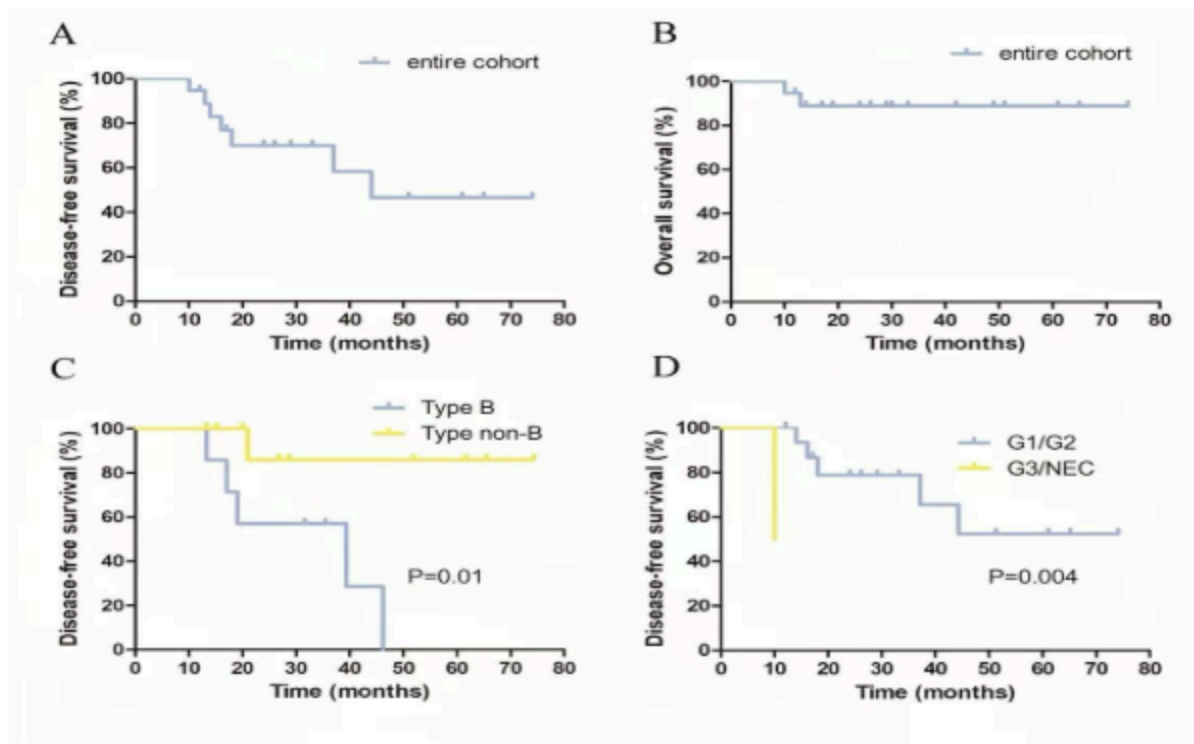


Figure 3

(A) Disease-free survival of patients with primary hepatic neuroendocrine; (B) Overall survival of patients with primary hepatic neuroendocrine; (C) Kaplan–Meier curves comparing disease-free survival status based on blood type B and type non-B in patients with primary hepatic neuroendocrine carcinomas($P=0.01$); (D) Kaplan–Meier curves comparing disease-free survival status based on G1/G2 and G3/NEC in patients with primary hepatic neuroendocrine carcinomas($P=0.004$).