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Total Parenteral Nutrition Induced Pancytopenia: A Case Report

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Abstract **Case Report**

Total parenteral nutrition is a mean of delivering nutrition intravenously. Its use is associated with vitamin deficiency. Folic acid and vitamin B12 deficiencies are a rare cause of pancytopenia, whose existence compromises the prognosis of a critically ill patient. In this report, we present the case of a 48 year old man with septic shock secondary to a gangrenous cholecystitis complicated postoperatively by an abscessed collection of the hepatic hilum, and was given total parenteral nutrition. The patient was referred to our department for specialized care, and displayed signs of severe hypovolemia and anemia, with refractory shock. Lab findings were in favor of pancytopenia, with an abdominal CT-Scan showing multiple hematomas. Patient underwent surgical intervention and was diagnosed with folic acid deficiency. He was supplemented with folic acid and vitamin B12, transfused, and switched to mixed enteral and parenteral nutrition following vasopressor drug withdrawal. Outcome was marked by the increase of platelets, hemoglobin and white blood cells, without recurrence of hemorrhage, and transfer of the patient to the surgical ward after complete recovery from the septic shock. This case highlights the importance of vitamin supplementation in patients receiving total parenteral nutrition, and the regular assessment of their complete blood count in the absence of any supplementation.

Keywords: Pancytopenia, folic Acid, total parenteral nutrition, case report.

INTRODUCTION

Nutritional therapy is an essential part of the patient's intensive care. Total parenteral nutrition suppose intravenous feeding without enteral nutrition. It is a source of vitamin deficiencies, such as folic acid [1]. Pancytopenia is one of the numerous complications of folate deficiency [2, 3]. We describe a rare case of folate deficiency induced pancytopenia, following total parenteral nutrition.

PATIENT AND OBSERVATION

Patient Information: We present the case of a 48 year old man with no specific medical or surgical history. He was referred from a private hospital to our department for the management of a septic shock secondary to a gangrenous cholecystitis complicated postoperatively by an abscessed collection of the hepatic hilum. The patient was given total parenteral nutrition, in association with antiobiotics (amikacin, imipenem-cilastatin), fluid resuscitation and norepinephrine.

Clinical Findings: On admission, our patient was pale, with signs of dehydration and bruises at puncture sites. The blood pressure was 110/70 mm Hg under high-dose norepinephrine (1.8 ug/kg/min) and the pulse rate was 127 min^{-1}. The patient was confused, with a glasgow coma scale of 12 (Eye opening at 3, verbal response at 4, and motor response at 5), tachypneic at 25 c/min, and hypoxemic. There was issue of blood through the abdominal drain.

Timeline of Current Episode:

- January 9, 2023: Cholecystectomy for a gangrenous cholecystitis.
- January 10, 2023: Introduction of low molecular weight heparin.
- January 11, 2023: Introduction of enteral nutrition.
- January 12, 2023: Septic shock secondary to postoperative abscesses collection of the hepatic hilum. Introduction of norepinephrine, amikacin (single shot), imipenem-cilastatin, cessation of enteral nutrition and introduction of total parenteral nutrition.
- January 13, 2023: Surgical drainage of the abscessed collection.

- January 24, 2023: Admission in our department for refractory shock.

Diagnostic assessment

Lab findings (Table 1) were in favor of bicytopenia, with thrombopenia and normochromic macrocytic anemia, impaired renal function, and severe hypernatremia. The abdominal CT-Scan showed hematomas at the level of the cholecystectomy site and the right anterior abdominal wall without vascular lesion.

After interruption of low molecular weight heparin, correction of hypernatremia, and hemodynamic stabilisation, the patient underwent surgery under general anesthesia, two days after his admission.

No vascular lesion was described. A surgical hemostasis was performed. Given the ongoing decrease of platelets and hemoglobin, and the apparition of a leucopenia, cessation of parenteral nutrition and imipenem-cilastatin was decided.

Given the improvement of septic shock, with withdrawl of vasopressors, a pancytopenia secondary to sepsis was not retained. The involvement of parenteral nutrition or imipenem-cilastin's toxicity seemed very likely.

We started a therapeutic test with folic acid and vitamin B12, after dosing folic acid, blood iron, ferritin and reticulocyte.

Blood copper, blood zinc and vitamin B12 assays were not available in our hospital.

Diagnosis: Folate deficiency induced pancytopenia secondary to total parenteral nutrition. The lab findings were in favor of a folate deficiency (1,8 ng/ml).

Therapeutic interventions: We continued folic acid (1 mg daily, orally for 6 days) and vitamin B12 supplementation (1000 mg daily for 6 days). Given the concomitant presence of anemia, we initiated a transfusion with 3 packed red blood cells. We switched to a mixed enteral and parenteral nutrition strategy.

Follow-up and outcome of interventions: Outcomes were marked by the increase of platelets, hemoglobin, and white blood cells, correction of hypernatremia and renal function. Patient recovered from his shock, was conscious, and eupneic. He was transferred to the surgical ward, and discharged at home 10 days later with a normal complete blood count.

Patient Perspective: When asked, the patient didn't remember his initial state on admission, but recognised that he felt less tired on his last 6 days in the intensive care unit. When asked, his family told our staff they could see an improvement of his overall state after the introduction of folic acid.

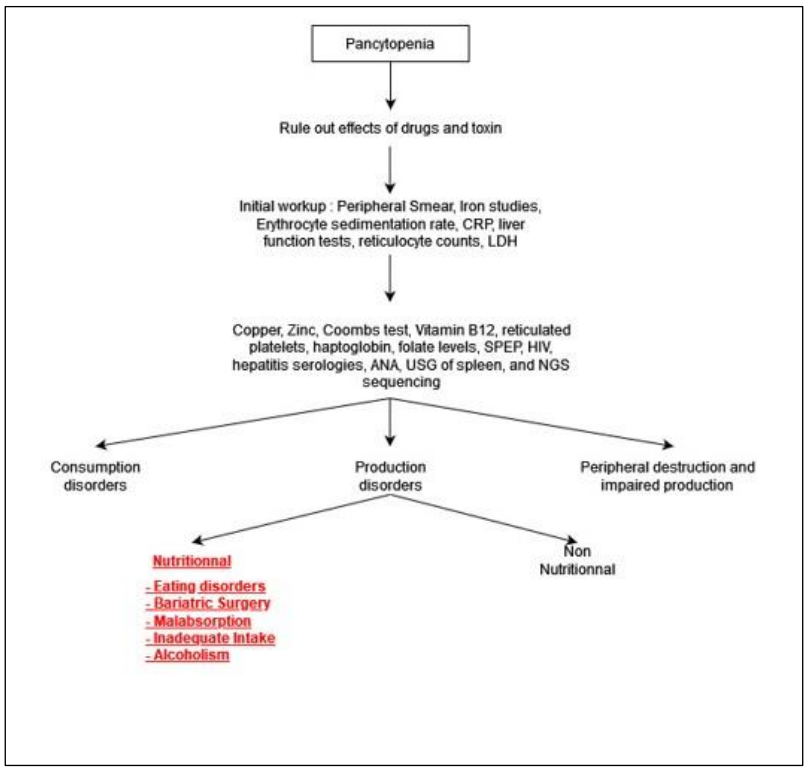

Figure 1: General algorithm to help diagnose the cause of pancytopenia (1)

Table 1: Biological findings and timeline of events

Date	24/01/2023	26/01/2023	27/01/2023	29/01/2023	01/02/2023	07/02/2023	17/02/2023
Hb *g/dL*	10.2	7.6	8.3	8.9	7.1	9.4	8.7
MCV *um3*	102	101	103	102	104	85.4	85.3
MCHC *%*	34.3	33.7	34.6	33.8	33.6	34	34.6
Iron *mg/L*					1.23		
Ferritin *ng/ml*					270		
WBC 10^3/*uL*	19.1	11.5	11.3	6.3	2.0	6.4	4.5
Neutrophils 10^3/*uL*	16.1	9.7	9.8	4.6	1.4	4.5	3.0
PLT 10^3/*uL*	272	69	64	38	45	249	253
Na *meq/L*	183		173	169	147	147	144
Creatinine *mg/L*	41		18.6	13.6	7.4	6.9	6.9
CRP *mg/L*	69			58		64	58
PCT *ng/ml*	2.48			0.53		0.59	
Folate *ng/ml*					1.8		
New event		Post surgery	Transfusion of 3 Packed Red Cells Norepinephrine withdrawal No Microbiological finding Cessation of LMWH	Cessation of ImipenemCilastatin and total parenteral nutrition	Initiation of folic acid and vitamin B12 intake introduction of enteral nutrition with parenteral nutrition	Day 7 of vitamins.	One day before discharge, 10 days after the end of vitamins intake

MCV: Mean corpuscular volume, MCHC: Mean corpuscular hemoglobin concentration, WBC: White blood Cells, PLT: platelets, PCT: Procalcitonin, Na: Natremia

DISCUSSION

Pancytopenia is a condition related to a poor outcome. It reflects many underlying causes that should be sought in a systematic way. That could be a real challenge because of the wide range of conditions leading to pancytopenia.

Ruling out the causes that can worsen pancytopenia, such as drug toxicity, is a first-line attitude.

In case of lack of improvement, the second line attitude includes ordering an array of biological analysis such as iron studies, reticulocyte count. In case of normochromic macrocytic anemia, ordering serum vitamin B12 and folate levels may help to approach the diagnosis as folic acid deficiency should be suspected in patients with pancytopenia and macrocytosis (Figure 1) [1].

Folic acid deficiency leads to aregenerative normochromic anemia, with an increased mean corpuscular volume, and less frequently to pancytopenia. Serum folate levels <2ng/ml defines folic acid deficiency, and its clinical signs include impaired consciousness, asthenia, glossitis, oral ulcers, and manifestation of anemia [2]. Folic acid deficiency may be secondary to or accompanied by a vitamin B12 deficiency, as their role and metabolism are closely linked [3]. As a result, it is necessary to determine vitamin B12 levels before initiating treatment by folic acid in order to treat them both and avoid worsening of a neuropathy, which may become irreversible [4].

Management of folic acid deficiency relies on oral supplementation of 1 to 5 mg daily of folic acid [2].

Folate deficiency may develop in patients fed by total parenteral nutrition rather quickly despite sufficient stocks under certain conditions such as infections (5). It should be prevented by systematic supplementation of folic acid and vitamin B12. We remind that the recommended dietary allowance for an adult in 24 h are 0.4 mg IV of folic acid and 0.005 mg of vitamin B12 [6].

In our case, the patient was infected, and was fed with total parenteral nutrition for 13 days without any supplementation. He presented with macrocytic

anemia and thrombopenia, which led us to stop imipenem-cilastatin and heparin. With the apparition of pancytopenia, we ordered iron studies, reticulocyte count, folate levels. Once we diagnosed folic acid deficiency, we started supplementation of both vitamin B12 and B9, as we could not order vitamin B12 levels. Outcome was good, with disparition of pancytopenia. We did not take into account the neurological improvement in the judgment of the effectiveness of our treatment given the concomitant existence of hypernatremia.

Pancytopenia is a rare manifestation of folate and vitamin B12 deficiencies [7, 8]. The most commonly hematologic abnormalities induced folate and vitamin B12 deficiencies seem to be anemia (37%), followed by leukopenia (13,9%) and thromocytopenia (9,9%) [7, 9]. Pancytopenia is seen in 5% of patients [7, 9].

Folic acid is a water-soluble vitamin whose deficiency is mainly related to insufficient food intake.

Without supplementation, folate deficiency might be documented after two weeks of total parenteral nutrition [10].

Multiple factors could lead to an early development of folate deficiency after initiation of total parenteral nutrition. That could include chronic alcoholism, poor dietary intake before hospitalisation, infection, and lack of folate in the intravenous alimentation fluid. Some of these factors were present in our case.

CONCLUSION

Total parenteral nutrition without vitamin supplementation can lead to folate and vitamin B12 deficiency, which may result in pancytopenia. While nutritional therapy is a necessary support in treating the critically ill, its numerous complications must be prevented by narrowing its indication and anticipating its complications by standardizing and applying best practice protocols.

Competing interests: The authors declare no competing interest.

Authors' Contributions

Asmae Chaker: Is the main author of the manuscript.

Idriss Chajai: Has been involved in drafting in the manuscript.

Yassine Regragui: Has been involved in drafting in the manuscript.

El Mahdi Awab: Has been involved in drafting the manuscript.

Rachid El Moussaoui: Has been involved in drafting in the manuscript.

Abderrahim Azzouzi: Has been involved in drafting in the manuscript.

Ahmed El hijri: Has given final approval of the version to be published.

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