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A rare case of hematologic peritonitis complicating secondary myelofibrosis

(Un Un cas rare d'une péritonite hématologique compliquant une myélofibrose secondaire)

Charlotte Gabilan, Marie-Béatrice Nogier, Clotilde Gaible, Hélène El Hachem

Département de Néphrologie et Transplantation d'Organes, CHU de Toulouse, France

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Summary

Peritonitis is a frequent complication of peritoneal dialysis. Its diagnosis is based on clinical signs (pain, cloudy effluent), intraperitoneal hyperleukocytosis (> 0.1×10^9/L with more than 50% polynuclears), or a positive culture. Although the majority of peritonitis cases are of infectious origin, there are also cases due to non infectious origin, which can lead to the inappropriate use of antibiotics and delayed diagnosis. We report the case of a 78-year-old male patient with a complex haemopathy that combined paroxysmal nocturnal haemoglobinuria, despite treatment with ravulizumab, and essential thrombocythemia, which transformed into myelofibrosis. After the initiation of peritoneal dialysis treatment, he presented with occasionally cloudy dialysis fluid rich in leukocytes (up to 0.442 ×10^9/L), with no evidence of infection (negative cultures and DNA16S PCR, moderate CRP, and an absence of atypical cells). The origin of the intraperitoneal hyperleukocytosis was attributed to myelofibrosis-related blood hyperleukocytosis. The clinical course was unfavorable, leading to palliative management.

This case illustrates the difficulty of managing this complication in peritoneal dialysis patients. Although infectious peritonitis is the most common first-line diagnosis, it is important to consider various differential diagnoses in cases of culture-negative peritonitis, particularly hematological causes (leukemia, lymphoma, myelofibrosis). However, forms with a predominance of neutrophils in the dialysate may simulate an infection. The absence of fever, elevated CRP, and a correlation between blood and peritoneal hyperleukocytosis should help in making a differential diagnosis. Immunophenotyping or molecular biology in the dialysate could refine the diagnosis. This case highlights a possible cause of sterile peritonitis due to myelofibrosis with hyperleukocytosis, and calls for recommendations to be adapted to increasingly complex clinical situations.

Keywords: peritoneal dialysis, peritonitis, cloudy peritoneal dialysate, culture-negative peritonitis, secondary myelofibrosis

Résumé

La péritonite est l'une des complications fréquentes de la dialyse péritonéale. Son diagnostic repose sur des signes cliniques (douleur, effluent trouble), une hyperleucocytose intrapéritonéale (> 0,1×10^9/L avec plus de 50 % de polynucléaires), et/ou une culture positive. Bien que la majorité des péritonites soient d'origine infectieuse, il existe des formes d'origine non infectieuse qui peuvent entrainer un usage inapproprié d'antibiotiques et un retard diagnostic. Nous rapportons le cas d'un patient de 78 ans, atteint d'une hémopathie complexe qui associait hémoglobinurie paroxystique nocturne, malgré un traitement par ravulizumab, et une thrombocytémie essentielle transformée en myélofibrose. Après initiation d'un traitement par dialyse péritonéale, il a présenté un liquide de dialyse parfois trouble et riche en leucocytes (jusqu'à 0,442 ×10^9/L), aucune infection n'a été mise en évidence (cultures et PCR ADN16S négatives, CRP modérée, absence de cellules atypiques). L'origine de l'hyperleucocytose intra-péritonéale a été attribuée à l'hyperleucocytose sanguine liée à la myélofibrose. L'évolution clinique a été défavorable, menant à une prise en charge palliative.

Ce cas illustre la difficulté de la prise en charge de cette complication chez les patients en dialyse péritonéale. Bien que le diagnostic de première intention, par argument de fréquence, soit la péritonite infectieuse, il parait nécessaire d'évoquer les différents diagnostics différentiels en cas de péritonite à culture négative et notamment les différentes causes hématologiques (leucémies, lymphomes, myélofibrose). Cependant, les formes avec prédominance de polynucléaires neutrophiles dans le dialysat peuvent simuler une infection. L'absence de fièvre, de CRP élevée, et une corrélation entre hyperleucocytose sanguine et péritonéale devraient aider au diagnostic différentiel. L'immunophénotypage ou la biologie moléculaire dans le dialysat pourrait affiner le diagnostic. Ce cas met en évidence une cause possible de péritonite stérile, la myélofibrose avec hyperleucocytose, et invite à adapter les recommandations à des situations cliniques de plus en plus complexes.

Mots-clés : dialyse péritonéale, péritonite, dialysat trouble, péritonite à culture négative, myélofibrose secondaire

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Introduction

Peritoneal dialysis is one of the techniques used for renal replacement therapy. It is commonly used in France, although much less than hemodialysis [1]. Like any technique, it is not without complications, the most well-known of which is peritonitis [2, 3].

The diagnosis of peritonitis is based on the presence of at least two of the following [4]:
- clinical features consistent with peritonitis, i.e., abdominal pain or cloudy dialysis effluent;
- a white blood cell count in dialysis effluent > 100/μL or > 0.1 × 10^9/L (after a stasis time of at least 2 hours), with > 50% polymorphonuclear leukocytes (PMNs);
- a positive culture in the dialysis effluent.

The majority of peritonitis cases are infectious in origin, but other etiologies must be considered and investigated [5, 8]. Signs of peritonitis are usually interpreted as infectious in origin to avoid delays in treatment, which can lead to significant morbidity and mortality. However, this can lead to complications, including the excessive use of antibiotics, which risks altering the bacterial ecology and promoting antibiotic resistance; it can also lead to delayed management of the underlying disease (which may be iatrogenic, an allergy, an oncological or hematological condition, or a surgical pathology).

The recommendations for managing peritonitis [4] emphasize the need to initiate antibiotics promptly, given the potential severity of the infection; however, this recommendation must be qualified, and management must be adapted on a case-by-case basis.

Nephrology patients are often elderly, have multiple pathologies, and are on multiple medications. This presents us with a complex pattern of complications and observations, particularly in oncological and hematological contexts.

We report here a case of non-infectious peritonitis manifesting as sometimes cloudy peritoneal dialysis effluent associated with excess intraperitoneal white blood cells secondary to blood hyperleukocytosis, itself itself a consequence of a hematological disease.

Case presentation

A 78-year-old man developed stage V chronic kidney disease in the context of paroxysmal nocturnal hemoglobinuria that progressed despite treatment with ravulizumab (Ultomiris®, Alexion Pharma France) and then eculizumab (Soliris®, Alexion Pharma France).

He had a history of paroxysmal nocturnal hemoglobinuria and also essential thrombocythemia with a cytogenetic diagnosis of MPL W515L and associated DNMT3A mutation, which secondarily transformed into myelofibrosis and had been treated with hydroxyurea (Hydrea®) and ruxolitinib (Jakavi®) since 2023 (with known hyperleukocytosis at 30G/L). He also presented with flutter and high blood pressure.

He began emergency extrarenal purification by hemodialysis after placement of a right internal jugular tunneled catheter on October 28, 2024, followed by peritoneal dialysis on January 6, 2025 (after placement of a peritoneal dialysis catheter accompanied by treatment for an inguinal

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hernia on December 9, 2024). His protocol included a short exchange (4 hours) of isotonic solution (Physioneal 40® with 1.36% glucose, Baxter International Inc.) and a long exchange of hypertonic solution (Extraneal®, Baxter International Inc.) for the rest of the nycthemeral cycle. The protocol was adapted to the patient's needs, his residual renal function, and the availability of registered nurses.

On January 13, 2025, his nurses reported difficulty with drainage and that the patient was suffering from abdominal pain. He was admitted to the day hospital and underwent an exchange, which restored the drainage fluid to a clear state. However, cytological examination revealed a white blood cell count of 0.139 × 10^9/L, with 53% polynuclear cells. Blood tests showed a CRP of 8 mg/L, a hemoglobin level of 9 g/dL, and a white blood cell count of 63 × 10^9/L, with 36 × 10^9/L of polynuclear cells.

Bacteriological samples of dialysis fluid and blood were cultured. The ASP found the catheter in place but with an accumulation of fecal matter. Because of the possibility of infectious peritonitis related to peritoneal dialysis, he was given empirical intraperitoneal antibiotic treatment with cefazolin and ceftazidime (in accordance with the Toulouse University Hospital protocol). Given his stable clinical condition, the patient was discharged home.

On January 14, 2025, he was re-evaluated in consultation due to persistent abdominal pain and slightly cloudy drainage fluid. Cytological examination revealed an elevated white blood cell count of 0.197 × 10^9/L, with 51% polymorphonuclear cells. He was admitted to the nephrology department on the same day.

Physical examination on admission showed no fever, a blood pressure of 160/80, and a heart rate of 70 bpm. Cardiopulmonary auscultation was normal. The abdomen was tender with no guarding or contracture. The results of laboratory and imaging tests after admission were as follows:
- Cytological analysis of the dialysis fluid revealed a white blood cell count of 0.201 × 10^9/L, with 29% polynuclear cells.
- The effluent culture was negative, as was the 16S DNA (bacterial DNA by PCR),
-Blood te sts revealed a CRP of 4.4 mg/L, a hemoglobin level of 8.7 g/dL, and a white blood cell count of 67 × 10^9/L with a predominance of PNN.
- All blood cultures were negative.
- Computed tomography revealed parietal thickening of the colon associated with infiltration of peritoneal fat.

Given the results and despite no increase in CRP, a diagnosis of colitis without peritonitis was made, prompting a change in antibiotic therapy to intravenous tazocillin for a total duration of 7 days. The patient was discharged home.

On February 3, due to persistent asthenia, tests were performed to assess the progression of the patient's hematological disease:
- A myelogram showed poor bone marrow with hypoplasia of the erythroid lineage and moderate dysmyelopoiesis, without excess blasts.
- Lymphocyte phenotyping of the bone marrow showed no significant expansion of lymphocyte subpopulations.
- Molecular biology analysis to detect hematological disorders revealed the previously described DNMT3A mutation.

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On February 5, 2025, the patient was hospitalized due to a deterioration in his general condition and spontaneous bleeding. Physical examination on admission showed a blood pressure of 130/60 and a heart rate of 70 bpm, with no fever. Cardiopulmonary auscultation was normal. The abdomen was still tender. Drainage of PD fluid revealed it to be cloudy without fibrin. Analysis of the fluid showed a white blood cell count of 0.442 × 10^9/L, with 41% polynuclear cells. Blood tests revealed a CRP of 2.9 mg/L, a hemoglobin level of 10.2 g/dL, and a white blood cell count of 62 × 10^9/L *(Table I)*. All cultures were negative. It should be noted that none of the dialysis fluid analyses revealed any atypical cells on the slides examined. We did not perform phenotyping of the dialysis effluent, as phenotyping of the bone marrow was normal.

Table I. Evolution of clinical and biological parameters

Date	Effluent aspect	Blood WBC (x10^9/L)	CRP (mg/L)	Effluent WBC (x10^9 /L)	Effluent Neu (in %)	Effluent Baso (in %)	Effluent Lymp (in %)	Effluent Mono (in %)
13/01/2025	Clear	63	8	0.139	53	1	2	44
14/01/2025	Cloudy	NA	NA	0.197	51	1	3	45
15/01/2025	Cloudy	67	4.4	0.201	2	1	7	63
05/02/2025	Cloudy	62	2.9	0.442	41	1	2	56

WBC: white blood cells; Neu: neutrophils; Baso: basophils; Lymphs: lymphocytes; Mono : monocytes

The diagnosis was terminal hematological disease with intraperitoneal hyperleukocytosis secondary to blood hyperleukocytosis refractory to medical treatment. However, this remains a hypothesis since we did not perform molecular biology analysis on the effluent, which would have allowed us to confirm the presence of pathological cells associated with the previously described mutation.

The prognosis was poor, and the patient was shifted toward palliative care.

Discussion

Infectious peritonitis during peritoneal dialysis is a classic complication with an initially low morbidity and mortality rate, which increases significantly if treatment is delayed. Peritoneal infections are a fairly common reason for discontinuing peritoneal dialysis and switching to hemodialysis. In 2018, according to the RDPLF, 14% of such transfers were secondary to peritonitis [9].

In addition, sterile peritonitis is a common problem in patients receiving peritoneal dialysis. It is, therefore, essential to be able to diagnose and manage the various causes of peritonitis. Previous studies found peritoneal dialysate cultures to be negative in 20% of cases [10], but more recent work has found negative cultures in between 10 and 15% of cases (14.6% according to the RDPLF in 2017, and 13.7% at Toulouse University Hospital between January 1, 2020, and January 1, 2025). In these situations, it is essential first to rule out an infectious cause that

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is difficult to identify, such as mycobacteria, fungi, or parasites. It is then useful to look at the distribution of different types of cells in the dialysate sample. When the sample is predominantly composed of neutrophils, the possibility of infectious peritonitis remains, and it is sometimes difficult to justify continuing antibiotic therapy in cases of culture-negative infectious peritonitis.

However, when the white blood cells are predominantly neutrophils and an infectious cause cannot be determined, it is necessary to look for other etiologies [8], such as:
- Inflammation of intraperitoneal organs (appendicitis, cholecystitis, etc.),
- Inflammation of retroperitoneal organs (such as splenic infarction, splenic abscess, or pancreatitis) [11, 15],
- Malignant tumors of solid organs (such as renal carcinomas or endometrial cancer) [16, 19].

After reviewing the literature, we created a table *(Table II)* of possible etiologies of neutrophil-predominant leukocytosis in peritoneal dialysis fluid with a sterile culture.
Hematological causes are mainly found when the dialysis fluid is predominantly lymphocytic, with lymphoma being the most common etiology. After reviewing the literature, we found six reported cases of lymphoma diagnosed in the context of suspected peritonitis [20, 25]. The

⬇ *Table II. Possible causes of neutrophilic leukocytosis with sterile peritoneal dialysis fluid*

CATEGORY	ETIOLOGIES	PROPOSALS
Actual infection but negative culture	• Mycobacteria (TB) • Fungi (Candida, Aspergillus, Mucormycosis) • Fastidious bacteria (Brucella, Legionella) • Poor sampling of anaerobes	• Germs that are difficult to isolate: prolonged cultures or PCR often necessary
Prior antibiotic therapy	• Antibiotics started before sampling	• Antibiotic therapy window to be discussed
Technical error	• Inadequate sampling or transport • Contamination of the vial	• Repeat sampling
Chemical peritonitis	• Irritation from antiseptic (iodine, chlorhexidine) • Rupture of the dialysis bag	
Hemoperitoneum	• Secondary trauma to the catheter with digestive perforation	• Imaging • +/- endoscopy • +/- surgical management
Inflammatory or autoimmune disease	• Systemic lupus erythematosus • Vasculitis	
Inflammation of intraperitoneal organs	• Appendicitis • Cholecystitis	• Imaging
Inflammation of retroperitoneal organs	• Acute pancreatitis • Splenic abscess • Splenic infarction	• Imaging • Biology (including lipase/amylase)
Malignant tumor of solid organs/peritoneal carcinomatosis	• Renal carcinomas • Endometrial cancer • Peritoneal metastases • Lymphoma	• Imaging • +/- biopsy or excision • +/- PD effluent analysis in anatomopathology, immunophenotyping, molecular biology
Hollow organ rupture	• Perforated ulcer, diverticulitis, appendicitis	• Imaging • +/- surgical managemen
Ischemia	• Mesenteric ischemia (AMS occlusion)	• Imaging

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pathophysiological explanation is the presence of an increased number of atypical lymphocytes secondary to intraperitoneal diffusion. It is, therefore, possible that other hematological diseases may be complicated by aseptic peritonitis. However, we have not found any other cases in the current literature.

Essential thrombocythemia can, in some cases, develop into secondary myelofibrosis. The complications of secondary myelofibrosis can be divided into three groups:
- General signs including asthenia, sweating, and hyperthermia,
- Myeloproliferation, including splenomegaly and hyperleukocytosis,
- Cytopenias, including anemia and thrombocytopenia.

These complications develop at varying rates and can therefore sometimes mimic infections (particularly hyperthermia and hyperleukocytosis). In some cases, significant hyperleukocytosis is present, which is a marker of poor prognosis with a risk of resistance to ruxolitinib and unfavorable disease progression [26].

In this clinical case, we collected clinical and biological data from a patient who presented with sterile peritonitis during peritoneal dialysis. The data suggested that this peritonitis was secondary to his hematological disease, namely essential thrombocythemia with secondary myelofibrosis. However, this case shows the limitations of such a diagnosis as a first-line approach. Indeed, it is difficult not to consider infectious peritonitis when intraperitoneal leukocytes are present above the threshold considered pathological and when the percentage of neutrophils is greater than 50%. Moreover, the initial observation of the case may have been related to a digestive infection, an initial flare-up of the patient's hematological disease, or a combination of the two. It is difficult to choose between the two hypotheses. We observed that the dialysis fluid became more mixed than it was initially, which points toward a hematological cause.

When hematological peritonitis is suspected, it may be useful to perform lymphocyte immunophenotyping or molecular biology analysis of the dialysis effluent, depending on the suspected cause and diagnostic method. This could have helped us confirm the diagnosis of hematological peritonitis.

These results show that certain clinical and biological markers should alert us to seek differential diagnoses for infectious peritonitis, particularly apyrexia and the absence of associated biological inflammatory syndrome (CRP). In addition, they highlight a new possible cause of culture-negative peritonitis.

Conclusion

This observation highlights a new alternative diagnosis for sterile peritonitis, encouraging the consideration of new causes of culture-negative peritonitis. Nevertheless, physicians should remain vigilant for infectious peritonitis, which should be considered as the primary diagnosis.

Authors' contributions

ChG contributed to data collection and analysis, study design and methodology, and the writing of the original manuscript. HEH reviewed the literature and revised the manuscript. ClG and MBN performed the final review and approved the manuscript for publication.

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Ethical considerations

In accordance with ethical requirements, we specify that informed consent could not be obtained, as the study was conducted retrospectively after the patient's death.

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Conflicts of interest

No conflicts of interest to declare.

ORCID iDs
Charlotte Gabilan https://orcid.org/0009-0002-5048-7657
Marie Béatrice Nogier https://orcid.org/0000-0001-9888-2547

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