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Rare Case of Pralsetinib-Induced Chylous Ascites: A Case Report of a Young Woman

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1. Abstract

The observation of adverse drug reactions is still a problem that needs continuous attention, although the drug has been marketed. Because it is related to the drug safety of patients. Pralsetinib, as a new RET inhibitor, has been approved for the treatment of lung cancer, but due to the low RET mutation rate, the small number of enrolled cases in clinical studies, and the short clinical marketing time, the observation of adverse events is not comprehensive. Here, we discuss a case of pralsetinib-induced chylous ascites in a 30-year-old female patient with RET-fusion-positive NSCLC.

2. Background

The observation of adverse drug reactions is still a problem that needs continuous attention, although the drug has been marketed. Because it is related to the drug safety of patients. Pralsetinib, as a new RET inhibitor, has been approved for the treatment of lung cancer, but due to the low RET mutation rate [1], the small number of enrolled cases in clinical studies, and the short clinical marketing time, the observation of adverse events is not comprehensive. Spontaneous chylous effusions are rare,however, they have been observed by independent investigators in patients treated with RET tyrosine kinase inhibitors (TKIs). However, none of these were observed with pralsetinib [2], the exact pathophysiology of this rare occurrence remains unclear. Here, we discuss a case of pralsetinib-induced chylous ascites in a 30-year-old female patient with RET-fusion-positive NSCLC.

3. Case Presentation

A 29-year-old female who underwent right salpingectomy and left tubal ligation in 2019 for an ectopic pregnancy was admitted to our hospital with the complaint of progressive dyspnea in July 2021(Figure 1A). She had been diagnosed with non-small cell lung cancer (adenocarcinoma, T4N3M1c), metastatic malignant tumor located in the pericardium, bilateral pleura, cervical lymph node, and abdominal lymph nodes, and the results of the tissue genetic tests were CCDC6 (Exon1)-RET(Exon12-20) fusion. She received pralsetinib orally at doses of 400 mg once daily from August 2021, and received follow-up every 3-5 months. The response was assessed as partial (Figure 1B). From February to March 2022, the dose was reduced by 200–300 mg/day owing to adverse reactions (diarrhea), and diarrhea continued after the dose reduction. In April 2022, oral administration of 400 mg/day continued.

A follow-up six months later (October 2022) revealed fluid accumulation in the abdomen (Figure1C), which was drained under ultrasound guidance to reveal hylous fluid (Figure 2A). Biochemical analysis of the abdominal fluid revealed exudative effusion, with a triglyceride level of 8.86 mmol/L(785 mg/dl) (Table 1). Thorough blood investigations and abdominal fluid cytology results were noncontributory to the etiology of chylothorax. Tumor cells were not detected by cytological examination of ascites, abdominal CT tomography showed that the abdominal metastatic lymph nodes were smaller than the anterior, and peritoneal dissemination was not observed.

Furthermore, PET-CT failed to identify any features of abdominal tumor progression. Although focal radioconcentration was observed in the left pelvic cavity (SUVmax=10.5), physiological metabolism of the ovaries was considered, hyle leak or blockage was not identified via lymphangiography, and developer uptake was not observed in the abdominal effusion (Figure 2B). After a multidisciplinary discussion, the patient was advised to stop taking Pralsetinib orally, 2 weeks after of discontinuation, the ascites did not regrow. To control the disease, pralsetinib was initiated with a dose reduction of 200 mg/day. Chest and abdominal CT examinations 8 months later showed that the lung tumor was stable and there was no abdominal fluid (Figure 1D); the patient's condition was stable and his daily life was not affected.

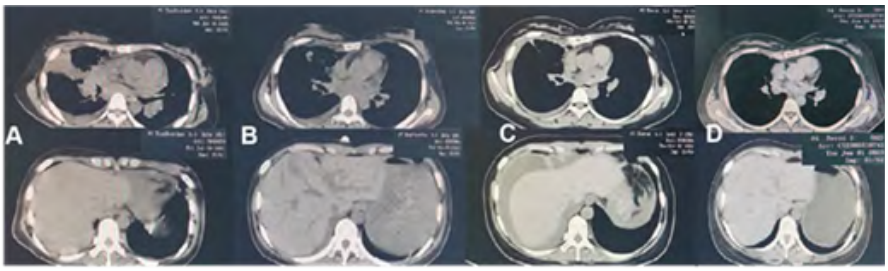

Figure 1:

A: 2021.7 CT of the chest and abdomen at the time of the first discovery of lung cancer shows lesions in the middle lobe of the right lung without abdominal effusion.

B: 2021.9 One month after oral administration of pralsetinib, reexamination showed that the primary lesion was smaller than before, and there was no abdominal fluid.

C: 2022.10 fter 14 months of oral pralsetinib, the lung lesions were smaller than before, but there was abdominal fluid.

D: 2023.6 Four months after the reduction of pralsetinib, the pulmonary lesions were stable and the abdominal fluid was obviously absorbed

Table 1: Characteristics of ascites

Laboratory data	
Triglyceride (mmol/L)	8.86
Cell count (× 10^6/L)	750
Total protein (g/L)	55.7
Total cholesterol (mmol/L)	2.95
Lactate dehydrogenase (U/L)	44.5
Ascites/serum ratio of albumin gradient	0.73

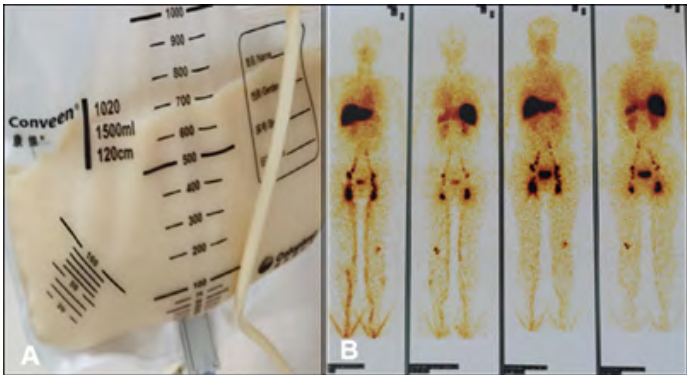

Figure 2:

A: The abdominal fluid is chylous

B: Lymphangiography showed no lymphatic leakage and no developer for abdominal effusion

4. Discussion

Chylous ascites is rare and is characterized by triglyceride-rich peritoneal fluid [3]. Chylous ascites is caused by thoracic duct obstruction or disruption (trauma/surgery, infections, radiotherapy, autoimmune disease), or increased lymph production (cirrhosis, cardiovascular disease). Invasion and disruption of the normal lymph flow (lymphomas, neuroendocrine tumors, sarcomas, leukemia, solid organ malignancies) is also the cause of chylous ascites. We performed tests to determine whether chylous ascites were due to disease progression or other diseases. Cytological examination of the ascites was negative in the present case, and there was a low probability that peritoneal dissemination of the lung cancer had occurred. In addition, her liver function was normal, and chyle leak or blockage was not discovered on lymphangiography despite she had undergone surgery of the fallopian tube.

According to the above examination results, we have no evidence to prove that chylous ascites is caused by disease, so we consider whether it is a drug-related adverse reaction. The literature reported, chylous effusions can emerge during treatment with selected RET TKIs, such as selpercatinib, agerafenib, cabozantinib, and lenvatinib, but none have been observed with pralsetinib [2]. Finally, we decided to observe the changes of the patient's chylous abdomen by stopping the drug, and the result was that the patient's chylous abdomen was quickly controlled after stopping the drug. Due to the effectiveness of RET inhibitors, we did not give up this drug, and decided to decrease the dose in order to achieve a balance between drug efficacy and side effects. Fortunately, at present, the patient was taken pralsetinib 200mg/ day, and there was neither chylous ascites nor tumor progression. To our knowledge, this is the first case of chylous abdominal fluid in a patient treated with prasetinib, and there is no evidence to prove that chylous effusion was the result of disease progression. The mechanism of chylous effusion development in patients treated with RET inhibitors is a pivotal unanswered question. The same is true for other TKI/MKI drugs, as far as we know, there are only 11 dasatinib-related chylothorax and one Pazopanib-induced chylothorax that have been published in the scientific literature, and the mechanism is also unclear [4, 5].

Although relatively comprehensive observation of adverse events has been carried out before the drug is marketed, many adverse events will be continuously observed after the drug is marketed due to various factors such as the time of observation and administration and the complexity of the human body. The observation and timely report of these adverse events will help improve the vigilance of doctors. So that the patient's pain can be found in time and be well handled.

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