

A PROPOS D'UN CAS

Blue-green inclusions in leukocytes and Covid-19: a case report and review of literature

Les inclusions bleues-vertes des leucocytes et Covid-19: à propos d'un cas et revue de littérature

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Abstract

Blue-green cytoplasmic inclusions in neutrophils and/or monocytes are uncommon anomalies observed in peripheral blood smear which were described in few case reports in patients with acute liver injury, lactic acidosis and more recently, in cases of Covid-19. These inclusions are associated with a critical prognosis and death shortly time after identification. Herein, we report a case of blue-green cytoplasmic inclusions finding in neutrophils and monocytes cytoplasm's in a patient with Covid-19.

Keywords: Covid-19, inclusion Bodies, neutrophils, monocytes, coronavirus

Résumé

Les inclusions cytoplasmiques bleues-vertes des neutrophiles et/ou des monocytes sont des anomalies rares de frottis sanguin décrites chez les patients atteints d'une lésion hépatique aiguë, d'acidose lactique et récemment de Covid-19. La présence de ces inclusions est associée à un pronostic critique et péjoratif à court terme.

Nous rapportons un cas des inclusions cytoplasmiques bleues-vertes dans le cytoplasme des neutrophiles et des monocytes.

Mots clés : Covid-19, inclusions cytoplasmiques, neutrophiles, monocytes, coronavirus

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-Covid 2) was responsible of an increased mortality rates in the 21 century (1). Prognostic indicators are performed markers that can help in the therapeutic care of critically ill patients and were frequently described in many studies (2). Recently, reporting of blue-green cytoplasm inclusions named “crystal of death” in few series of case in the literature should be considered as a simple cytological marker to identify patients at greater risk of short-term mortality (3-7). Herein, we report a clinical case of covid-19 patient died after 24 hours of identification of blue green inclusions in the peripheral blood smear.

CLINICAL CASE

A 78 years old man with a history of diabetes and high blood pressure was hospitalized for a severe acute respiratory syndrome covid-19 in the intensive care unit

requiring a mechanic ventilation. Chest X-ray showed bilateral peripheral alveolar infiltrates. Laboratory tests showed an increased leucocytes number ($94 \times 10^3/\mu\text{L}$) with a predominance of polymorphonuclear cells ($92.4 \times 10^3/\mu\text{L}$), lymphopenia ($0.8 \times 10^3/\mu\text{L}$), aregenerative normochrome anemia (Hemoglobin = 5.6 g/dL), normal platelets number, and elevated D-Dimers (6961 ng/mL). Biochemical report showed an elevated lactate dehydrogenase (LDH=877 U/L), renal failure (urea = 76.4 mmol/L, creatinine = 277 $\mu\text{mol/L}$), CRP=90.97 mg/L, hyperkalemia=7.62 mmol/L, hypernatremia =147 mmol/L, lactate =1 mmol/L) but with a normal hepatic function (Aspartate transaminase = 38.2 UI/L, Alanine transaminase =24.9 UI/L).

Peripheral blood smear examination revealed multiple blue-green inclusions in 4% of neutrophils and 1% of monocytes (Figure 1).

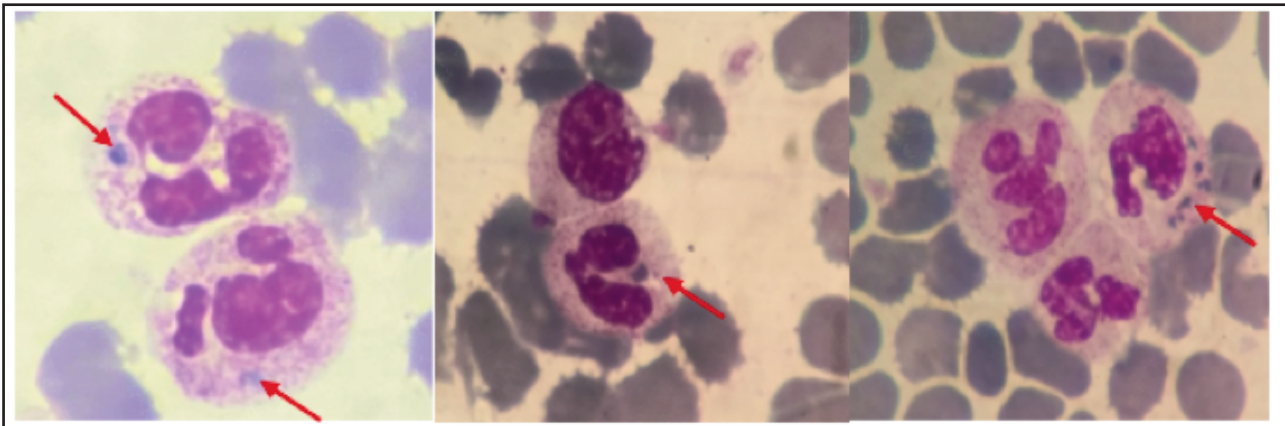


Figure 1: Blue-green inclusions in neutrophils cytoplasm cells (red arrows).

The patient died after 48 hours of this microscopic finding and 10 days after initial Covid-19 testing.

DISCUSSION

Most reports described this crystal inclusion as a critically anomaly in patients with tissue injury seen in liver failure and sepsis (3) and recently described in rare cases of Covid-19 patients (5-7). Three publications documenting 8 cases of prominently green inclusions in Covid-19 patients have been reported. These cases were frequently linked to elevated transaminase levels and lactic acidosis (table 1). Such blue-green inclusions called «crystals of death» were associated with a short-term mortality in 60% with a median of 3 days, range 1-599 days (4) and represent a prognostic factor for higher early mortality rate within 24–72 hours (6). The higher the transaminase levels, the greater the number of inclusions within neutrophils, and the more extensive the tissue damage becomes. The percentage of neutrophils inclu-

sions could be useful as a prognostic value in the patient follow-up (8). However, the clinical significance of this finding is still uncertain. In fact, prognosis is related to various factors like age, comorbidity, and severe illness. Green inclusions could be simply a transient morphologic anomaly (9).

In this case, blue-green inclusions were detected in peripheral blood smear of a critically ill coronavirus disease patient without any signs of hepatic necrosis with large inclusions in neutrophils and monocytes cytoplasm. These markers were also reported in a healthy patient affected with covid-19 (5). The pathogenesis of these inclusions is unclear and need more exploration of their etiology and clinical implications.

Peripheral blood smear is important since these anomalies are not detected in hematology analyzer.

Table 1 : Overview of literature for green-blue inclusions cases in covid-19 patients

Study (author,years)	Number of case report	Patient disease	Multisystem organ failure	Days from inclusion to death	Pourcentage of green inclusions
Dienstmann et al,2020	1	Covid-19	-	2 days	-
Cantu et al,2020	6	Severe	Lactic acidosis covid-19	1-10 days Liver necrosis	5% in neutrophils 1% in monocytes
Kritikou et al,2021	1	Severe covid-19	Lactic acidosis Liver necrosis	22 days	-

These inclusions are underdiagnosed, and their detection requires an extremely vigilance from the cytologist. Green inclusions were mostly described as birefractory, blue-green, cytoplasmic inclusion with variable size and circular shape with poorly defined edge (1). Regularly multiple, they are found in the cytoplasm of neutrophils and, less commonly in monocytes. Many hypotheses suggest that these crystals was rich of lipofuscin released from lysosomal degradation of necrotic hepatocytes phagocytized by neutrophils and monocytes (6). In addition, it should not be confused with Döhle bodies, Howell–Jolly pseudobodies, cryoglobulins, and May–Hegglin anomaly. It is essential that the cytologist immediately reports this finding to alert the clinician on the critical status of

the patient and aware of a possible tissue damage since almost 100% of COVID-19 patients died after the microscopic discovery of these inclusions (6). In the setting of COVID-19, this case reminds us that critically blue-green inclusions may aid to identify patients with higher risk of short term mortality. The information provided by the laboratory is crucial to establish prognosis. However, it's not systematically related to patients with acute liver failure or concurrent lactic acidosis (5). It is possible that tissue injury from other organs could also contribute to this finding. Therefore, further studies are required to ascertain the composition of these crystals and to develop a prognostic score, that encompass factors such as the percentage of inclusion and indicators of tissue damage.

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