# Obstruction of the biliary tract as a rare presentation of acute myeloid leukemia: A case report

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**Abstract.** To investigate the clinical characteristics of acute myeloid leukemia (AML) with biliary obstruction as the first manifestation and explore the treatment options. A retrospective analysis was performed on a case of AML with biliary obstruction as the first manifestation admitted to the First Affiliated Hospital of Jishou University (Jishou, China). The relevant laboratory examination, imaging, pathological results and treatment strategies were analyzed. The patient was a 44-year-old male with an initial manifestation of biliary obstruction. Combined with the results of laboratory tests and bone marrow aspiration, the patient was diagnosed with AML and was treated with an IA regimen (idarubicin 8 mg d1-3, cytarabine 0.2 d1-5). After 2 courses of treatment, complete response was achieved, the liver function returned to normal and the biliary obstruction disappeared. The initial symptoms of AML are varied, and always combine with multi-system organ damage. Early diagnosis and active treatment of primary diseases are the keys to improving the prognosis of these patients.

## Introduction

Acute myeloid leukemia (AML) is a common hematopoietic tumor involving myeloid precursor cells. It is characterized by clonal proliferation, decreased number of mature cells, and invasion of multiple tissues and organs. AML accounts for nearly 70% of acute leukemia (AL) cases. Common clinical manifestations include fever, anemia, thrombocytopenia, and secondary infection. Gastrointestinal infiltration is present at diagnosis in some patients but a biliary obstruction is rare (1). The characteristic karyotype in acute myelomonocytic leukemia with eosinophilia (M4E0) is inv(16). In general, inv(16) is a marker of good prognosis. In this case, AMML (M4E0) could be diagnosed, accompanied by inv(16)(p13q22) and biliary infiltration with poor prognosis, which is rare in such cases. In the present case, the patient developed biliary obstruction. After 2 cycles of the IA regimen chemotherapy, bone penetration was perfected again, indicating complete remission, and the transaminase and bilirubin levels returned to normal. A case of AML with biliary obstruction as the first manifestation was treated in our hospital, and the treatment effect was good. Below we report the details of this case.

## Case report

A 44-year-old male patient was admitted to the Department of Gastroenterology of our hospital with poor appetite, nausea, and icterus for more than 20 days. Physical examination showed an anemic appearance, icterus in skin mucosa and sclera, and limited movement of the spine. Preliminary diagnosis of jaundice etiology by gastroenterology suggested acute icteric hepatitis or obstructive jaundice. Relevant laboratory examination (Table I).

Color Doppler ultrasonography of the abdomen showed the following results (Fig. 1A, B): 1. enhanced liver parenchyma echo and thick light spot, indicative of cholestatic liver disease; 2. the intrahepatic and extrahepatic biliary systems were extensively dilated, indicating the possibility of distal common bile duct obstruction; 3. sand-like stones of the gallbladder, and 4. splenomegaly. Enhanced CT scan of the whole abdomen yielded the following observations (Fig. 2A, B): 1. enlarged gallbladder indicative of possible cholecystitis; 2. the intrahepatic and extrahepatic bile ducts were dilated, and distal common bile duct stones were suspected. Additionally, endoscopic retrograde cholangiopancreatography (ERCP) was performed in May 2019 and was unsuccessful because the patient had a history of ankylosing spondylitis and could not cooperate in maintaining his position. Subsequently, magnetic resonance cholangiopancreatography (MRCP) was performed in May 2019 and the following was observed (Fig. 2C.a, C.b): 1. middle and lower segments of the common bile duct were resected for unknown reasons; 2. gallbladder enlargement and cholecystitis; 3. atrophy of the left kidney, lymph nodes at the posterior edge of the pancreatic head, and bilateral renal cysts. The interval between abdominal color Doppler ultrasound and

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*Key words:* acute leukemia, biliary obstruction, neuroblastoma RAS viral oncogene homolog gene mutations, inv(16)(p13q22)

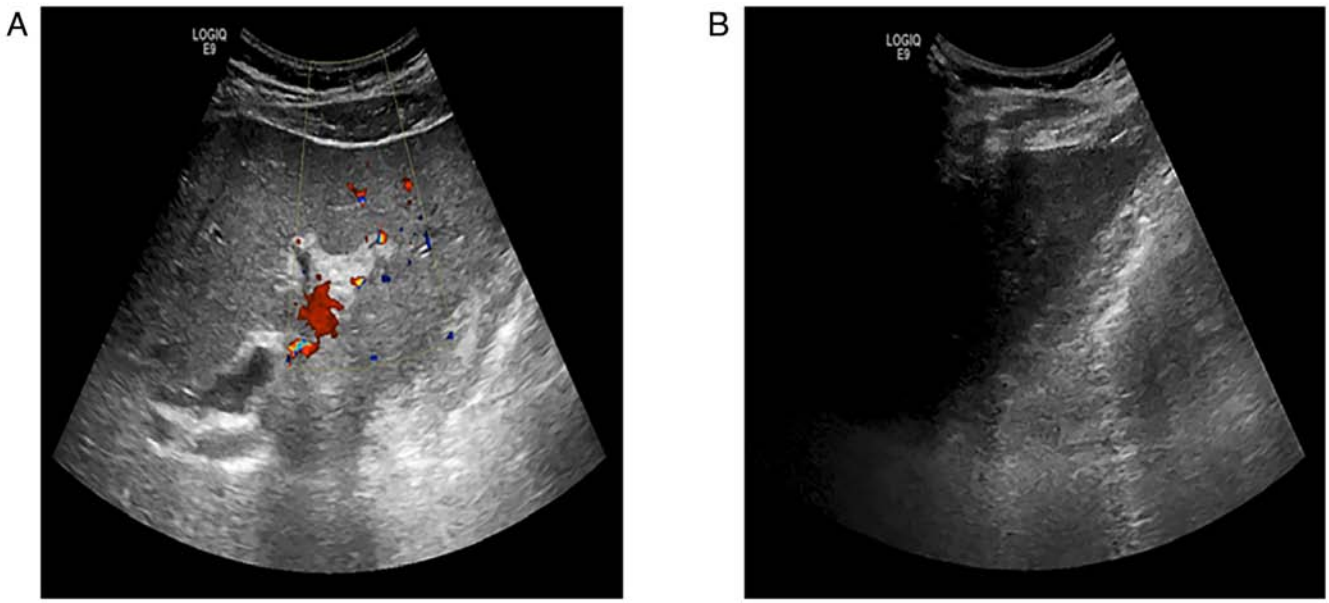


Figure 1. (A and B) Observations from color Doppler ultrasonography of the abdomen. (A) Enhanced liver parenchyma echo and thick light spot were observed, indicative of cholestatic liver disease and the intrahepatic and extrahepatic biliary systems were extensively dilated, indicating the possibility of distal common bile duct obstruction. (B) Sand-like stones in the gallbladder and splenomegaly were observed.

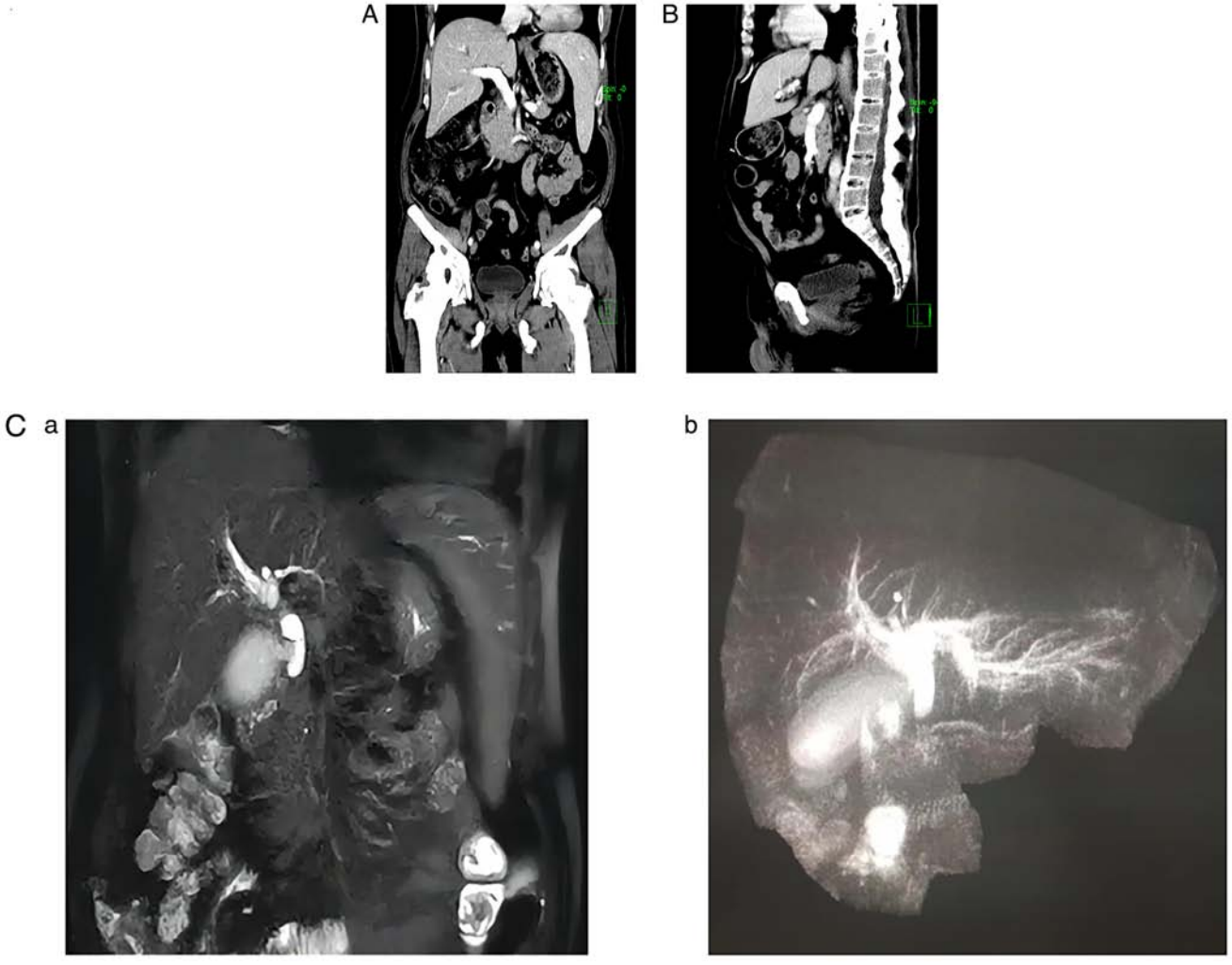


Figure 2. (A and B) Observations from enhanced computed tomography scan of the whole abdomen. (A) The intrahepatic and extrahepatic bile ducts were dilated, and distal common bile duct stones were suspected. (B) Enlarged gallbladder indicative of possible cholecystitis. (C-a and C-b) Observations of magnetic resonance cholangiopancreatography. (C-a) Middle and lower segments of the common bile duct were resected for unknown reasons. Atrophy of the left kidney, lymph nodes at the posterior edge of the pancreatic head and bilateral renal cysts. (C-b) Gallbladder enlargement and cholecystitis.

Table I. Laboratory test results.

| Project | Laboratory test value | Normal range |
|---|---|---|
| White blood cell, /l | $2.43x10^9$ | $4.0\text{-}10x10^9$ |
| Hemoglobin concentration, g/l | 99.00 | 120.00-160.00 |
| Fibrinogen content, g/l | 4.15 | 2.00-4.00 |
| Aspartate aminotransferase, U/l | 128.00 | 0.00-40.00 |
| Direct bilirubin, $\mu$mol/l | 199.60 | 0.00-6.80 |
| Cholinesterase, U/l | 3979.00 | 4000.00-11000.00 |
| γ-glutamyltransferase, U/l | 291.00 | 0.00-50.00 |
| A/G | 1.20 | 1.50-2.00 |
| Sodium, mmol/l | 146.00 | 135.00-145.00 |
| Ceruloplasmin, g/l | 0.33 | 104.00-245.00 |
| Red blood cell, /l | $3.02x10^{12}$ | $4.00\text{-}5.50x10^{12}$ |
| Platelet count, /l | $51.00x10^9$ | $100.00\text{-}300.00x10^9$ |
| Alanine aminotransferase, U/l | 208.00 | 0.00-40.00 |
| Total bilirubin, $\mu$mol/l | 228.50 | 3.40-20.50 |
| Indirect bilirubin, $\mu$mol/l | 28.90 | 0.00-18.00 |
| Alkaline phosphatase, U/l | 437.00 | 39.00-117.00 |
| Albumin, g/l | 33.20 | 35.00-55.00 |
| Blood glucose, mmol/l | 16.92 | 3.89-6.11 |
| Chloride, mmol/l | 112.00 | 96.00-106.00 |
| Urine bilirubin, $\mu$mol/l | 2.00+ | - |

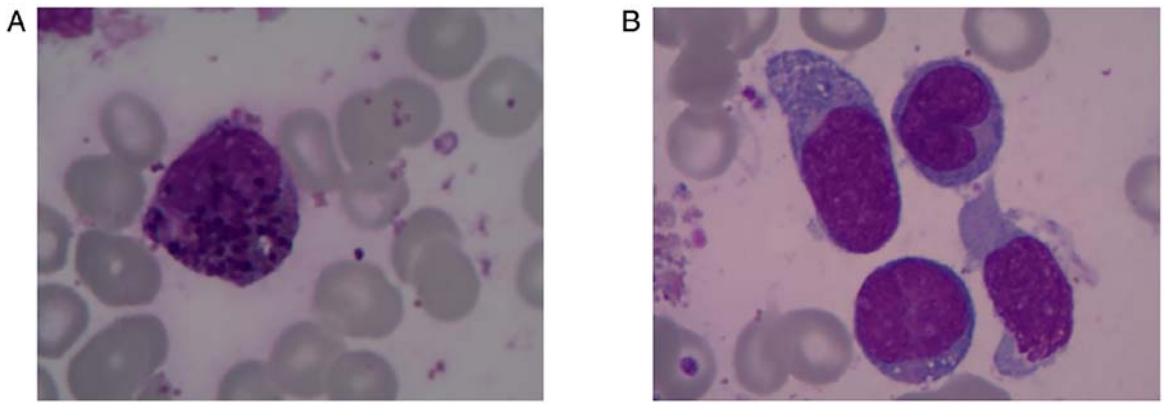


Figure 3. (A) Peripheral blood cell morphology revealed myeloid blasts at 45%. (B) Bone marrow smear cytology showed that myeloid blast cells accounted for 55%, and Auer bodies were seen in some cells.

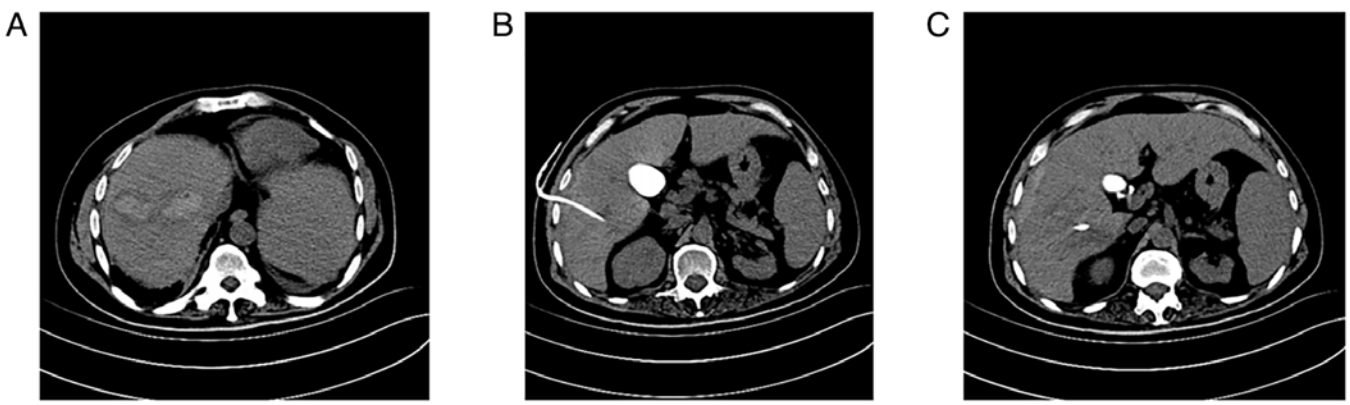


Figure 4. (A) After repeated reviews, abdominal cavity hemorrhage was gradually absorbed and the size of the intrahepatic hematoma was found to decrease. (B and C) After the operation, multiple intrahepatic hematomas and intra-peritoneal hemorrhages were found.

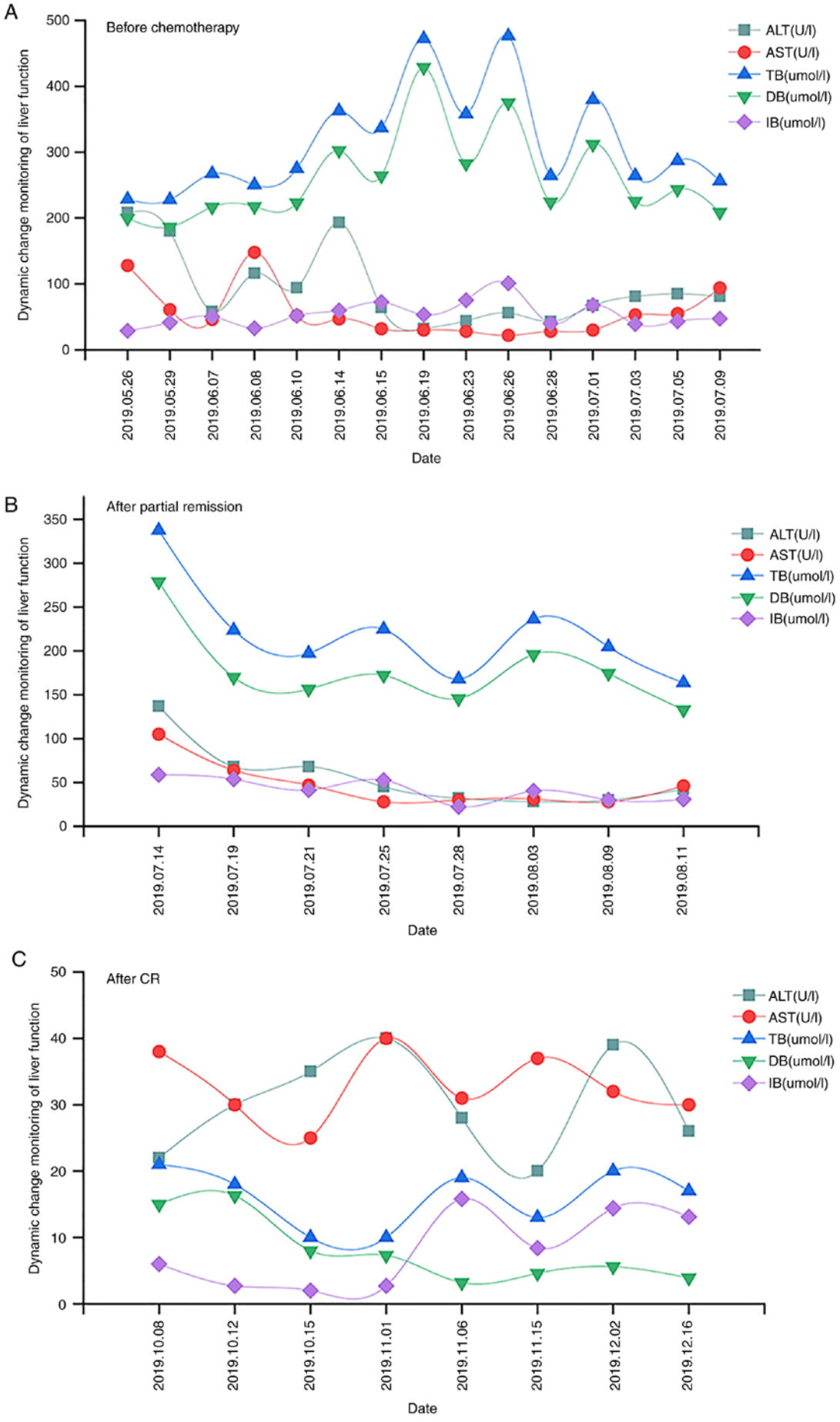


Figure 5. Conditions of liver function liver function test (A) before chemotherapy, (B) after partial remission, and (C) after CR. (A and B) Liver function after partial remission was better compared with that before chemotherapy. (C) Liver function basically returned to normal after CR. CR, complete remission.

enhanced CT was 1 week, and the interval between abdominal color Doppler ultrasound and MRCP was 2 weeks.

Given pancytopenia, the patient was referred to the Department of Hematology, and a bone marrow aspiration was performed in May 2019. The relevant examination results were as follows: peripheral blood cell morphology revealed myeloid blasts at 45% (Fig. 3A). Bone marrow smear cytology showed that myeloid blast cells accounted for 55%, and Auer bodies were seen in some cells (Fig. 3B). NRAS gene mutation was detected, with a mutation frequency of 33.7% (1683X). Karyotype analysis showed 46, XY, inv(16)(p13q22), and inversion of chromosome 16 in the analyzed cells. Flow cytometry results were consistent with the immunophenotype of AML (non-M3). The results of flow cytometry showed that CD117+ cells accounted for about 45.36% of the total nuclear cells, with an immunophenotype of CD34+, CD117+, HLADR+, CD33+, CD13+, CD7-, CD10-, CD11b-, CD14-, CD16-, CD19-, and CD56-. The relative proportion of monocytes increased and accounted for 12.91%. The immunophenotype of monocytes was CD34-, CD117-, CD11b+, CD13+, CD14+ part, CD15+ part, CD33+, CD36+, and CD64+.

Combined with the results of the above auxiliary examinations, the patient was definitively diagnosed with AML (M4E0). Since the liver function did not obviously improve in the patient, a puncture through the liver and gallbladder main drainage was performed on June 6. After the operation, multiple intrahepatic hematomas and intra-peritoneal hemorrhages were found (Fig. 4A, B, C). After several review exceeds, abdominal cavity hemorrhage was gradually absorbed and the size of the intrahepatic hematoma was found to reduce. On June 11, the patient began to receive an IA regimen (idarubicin 8mg from day 1 to day 3, cytarabine 0.2 from day 1 to day 5), and palonosetron injection for the prevention and treatment of emesis. After surgery, the patient entered the myelosuppression stage and received an active blood transfusion, plasma exchange, blood raising, and anti-infection treatment. The patient had no severe active bleeding, no obvious fever, and no cough. The first cycle of chemotherapy was completed on July 5, 2022. A bone marrow biopsy at our hospital showed hypoplasia. A small sample was taken, and about 0.5% of blasts were visible on the blood smear along with 1% of blasts. Bone marrow biopsy in our hospital showed reduced proliferation. In a small sample, about 0.5% of blasts could be seen, and 1% of blasts could be seen in blood slides. Flow cytometry showed that about 0.44% of myeloid blasts in bone marrow were CD34+, CD117+, CD13+, CD33+, HDA-DR+, CD10-, CD11b-, CD14-, CD19-, CD56-, and CD64+. Taken together, a partial response was suggested. Liver function was re-examined (Fig. 5B) and was found to be better than that before chemotherapy (Fig. 5A). The patient received the second cycle of the IA regimen (idarubicin 8 mg from day 1 to day 3, cytarabine 0.2 mg from day 1 to day 5) on July 18, 2019. The re-examination of the bone marrow biopsy (Fig. 6) after the end of chemotherapy showed CR, and the liver function returned to normal (Fig. 5C).

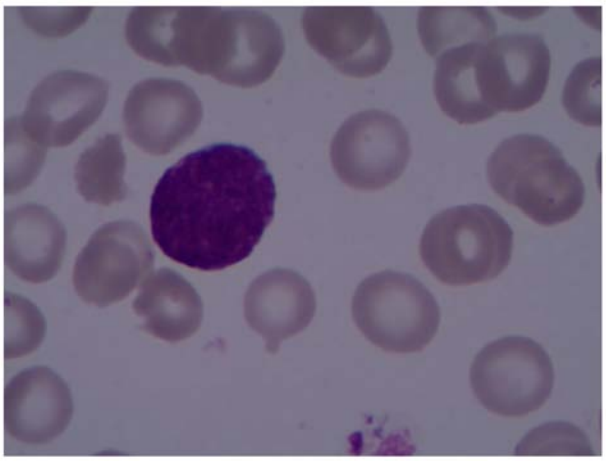

Figure 6. Re-examination of the bone marrow biopsy after the end of chemotherapy showed complete remission.

## Discussion

The characteristic karyotype in acute myelomonocytic leukemia with eosinophilia (M4E0) is inv(16) (1,2). Pulikkan and Castilla (3) have confirmed that the molecular result of inv(16) was the fusion gene of CBFβgene in the long arm of chromosome 16 and MYH11 gene in the short arm, and some foreign studies have also been reported (4) with the appearance of the fusion gene as a marker of good prognosis. In this case, AMML (M4E0) could be diagnosed, accompanied by inv(16)(p13q22) and biliary infiltration with poor prognosis, which is extremely rare in such cases.

In this case, the patient developed biliary obstruction. After 2 cycles of the IA regimen (idabicin, 8 mg d1-3; cytidine 0.2 d1-5) chemotherapy, bone penetration was perfected again, indicating complete remission, and the transaminase and bilirubin levels returned to normal. Abdominal B-ultrasound showed no biliary obstruction. Therefore, we considered that the patient's biliary obstruction might be caused by extramedullary infiltration of leukemia cells. However, myeloid sarcoma (MS) is a neoplastic mass formed by immature myeloid cells in the extramedullary position with a low incidence and is more common in children and adolescents (5,6). Studies have shown that (7-10) MS mainly accumulates connective tissue/soft tissue, and the involvement of the biliary tract is extremely rare. Although inv(16) is a marker of good prognosis, it has been reported (11) that extramedullary infiltration is also likely to occur in the presence of hyperleukocytes, thrombocytopenia, or gene mutation, mostly in the central nervous system. However, the patient had an NRAS gene mutation. Previous studies (12,13) have found that NRAS mutation mostly occurs in codon 61, and the amino acid encoded by the codon constitutes the action site of Ras protein and GTPase activating protein (GAP). The mutation led to a state of continuous activation of RAS-GTP, thus causing malignant cell proliferation and metastasis. Therefore, biliary infiltration may occur when inv(16) is combined with NRAS gene mutation.

After the diagnosis is clear, the patient generally needs to undergo chemotherapy but at present, almost all chemotherapy drugs have toxic side effects on the liver. In this case, the patient's liver function was seriously abnormal. We needed to avoid further liver function damage while undergoing chemotherapy. Therefore, based on clinical practice, percutaneous transhepatic cholangial drainage (PTCD) was performed to relieve jaundice and prevent further liver function. PTCD is a technique

for (14) percutaneous transhepatic placement of a catheter in the biliary tract by imaging. PTCD is the preferred treatment for many biliary diseases and is often applied for (14,15) malignant biliary tumors for palliative care, acute suppurative cholangitis for biliary decompression, preoperative preparation for biliary diseases, and other hepatobiliary surgery diseases. In this case, the liver function of the patient was seriously impaired before chemotherapy. After timely PTCD was performed to reduce jaundice and improve liver function, good results were achieved in chemotherapy. Therefore, we believe that for biliary obstruction caused by leukemia invasion, PTCD should be performed before chemotherapy. Simultaneously, abdominal and abdominal color Doppler ultrasound was reviewed timely after the operation to evaluate whether there was abdominal bleeding and hematoma formation.

Overall, we present a rare case report of AML involving the biliary tract and found that biliary drainage in combination with chemotherapy may prove a viable strategy for the treatment of leukemia biliary obstruction. Although inv(16) is a marker of good prognosis in the present study, extramedullary infiltration is also prone to occur in the presence of hyperleukocyte, thrombocytopenia, or gene mutation. AML is relatively common clinically, with diverse initial symptoms, and often complicated with multi-system organ damage. We should pay attention to whether it is caused by the primary disease. Active treatment of the primary disease is the key to a good prognosis for these patients.

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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**

SKT, ML, HJF, XLL and KS conceived and designed the study. SKT, ML, HJF and ZWS collected and interpreted all relevant clinical and laboratory data. SKT, ML, HJF, ZWS, XLL and KS prepared the manuscript. XLL and KS revised the manuscript. All authors read and approved the final manuscript. SKT, ML, HJF, ZWS, XLL and KS confirm the authenticity of all the raw data.

**Ethics approval and consent to participate**

Not applicable.

**Patient consent for publication**

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

**Competing interests**

The authors declare that they have no competing interests.

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