Dear Editors and Reviewers:

Thank you for your precious comments and advice. Those comments are all valuable and very helpful for revising and improving our paper（manuscript NO:87260）.We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in yellow highlight in the manuscript. The main corrections in the paper and the responds to the reviewer's comments are as following:

Comment 1: "*The patient, a 12-year-old female, presented with a medical history of recurring respiratory infections and hemoptysis. Upon diagnosis, Abernethy malformation was identified, as confirmed by chest computed tomography (CT) revealing bronchial dilatation. Notably, the physician's attention was drawn to the presence of splenomegaly during the progression of the disease. The enhanced CT of the abdomen showed tortuous and dilated splenic vessels, irregular liver morphology, and pancreatic atrophy, which was considered a possible Abernethy malformation. Intraoperatively, the abnormal blood flow was seen to merge into the inferior vena cava through the left renal vein without hepatic processing*" This part of the abstract needs to be re-written to clarify the sequence of clinical suspicion and detailed diagnosis of the case.

Response: We are grateful for the suggestion. we have re-written this part according to the Reviewer's suggestion. A 12-year-old girl presented with a medical history of recurring respiratory infections and hemoptysis, and chest computed tomography (CT) showed bronchiectasis. Whole exome sequencing was performed for the patient, yielding findings that revealed a compound heterozygous variant of the CFTR gene: c.233_c.234insT/p.Trp79fsTer3 (maternal origin); c.2909G>A/p.Gly970Asp (paternal origin). CF was diagnosed. The physician's attention was drawn to the presence of splenomegaly during disease progression. Abdominal enhanced CT revealed splenomegaly, compression of the left kidney, and multiple tortuous dilated vascular shadows were seen at the splenic hilum, which flowed back into the left renal vein and portal vein, suggesting Abernethy malformation type II. Intraoperatively, the abnormal blood flow was seen to merge into the inferior vena cava through the left renal vein without hepatic processing, and the pathology of liver biopsy showed hypoplastic, dilated or absent portal vein branches, both of which supported the diagnosis of Abernethy malformation type II. This represents the initial documented instance of Abernethy malformation accompanied by a CFTR gene mutation in the existing body of literature.

Comment 2: The conclusion in ABSTRACT section needs to be re-written as well to conclude what the authors actually reported in their case. "*Children who have Abernethy malformation in combination with CF are exceptionally uncommon in clinical cases and necessitate a detailed clinical history, as well as comprehensive laboratory and imaging assessments, in order to augment the precision of the diagnosis.*"

Response: We agree with the comment. We have re-written the sentence in the revised manuscript as the following: Coexisting Abernethy malformation and CF are rare. Detailed medical history information, abdominal enhanced CT, venography and genetic testing contribute to diagnosis as well as differential diagnosis.

Comment 3: In the Case Summary, the part on Laboratory data is very irrelevant to the case :"*Laboratory test findings were as follows: Blood routine: WBC 3.28×10^9/L, PLT 84×10^9/L; fecal occult blood: negative; blood biochemistry: ALT 28.0 U/L, AST 38.0 U/L, CK-MB 15.0 U/L; serum thyroid function test:TT3 2.33mmol/L, FT3 6.22pmol/L. FT3 6.22pmol/L, TT4 97.58mmol/L, FT4 16.61pmol/L; sputum culture: positive for mycoplasma antibodies; bone marrow aspiration: partial dilution bone marrow image; the four tumor tests : AFP 1.66ng/m, CEA 1.63ng/mL, NSE 10.87ng/mL, CA19-9 90.95↑ng/mL; fiberoptic bronchoscopy alveolar lavage: numerous erythrocytes and inflammatory cells, 74% neutrophils,6% lymphocytes,20% macrophages were seen.*" Lab results have to be relevant to the case. The most relevant is sputum culture which showed mycoplasma antibodies!!!

Response: We are very sorry for our incorrect writing. The correct expression is as follows: positive for mycoplasma antibodies; sputum culture: Pseudomonas aeruginosa; bone marrow smear: normal proportions and morphology of the erythroid, myeloid, megakaryocytic, and lymphoid populations; This part of the laboratory test is related to the diagnosis or differential diagnosis of Abernethy malformation and CF. The child had splenomegaly, and the peripheral blood count showed thrombocytopenia, which needed to be differentiated from haematological neoplastic diseases, so the tumour indicators were detected, and the bone marrow aspiration was performed. CF and Abernethy malformation may lead to liver function damage, and liver function damage may lead to coagulopathy， so tests of liver function and coagulation function are required. The child had recurrent respiratory tract infections and haemoptysis, so fibrinoscopic alveolar lavage was performed. Similarly, respiratory pathogenetic testing was required. Thyroid function results were removed.

Comment 4: Abdominal ultrasound and Doppler study are messed up; results of abdominal imaging needs to be written in a clearer way to be able to reach such a diagnosis as Abernathy malformation. "*Ultrasound of portal vein system:internal diameter of main trunk of portal vein 8mm, maximum flow velocity: 19.3cm/s, slightly tortuous, splenic vein the internal diameter of the splenic vein was 11 mm, with tortuous course and slowed flow velocity, and tortuous vascular echogenicity was seen around the stomach base. The whole abdomen was enhanced with CT (Figure 1C、1Dand 1E):plenomegaly, multiple tortuous dilated vessels at the splenic hilum, irregular liver morphology, and pancreatic atrophy*".

Response: We have made correction according to your comments. Ultrasound of the portal venous system showed that the internal diameter of the main trunk of the portal vein was 8 mm, with a maximum blood flow velocity of 19.3 cm/s, and a slightly tortuous course. The internal diameter of the splenic vein was 11 mm, with a tortuous course, slowed blood flow velocity, and tortuous vascular echoes around the fundus of the stomach, suggesting that the portal vein had a slightly tortuous course, and the splenic vein was thickened with a tortuous course. The whole abdomen was enhanced on CT imaging (Figure 1C–1E). The liver was irregular in shape, with a large caudate lobe and no abnormal density shadows in the parenchyma. The gallbladder was not significantly abnormal in shape or size, and no abnormal density shadows were seen. The spleen was enlarged, the left kidney was compressed, and multiple tortuous dilated vascular shadows were seen at the

splenic hilum, which flowed back into the left renal and portal veins. The pancreas was morphologically atrophic but no obvious abnormal density was seen. The findings were suggestive of splenomegaly and multiple tortuous dilated vessels at the splenic hilum, irregular liver morphology, and atrophy of the pancreas.

Comment 5: In the Treatment section, the diagnosis and management are messed up: a diagnosis has to be made before an intervention is done.

Response: This child had been diagnosed with Abernethy malformation type II and CF prior to surgery. The diagnosis of CF was determined through an analysis of medical history, chest CT, and whole exon gene detection. Abdominal enhanced CT supported the diagnosis of Abernethy malformation type II. Venography was performed during the procedure, and the findings support the diagnosis of Abernethy malformation type II. Some tissues of the liver were taken for pathological examination during the operation. Pathological analysis showed that portal vein branches were dysplastic, dilated or absent, which was consistent with Abernethy malformation type II.

Comment 6: Re=phrasing is needed for this part to delineate the abnormal anatomy revealed in this child: "*The intraoperative venography and postoperative pathology confirmed portal vein dysplasia, and the anomalous blood flow was unprocessed by the liver through the left renal vein into the inferior vena cava, which supported the diagnosis of Abernethymalformation type II. This abnormal shunt caused elevated portal vein pressure, tortuous changes in the splenic vessels, and varicose veins of the fundus, but did not present with vomiting or lower gastrointestinal bleeding*."

Response: We have made correction according to the Reviewer's comments. Intraoperative venography showed multiple tortuous dilated vessels in the splenic hilum, abnormal blood flow into the inferior vena cava through the left renal vein, and portal vein branches and side branches were present, which supported the diagnosis of Abernethy malformation type II.

Comment 7: The explanation of splenomegaly in the Discussion section is unclear : "*There is evidence suggesting a potential association between Abernethy malformation and cystic fibrosis (CF) with the occurrence of splenomegaly. However, the underlying mechanisms differ, with Abernethy malformation being attributed to inadequate blood return to the splenic vein, and CF being associated with congenital dysplasia[10-12]. Therefore, it is hypothesized that the splenomegaly observed in this child is a result of a combination of both diseases.*" What is "congenital dysplasia", what is "inadequate blood return to splenic vein?"

Response: We are grateful for your suggestion. We have re-written this part according to your suggestion. There is evidence suggesting a potential association between Abernethy malformation and CF with the occurrence of splenomegaly. Abernethy malformation results in splenomegaly due to obstruction of blood return from the splenic vein as a result of portal vein hypoplasia and

abnormal blood shunting. CF is a monogenic disorder resulting from mutations in the CFTR gene, which encodes the epithelial ion channel responsible for the transportation of chloride and bicarbonate ions. These mutations lead to impaired mucus hydration and clearance, resulting in the obstruction of lumens of the respiratory, pancreatic, and biliary tracts, as well as abnormal secretion from exocrine glands[10]. Cystic fibrosis liver disease (CFLD) frequently manifests with hepatic steatosis, cholestasis, and progressive cirrhosis, leading to portal hypertension and subsequent splenomegaly[11,12]. Additionally, noncirrhotic portal hypertension can arise in CFLD, potentially attributed to inflammatory and fibrotic paracaval portal vein lesions[13]. Therefore, it is hypothesized that the splenomegaly observed in this child was a result of a combination of both diseases.

Comment 8: Is it the aim of this case summary to emphasize the importance of differentiation in history taking between hematemesis and hemoptysis? "*Patients with Abernethy malformation accompanied with upper gastrointestinal varices may have hematemesis after food stimulation, and CF may also have massive hemoptysis due to bronchiectasis. When inquiring about the history, it is imperative to exercise caution in accurately identifying the two conditions.*"?

Response: Thank you for your comments. Because Abernethy malformation combined with CF is very rare, we wanted to enhance clinicians' knowledge and understanding of both diseases through the case report. Differentiation in history taking between hematemesis and hemoptysis is one of our recommendations. I am sorry that we failed to express the conclusion clearly in the first draft. Your suggestion inspired us, so we have rewritten the conclusion: Coexisting Abernethy malformation and CF are rare. In cases where patients present with unexplained thrombocytopenia, splenomegaly, and hypersplenism, it is advisable to use enhanced abdominal CT to detect Abernethy malformation. In instances where children exhibit symptoms such as hemoptysis, recurrent respiratory infections, and bronchiectasis, it is crucial to raise awareness regarding the possibility of CF, and genetic testing may be conducted to establish a conclusive diagnosis. The co-occurrence of Abernethy malformation and CF is a clinically infrequent phenomenon that necessitates a detailed clinical history, as well as comprehensive laboratory and imaging evaluation to improve diagnostic accuracy.

We tried our best to correct grammatical and expressive errors to improve the manuscript. We appreciate for Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.