Association of polycythemia vera with non-cirrhotic portal hypertension in five patients: A case series

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Abstract. Polycythemia vera (PV) and non-cirrhotic portal hypertension (NCPH) are relatively independent diseases, and few studies have linked them. However, in clinical settings, there may be a causal relationship. The aim of the present study was to analyze the clinical data of five patients with portal hypertension caused by PV and summarize the characteristics of PV with portal hypertension, to enhance the knowledge of this disease. The clinical data of five patients with PV and portal hypertension treated at Beijing You'an Hospital (Beijing, China) from January 2010 to March 2022 were retrospectively collected. The characteristics of these patients were then summarized and analyzed, including general information, laboratory tests, imaging and gastroscopy data. Overall, four patients were diagnosed with PV earlier compared with those with NCPH (ranging between days and years), whereas one patient was diagnosed with NCPH at the time of PV diagnosis. These four patients had blood cell elevations of 2-3 categories (red blood cells, white blood cells or platelets). The Child classification of liver functions in all five patients were found to be grades A-B. All five patients had splenomegaly, where three patients had portal vein thrombosis and cavernous degeneration. In addition, four patients had moderate or severe esophageal varices. In conclusion, to the best of our knowledge, this was the first case series of NCPH caused by PV. Among the patients, it was revealed that: i) NCPH caused by PV had milder liver function damage compared with cirrhosis-induced portal hypertension; ii) splenomegaly, ascites and esophageal varicose veins were prominent symptoms of NCPH caused by PV; iii) If PV is diagnosed, esophagogastroduodenoscopy should be performed as early as possible and regularly, where primary prevention measures for esophageal variceal hemorrhage are recommended; and iv) patients with PV with portal hypertension are at risk of thrombosis and bleeding, but it remains to be determined whether early antithrombotic therapy can reduce complications.

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Abbreviations: PV, polycythemia vera; NCPH, non-cirrhotic portal hypertension; EGD, esophagogastroduodenoscopy; MPN, myeloid proliferative tumor; PVT, portal vein thrombosis; ULN, upper limit of normal

Key words: polycythemia vera, portal hypertension, non-cirrhotic portal hypertension, cirrhosis

Introduction

Polycythemia vera (PV) is a relatively indolent myeloid-proliferative neoplasm (MPN) that is characterized by the clonal proliferation of red blood cells, bone marrow and megakaryocytes (1,2). In addition, PV has several unique molecular characteristics, such as mutations in the JAK2V617F gene or exon 12 (1,2). However, although patients with PV can have prolonged survival with general treatment (e.g., bleeding therapy) and medication (e.g., hydroxyurea), PV is generally incurable (1,2). The clinical manifestations of PV also lack specificity, typically presenting with visible skin redness, particularly on the face, neck and extremities (3). Neurological symptoms can include headache, dizziness and tinnitus (4). In addition, peptic ulcers (5) and water pruritus are common in some patients because of increased basophil and histamine release (6). Common complications of PV can include recurrent ischemic cerebrovascular lesions (7), aquagenic pruritus (6), hypertension (8), pulmonary hypertension (9) and coronary heart disease (8,10). Since a universally-recognized set of unique clinical manifestations from PV are not available, missed diagnosis and misdiagnosis often occur. For example, a previous case report mentioned that the hypochondromic mass was misdiagnosed as hepatosplenomegaly caused by PV because the patient had concomitant polycythemia vera (11). That may delay the best opportunity and time for treatment.

Patients with PV have an increased risk of venous and arterial thrombotic events, with an incidence of 0.4-2.8 cases per 100,000 individuals per year and with a lifetime prevalence of 20-30% in an international study (12,13). Portal vein

thrombosis (PVT) in patients with PV is a common risk factor for non-cirrhotic portal vein thrombosis (14). PV with PVT may result in cavernous transformation of the liver, which may lead to collateral circulation formation, ascites, portal hypertension, biliary disease, esophagogastric varices and gastrointestinal bleeding (15-17).

Portal hypertension is an abnormal hemodynamic syndrome that causes ascites, variceal hemorrhage, hepatic encephalopathy and other serious complications, the most common of which is cirrhosis (18). Portal hypertension can be classified as cirrhotic or non-cirrhotic, where the latter, non-cirrhotic portal hypertension (NCPH), is the second leading cause of portal hypertension (19) and can be caused by PVT (20,21). PVT is a hepatic vascular disease that refers to thrombosis of the portal vein trunk and/or left and right branches of the portal vein of whichever cause, with or without thrombosis of the superior mesenteric vein, inferior mesenteric vein and splenic vein (12). When PVT occurs, the liver compensates by increasing hepatic artery blood flow to maintain normal liver function (22). NCPH is clinically characterized by features of portal hypertension, moderate to massive splenomegaly, with or without hypersplenism, but preserved liver functions (15). Liver pathology of NCPH is characterized by phlebosclerosis, periportal and perisinusoidal fibrosis, fibroelastosis, hepatic lobules that are structurally intact and differential atrophy (15). According to the location of blood flow resistance, portal hypertension can be classified into prehepatic, intrahepatic and posthepatic (20,21). The common pathogenesis of NCPH includes PV (23). PV combined with portal hypertension is classified as prehepatic NCPH (21). At present, to the best of our knowledge, there are few studies on patients with PV or NCPH. Therefore, present study aimed to analyze the clinical data of patients with PV and NCPH, to enhance the awareness of this disease.

Patients and methods

Patients. The study was approved by Ethics Committee of Beijing You'an Hospital Affiliated to Capital Medical University (Beijing, China) and written informed consent was obtained from all patients. The age and sex distribution can be seen in Table I. Information of patients with PV and NCPH was obtained from the electronic medical record system. Patients with seropositive hepatitis B and C viruses were excluded, as were patients with a history of alcohol or drug-induced liver injury, patients who were positive for autoimmune liver disease-related indicators, and patients with inherited metabolic liver disease. Specific inclusion and exclusion criteria are further described subsequently. This was a retrospective study of cases. The diagnosis of polycythemia vera was a clear diagnosis of the patient in other hospitals (Beijing Friendship Hospital Affiliated to Capital Medical University, Beijing, China; Peking University People's Hospital, Beijing, China). Their diagnoses were recorded in the electronic medical records system but it was not clear whether pathological tests were carried out. Patients who were diagnosed with PV and NCPH and treated in Beijing You'an Hospital, Capital Medical University (Beijing, China) from January 2010 to March 2022 were included into the present study. The patient's hospitalization information was collected from the hospital's medical record database, and the patient's examination data, including laboratory blood test and imaging data (hematological examination, the nurse extracted the fasting venous blood of the patient in the morning on the day after admission and sent it to the biochemical laboratory; imaging examination, during the hospitalization of the patient, the imaging physician used a Siemens AG 64 CT scanner to conduct CT scanning of the abdomen; electronic gastroscopy, an experienced gastroenterologist completed the electronic gastroscopy for the patient.), were collected from the electronic medical record system of Beijing You'an Hospital, Capital Medical University. All samples were processed at the Clinical Laboratory Center of Beijing You'an Hospital, Capital Medical University (Beijing, China). All patients included had complete biochemical, routine blood and coagulation results. Upper limb venous blood samples were tested using an automatic biochemical analyzer (AU400; Olympus Corporation), automatic blood cell analyzer (BC-5390CRP; Shenzhen Mindray Biomedical Electronics Co., Ltd.) and an automatic coagulation analyzer (Precil C3510; Shenzhen Mindray Biomedical Electronics Co., Ltd.). Enhanced abdominal CT examination was performed, and CT images and reports were collected from the Imaging Center of Beijing You'an Hospital. Gastroscopy images were collected from the Endoscopy Center of Beijing You'an Hospital, but no endoscopic histological samples were collected. All aforementioned examinations and examination information were recorded in the medical record system, and the results were collected from this and sorted in the present study. A total of 5 patients with PV and portal hypertension were included, of whom 3 were male and 2 were females. The mean age was 63.60±18.33 years. Table I summarizes the general characteristics of the 5 patients.

Inclusion criteria. Inclusion criteria were set in line with the diagnostic criteria of PV (2): Major criteria: i) Hemoglobin >16.5 g/dl in men and hemoglobin >16.0 g/dl in women; ii) bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis), including prominent erythroid, granulocytic and megakaryocytic proliferation with pleomorphic, mature megakaryocytes (differences in size); and iii) presence of JAK2V617F or JAK2 exon 12 mutation. Minor criterion: Subnormal serum erythropoietin level. (Diagnosis of PV requires meeting either all three major criteria, or the first two major criteria and the minor criterion). They were also in line with the diagnostic criteria of NCPH (21), as follows: The presence of esophageal and gastric varices or imaging manifestations (CT) of portal hypertension, such as splenomegaly, portal vein widening and/or collateral circulation.

Exclusion criteria. Serologically positive for hepatitis virus B or C; with history of alcoholic or drug-induced liver injury; indices associated with autoimmune liver disease were positive (such as anti-nuclear antibody, anti-mitochondrial antibody, immunoglobulin-G4, anti-Ro-52 antibody, scleroderma 70 antigen, double-stranded-DNA, anti-Jo-1 antibody and anti-nucleosome antibody); and with genetic metabolic liver disease (if the patient's medical record information in the medical record system indicated that genetic testing (ATPase copper transporting β gene mutation/homeostatic

Table I. General data of patients.

Case no.	Age/Sex	Chief complaint	Medical history	Diagnosis time of PV	Treatment of PV	Diagnosis time of portal hypertension
1	83/M	Abdominal discomfort	Coronary heart disease, atrial fibrillation, chronic bronchitis. Deny family history of hypertension, diabetes and liver disease	1 week	Hydroxyurea	1 day
2	49/F	Abdominal pain	Deny history of chronic liver disease. No history of long-term medication. No history of long-term alcohol consumption	During this hospital stay	Hydroxyurea	During this hospital stay
3	79/M	Swelling of the legs and feet	Deny history of hypertension, diabetes and coronary heart disease	10 years	Bloodletting, hydroxyurea, Peg-Interferon	2 years
4	66/M	Fatigue and yellowing of skin and eyes	Cerebral infarction, hypertension, coronary heart disease, myocardial infarction, hyperlipidemia, skin ulceration of bilateral lateral malleolus	19 years	Hydroxyurea, Peg-Interferon	4 days
5	41/F	Vomiting blood and black stool	Deny history of hypertension, diabetes and coronary heart disease. Deny family history of liver disease	3 years	Peg-Interferon	2 months

PV, polycythemia vera; F, female; M, male.

iron regulator gene mutation) had revealed hereditary liver disease that could lead to portal hypertension, such as hepatolenticular degeneration, hemochromatosis, etc., the patient was excluded).

Data analysis. This was a retrospective study. Patient clinical data, such as sex, age, major complaints, medical history, laboratory examination, and imaging findings of the abdomen and gastroscopy, were extracted from the hospital case system. Data were processed using the SPSS 26.0 software (IBM Corp.). The mean values of data conforming to a normal distribution are expressed as mean ± standard deviation. The mean values of data that did not conform to normal distribution were expressed as median (quartile 1, quartile 3).

Results

General data of patients. NCPH is relatively rare in the clinic (15), the patients included in the present study were serologically hepatitis virus B- and C-negative and had no history of alcoholic or drug-induced liver injury. In addition, their indices associated with autoimmune liver disease were negative and they had no genetic metabolic liver disease. The course since definite diagnosis of PV was longer than that of NCPH in cases 1, 3, 4 and 5; the duration of PV was 1 week, 10 years, 19 years and 3 years, respectively, while that of NCPH was 1 day, 2 years, 4 years and 2 months. The diagnosis of PV and NCPH of case 2 was simultaneous. PV treatment mainly entails the use of hydroxyurea and interferons (1). Overall, case nos. 1, 2, 3 and 4 received symptomatic treatment with hydroxyurea, whilst cases nos. 3 and 4 were treated with Peg-interferon in the later stages of the disease. By contrast, case no. 5 was treated with interferon. In the present study, case no. 4 showed obvious erythema on the cheek and auricle, where a history of bilateral lateral ankle joint ulcers was considered to be associated with the long-term use of hydroxyurea (Fig. 1).

Laboratory tests data of patients. Routine blood examination of four patients (case nos. 1, 2, 3 and 4) showed an elevation of 2-3 parameters (red blood cells, white blood cells or platelets). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were normal in all patients except for case 4, whose ALT and AST levels were elevated. Total bilirubin (TBIL) was elevated in four patients (case nos. 1, 2, 3 and 4). Albumin (ALB) protein levels were decreased in four patients (case nos. 1, 3, 4 and 5). Cases 3 and 4 had elevated glutamyl transpeptidase (GGT) and alkaline phosphatase (ALP) levels and cholestasis. Coagulation function showed 4 patients (case nos. 1, 2, 3 and 5) had decreased prothrombin activity (PTA), whilst 3 patients (case nos. 1, 2 and 3) had an elevated international normalized ratio. The Child-Pugh grade of liver function (24) was found to be A or B in all five patients (Table II). Case 1 died 9 days after admission. Cases 2, 3,

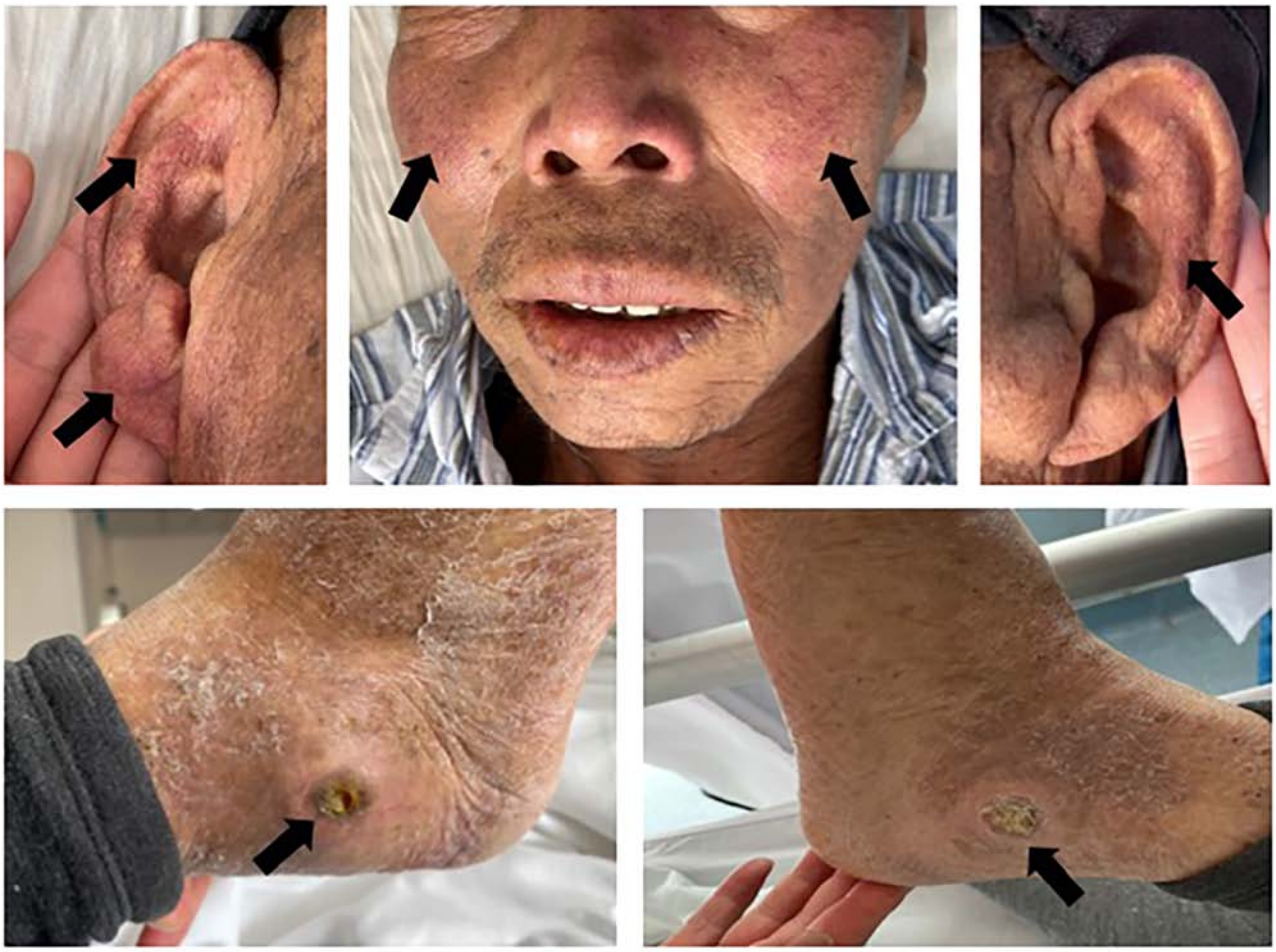

Figure 1. Features on patient case no. 4. Erythema on the cheek and auricle, with bilateral lateral ankles joint ulcers.

4 and 5 were followed up by telephone in December 2022. Cases 2, 3 and 5 survived, and case 4 died in June 2022.

Imaging and gastroscopy data of patients. Gastroscopy revealed moderate and severe esophageal varices in case nos. 1, 3, 4 and 5. Imaging examination (CT) revealed all patients had portal hypertension, of which case nos. 2, 4 and 5 had at least a venous emboli formation, whereas case nos. 2, 3 and 4 had hepatic perfusion abnormalities. All five patients had splenomegaly, where case nos. 2 and 3 found with associated spleen infarction. In addition, case nos. 1, 2, 4 and 5 had associated collateral circulation formation. Case nos. 1, 3, 4 and 5 had varying degrees of ascites (Table III).

Discussion

PV is an MPN, with a high risk of arteriovenous thrombosis (2,12,13). PVT is a common cause of NCPH, which can lead to the clinical manifestations of portal hypertension, such as collateral circulation, ascites, esophageal and gastric varices and gastrointestinal bleeding (15,23). PVT and a high coagulation state are common in patients with PV (12). Therefore, the present study hypothesized that PV can lead to NCPH.

In the present study, cases no. 3 and 4 exhibited increased D-Dimer levels, whereas three cases (nos. 2, 4 and 5) showed PVT accompanied by portal vein sponge appearance change (Table III). Table III specifically records the imaging findings of each patient. The venous embolus column shows the diagnosis of portal cavernous transformation. Cases no. 2 and 4 had mesenteric and splenic vein thrombosis, which are risk factors for portal hypertension. All five cases had splenomegaly, two of whom (case nos. 2 and 3) had splenic infarction. Chronic compression of bile ducts by collateral circulation (or ischemia caused by venule thrombosis) may lead to portal hypertension cholelithiasis (25,26).

Imaging reports of case no. 4 showed portal hypertension cholelithiasis with obvious elevations in ALP and GGT levels. Although the clinical symptoms were not obvious, abnormal liver function may have been caused by bile duct blockage in case no. 4. In the present study, the hematological manifestations of PV-induced NCPH included increased erythrocytes, white blood cells, hemoglobin and platelets in some of the patients. However, different patients behaved differently so these were not observed in all cases. These observations are different from the decreases in white blood cells and platelets due to hypersplenism in portal hypertension caused by cirrhosis (27). Among the patients included in the present study, only case no. 4 showed an increase in transaminases (ALT, AST, GGT and ALP). In addition, 4 patients (nos. 1, 3, 4 and 5) had slightly reduced ALB levels and 4 patients (nos. 1, 2, 3 and 4) had elevated bilirubin levels. The liver function index Child grade was A or B, indicating that the liver function

Table II. Laboratory test data of each patient.

Laboratory indices	Reference range	Case no.				
		1	2	3	4	5
Blood routine examination						
Red blood cell (x10^{12}/l)	4.3-5.8	7.76	6.58	4.8	5.36	3.27
White blood cell (x10^{9}/l)	3.5-9.5	11.49	8.88	43.03	28.96	2.35
Neutrophils (%)	40-75	74.8	76.2	93.2	91.4	55
Hemoglobin (g/l)	130-175	174	198	127	139	73
Platelet (x10^{9}/l)	100-300	455	699	480	782	91
Liver function						
Alanine aminotransferase (U/l)	9-50	19	9	15	56	10
Aspartate aminotransferase (U/l)	15-40	32	25	23	47	12
Total bilirubin (μmol/l)	5-21	46.9	30.8	21.2	90.5	20
Direct bilirubin (μmol/l)	<7	12	7.9	9.8	65.3	4.3
Albumin (g/l)	40-55	31.5	41.4	33.1	35.7	36
Glutamyl transpeptidase (U/l)	10-60	32	44	75	584	15
Alkaline phosphatase (U/l)	45-125	103	52	191	718	45
Coagulation function						
Prothrombin time (sec)	9.9-12.8	15	15	16	10.7	13.9
Prothrombin activity (%)	80-120	72.1	63	60	107	78.8
International normalized ratio	0.8-1.2	1.24	1.33	1.43	0.96	1.15
Activated partial thromboplastin time (sec)	25-36.5	46.7	57.1	49.2	33.4	51.2
Fibrinogen (g/l)	2-4	1.47	2.69	2	3.85	1.41
D-Dimer (μg/l)	<230	189	162.2	557	472	/
Child grade		B	A	B	B	A

damage in patients with portal hypertension caused by PV was relatively mild.

The gastroscopy and imaging examinations in the present study revealed manifestations of esophageal and gastric varices or portal hypertension, such as splenomegaly, portal vein widening and/or collateral circulation. The imaging and gastroscopy examinations provided a reliable basis for the initial diagnosis of portal hypertension in the patients, especially when the laboratory examination results were not consistent with clinical experience. As aforementioned, hyperplenism causes platelets and white blood cells (27). However, in the present study, the hematological manifestations of PV-induced NCPH included increased erythrocytes, white blood cells, hemoglobin and platelets.

Overall, cases nos. 1, 3, 4 and 5 developed ascites, whereas cases nos. 1, 2, 4 and 5 showed collateral circulation, all of which were considered to be associated with PV thrombosis and disease progression. A previous study has reported that even without varicose veins at baseline, the probability of developing varicose veins in patients with non-cirrhotic and non-neoplastic portal thrombosis is 2% after 1 year and 22% after 5 years (28). Once portal hypertension occurs, blood flows to the hepatic sinuses through the lateral branches of the portal vein or out of the liver through the lateral branches of the portal vein system, resulting in bleeding from the gastroesophageal, ectopic or rectal varices (29). Patients with moderate or severe esophageal varices that are red color sign-positive (RC-positive) are at higher risk of bleeding (30). In the present study, the esophageal veins of cases 1, 3 and 5 were severely varicose and RC-positive. It is recommended that after PV diagnosis, esophagogastroduodenoscopy (EGD) should be performed relatively early and regularly. Patients at risk of gastrointestinal bleeding should be treated prophylactically. Early prevention of primary esophageal variceal bleeding is recommended (30). However, there is no consensus on whether active antithrombotic therapy in patients with PV can delay or prevent venous thrombosis and various downstream complications, such as visceral infarction, ascites and variceal hemorrhage.

Inpatients diagnosed with PV in the case system of Beijing You'an Hospital from January 2010 to March 2022 were included in the present study. The clinical data for observation were the data of the patients at their first admission. In cases nos. 1, 3, 4 and 5 of the present study, the diagnosis of PV was earlier compared with that of NCPH, whereas in case no. 2 PV and NCPH were found simultaneously. Although the time and course of diagnosis of PV were different for the five patients, imaging examinations all patients indicated portal hypertension. Inpatient medical records showed that the symptoms of case nos. 2, 3, 4 and 5 were improved and discharged after acid suppression, gastric mucosa protection, upper gastrointestinal bleeding prevention and liver lowering enzyme treatment.

Due to their old age, case 1 was admitted to the hospital with abdominal and chest infections with numerous underlying

Table III. Imaging and gastroscopy.

Case no.	Venous embolus	Abnormality of hepatic perfusion	Splenomegaly	Infarction of spleen	Ascites	Collateral circulation	Varicose veins	Other gastroscopic findings
1	Portal and splenic veins widening	No	Yes	No	Yes	Yes	Esophageal varices (G3, severe, red-color sign positive)	Portal hypertensive gastropathy
2	Emboli of portal and superior mesenteric vein were extensively formed. Portal cavernous transformation	Yes	Yes	Yes	No	Yes	Chronic superficial gastritis	-
3	Portal vein widening	Yes	Yes	Yes	Yes	No	Esophageal varices (G3, severe, red-color sign positive)	Portal hypertensive gastropathy. Gastric polyp
4	Emboli of portal vein, superior mesenteric vein, splenic vein. Portal cavernous transformation	Yes	Yes	No	Yes	Yes	Esophageal varices (G2, moderate). Gastric varices	Reflux esophagitis. Portal hypertensive gastropathy. Duodenal ulcer (Stage A1)
5	Emboli of portal vein. Portal cavernous transformation	No	Yes	No	Yes	Yes	Esophageal varices (G3, severe, red-color sign positive)	-

diseases (coronary heart disease, atrial fibrillation and chronic bronchitis). After anti-infection and symptomatic treatment failed, the patient died clinically on the 9th day after admission. Case 4 was discharged from hospital after symptom improvement; however, the family confirmed that the patient had died during telephone follow-up 6 months later. In the present study, there was no difference between the treatment of patients with PV complicated with portal hypertension and that of hepatic portal hypertension. The present study suggested that clinicians should further consider whether patients with PV are complicated with portal hypertension and improve the examination for corresponding treatment. PV treatment mainly uses hydroxyurea and interferons (31). Among the five patients included in the present study, four patients (case nos. 1, 2, 3 and 4) received symptomatic treatment with hydroxyurea, with case nos. 3 and 4 also treated with interferon at the latter stages of the disease. However, case no. 5 was treated with interferon only.

Hydroxyurea is the first-line drug of choice, whereas Peg-interferon is typically administered to young women of childbearing age and to patients who show intolerance or resistance to hydroxyurea (31). Hydroxyurea is commonly used for treating various blood diseases, such as sickle cell anemia, thalassemia and chronic myelogenous leukemia. Long-term use of hydroxyurea can cause skin side effects, such as diffuse hyperpigmentation, heterochromia dermatitis and skin atrophy (32). Multiple ulcers occur in 64% patients treated with hydroxyurea long-term, where the most common ulcer site is the ankle (32). In a previous study, 30 of 993 patients treated with hydroxyurea for MPN developed painful ulcerative skin conditions, mainly in the ankle area. A total of 11 patients developed oral ulcers. In addition, 10 patients presented with non-ulcerative skin conditions, complicated by erythema and skin infiltration (by inflammatory exudate) (32). Furthermore, long-term sequelae of drug-induced liver injury can also be observed in portal hypertension (33). In a previous report, when thioguanine is used to treat acute and chronic myeloid leukemia (34) or when the adjuvant chemotherapy drug oxaliplatin was used, NCPH was found after several years of administration (35). Since liver injury caused by hydroxyurea has not been previously reported, portal hypertension in the patients of the present study was not considered for drug-induced liver injury.

In conclusion, the patients included in the present study were serologically hepatitis virus B and C negative, had no history of alcoholic or drug-induced liver injury, their indices associated with autoimmune liver disease were negative and had no genetic metabolic liver disease. The history is only a series of reports of NCPH caused by PV. However, due to the small sample size included in the present study, the mechanism of non-sclerosing portal hypertension caused by PV needs to be further explored. Analysis of patients' characteristics showed that decompensated manifestations of portal hypertension caused by PV, such as splenomegaly, cholecystitis and esophageal varicose veins, were more common. However, impairments in liver function was mild. After diagnosing PV, EGD should be performed as early as possible and regularly, where the primary prevention of esophageal variceal hemorrhage is particularly important. However, there is no consensus on whether active antithrombotic therapy in patients with PV can delay or prevent venous thrombosis and downstream complications, such as visceral infarction, ascites and variceal hemorrhage. If portal hypertension and related complications are consciously prevented in advance during PV, then the adverse outcomes of the disease may be improved.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

LZ, WL and JH were responsible for data acquisition. LZ, YW and CG were responsible for data interpretation and confirm the authenticity of all the raw data. CG, WL and JH critically revised this paper. WL and CG provided theoretical guidance for the single patient treatment protocol. CG and JH gave final approval of the version to be published. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present retrospective study was approved by an institutional review board of Beijing Youan Hospital, Capital Medical University (Beijing, China; approval no. LL-2022-089-K).

Patient consent for publication

Written informed consent was obtained from the relatives of patient 4. The Ethics Committee of Beijing You'an Hospital Affiliated to Capital Medical University (Beijing, China) waived the requirement of informed consent for the other 4 patients (cases 1, 2, 3 and 5). The study was also approved by the Ethics committee of Beijing You'an Hospital Affiliated to Capital Medical University (Beijing, China). The present study was a retrospective study. Clinical data were collected from medical records of eligible patients who had been hospitalized in our hospital. Patients who were diagnosed with PV and NCPH and treated in Beijing You'an Hospital, Capital Medical University (Beijing, China) between January 2010 and March 2022 were included into the present study. The patient's hospitalization information was collected from the hospital's medical record database, and the patient's

examination data, including laboratory blood test and imaging data, were collected from the electronic medical record system of Beijing You'an Hospital Affiliated to Capital Medical University (Beijing, China). The specific data were collected from the medical record management center of our hospital. The collected data do not involve patients' names and other privacy information.

Competing interests

The authors declare that they have no competing interests.

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