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Case Report

# Complications of a patient with chronic lymphocytic leukemia: A Case Report

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**ABSTRACT**:

**Introduction**: Chronic lymphocytic leukemia (CLL) and myasthenia gravis (MG) are chronic health conditions that require specific treatments and present distinct challenges for dental management, especially in surgical procedures such as tooth extraction. Patients with CLL often have coagulation dysfunctions due to hematological changes associated with the disease and immunosuppressant treatments. Myasthenia gravis, an autoimmune disease characterized by muscle weakness, often requires the use of corticosteroids and immunosuppressants, which can also increase the risk of bleeding. **Objective**: To discuss a clinical case of a patient with a previous diagnosis of Myasthenia gravis and chronic lymphocytic leukemia (CLL), with various complications, multiple hospitalizations and intercurrences, and to analyze the complications presented by the patient. **Method**: A descriptive study based on a case report. The clinical characteristics, evolution of the condition and specific complications faced by the patient were detailed. **Case Report**: After stabilization measures, a fistulectomy was performed on the wound site and corticosteroid therapy was started. The patient's general condition improved, his laboratory tests improved, the bleeding stopped and the wound closed. He was referred to the outpatient clinic for further follow-up and treatment. After a period of time, the patient returned to the same hospital complaining of asthenia, malaise, dyspnea on slight exertion, and an associated hyperglycemic peak of 300mg/dL. Tests again showed a drop in hemoglobin, with HB: 7.2, leukocytes of 9240 mm3 and a chest CT scan showing pneumonia. He was given 10 days of intravenous antibiotic therapy, ceftriaxone 2g a day. In addition, immunophenotyping was requested to assess the possibility of a recurrence of CLL, which showed a report of chronic lymphoproliferative B-KAPPA. On discharge, he was referred back to the hematologist to start a new cycle of chemotherapy. Due to his previous use of chemotherapy drugs, he opted for treatment with Venetoclax. He is currently undergoing treatment with Venetoclax, with no complications, and is being monitored on an outpatient basis. **Conclusion**: This case highlights the complexity of managing patients with hematological and autoimmune diseases undergoing invasive dental procedures. Multiprofessional coordination is essential to reduce risks and improve prognosis. The literature indicates that careful assessment of the hematological condition and immunosuppressive status is essential for the prevention of hemorrhagic complications.

***Keywords: Chronic lymphocytic leukemia; myasthenia gravis; hematological and autoimmune diseases***

## 1. INTRODUCTION:

Chronic lymphocytic leukemia (CLL) is a malignant lymphoproliferative disorder with sustained lymphocytosis for at least 3 months.[1] It is more common in Western countries and is often diagnosed in asymptomatic patients. Its clinical manifestations are not very specific, and it can present with fatigue, dyspnea, lymphadenopathy, splenomegaly,

hepatomegaly, weight loss of more than 10%, night sweats and fever (temperature greater than 38).[2]

The main risk factors for this disease are age (over 60), male gender, white ethnicity and a family history of chronic lymphoid leukemia.[2]

The most frequent complications are anemia, splenomegaly, infection, thrombocytopenia and lymphadenopathy. The rarest complications, but which can be fatal, are tumor lysis syndrome, leukostasis and secondary neoplasms. [3]

In CLL, various genetic mutations occur in the DNA of immature B cells, which lead to the formation of "abnormal" lymphocytes that are unable to carry out their role of defending the body against infections.[4]

These genetic mutations result in the neoplastic change in B lymphocytes that leads to leukemia. First-degree relatives of patients diagnosed with CLL are five to seven times more likely to develop CLL.[5]

For diagnosis, the most commonly used tests are blood count, histological infiltration pattern in biopsies, lymphocyte doubling time, serum markers, cytogenetic analysis to detect chromosomal aberrations, immunophenotyping, and evaluation of the mutation status of immunoglobulin variant region heavy chain (IgVH) genes using specific markers. Imaging tests are used to check the size of the tumor and metastasis sites. [5]

The evolution of patients with CLL is generally benign and they remain asymptomatic for many years. Because this disease affects more elderly patients, it is common for the cause of death to be due to a disease that coexists with CLL and not due to CLL itself. It is commonly related to complicated infections due to myelotoxic chemotherapy, granulocytopenia, hypogammaglobulinemia. The average survival period is around 4 to 6 years.[6]

Therapy goals are aimed at cure, improved survival, quality of life and comfort measures. They generally do not require initial treatment, and therapy is only indicated for those with systemic symptoms, worsening anemia or thrombocytopenia, bone marrow involvement or autoimmune etiology, splenomegaly and progressive lymphadenopathy.

## 2. OBJECTIVE:

The main objective of the study was to discuss a clinical case of a patient with a previous diagnosis of Myasthenia gravis, chronic lymphocytic leukemia (CLL), with various complications and multiple hospitalizations and intercurrences and to analyze the complications presented by the patient, contributing to clinical understanding and therapeutic approaches.

## 3. METHODS:

### 3.1 Type of study:

This is a descriptive study based on a case report. The clinical characteristics, evolution of the condition and specific complications faced by the patient were detailed.

### 3.2 Patient selection:

The case was selected from medical records, ensuring that the patient had CLL and had presented clinical complications throughout the course of the disease.

### 3.3 Data collection:

Data was extracted from the patient's medical records, including information such as:

- ✓ Demographic data: age, gender, relevant medical history.
- ✓ Diagnosis: initial examination and laboratory confirmations of CLL.
- ✓ Clinical evolution: details of complications during follow-up.
- ✓ Laboratory and imaging tests: results documenting the progression of CLL and its complications.
- ✓ Therapeutic interventions: therapies applied and patient response.

### 3.4 Ethical aspects:

The study will respect the ethical guidelines for research with data from medical records, guaranteeing patient anonymity and ethics committee approval, in accordance with current legislation for case reports.

### 3.5 Data analysis:

The data was organized and described qualitatively, emphasizing the complications related to CLL and the therapeutic responses observed. An analysis will be made of the possible correlations between the clinical history and the complications presented, using comparisons with the literature.

## 4. RESULTS:

### 4.1 Case report:

Patient H.L.L.A., male, 64 years old. He came to the emergency department of the Hospital Beneficência Portuguesa de Santos on March 12, 2023, due to active bleeding in the region of his right upper molar, where he had had a tooth extraction. The laboratory tests taken at admission are shown in Table: 1.

| Test | Result | Reference Value | Test | Result | Reference Value |
|---|---|---|---|---|---|
| Hemoglobin | 8.9 g/dL | 12-15.5 | Neutrophils | 3,520/ $mm^3$ | 1,890-6,510 |
| Hematocrit | 26.7 mL/ er./dL | 35-45 | Platelets | 147,000/ $mm^3$ | 150,000-450,000 |
| Leukocytes | 6,400/ $mm^3$ | 4,000-11,000 | Activated Partial Thromboplastin Time | 42 | 27-38 |
| Lymphocytes | 2,240/ $mm^3$ | 875-3,475 | Prothrombin Activity Time | 69.8 | 10-14 |

**Table 1: Routine laboratory tests.** ***Source: Authors***

The comorbidities, he reported Diabetes Mellitus, controlled with glicazide; myasthenia gravis, taking pyridostigmine, asymptomatic; and chronic lymphoid leukemia, currently untreated due to remission.

On March 10, 2023, he had a right upper molar tooth extracted due to local infection, with no possibility of clinical treatment. He was released with a prescription for analgesia. The following day, he started bleeding from the wound site non-stop. He went to the emergency department complaining of bleeding, associated with asthenia and weakness since the procedure.

On physical examination, he was conscious, oriented, in a regular general state, pale +/4+, normotensive, normocardic and normopneic. In the oropharynx, he had teeth in a regular state of hygiene, absence of total scarring in the region of the extraction on the hard palate, no signs of infection, with active bleeding.

On March 19, 2023, the patient's general condition deteriorated, associated with increased bleeding, hypotension 70x50 mmHg, tachycardia 120bpm and syncope assisted by family members. Tests showed worsening anemia HB: 7.6 and fibrinogen 127. He was sent to the intensive care unit (ICU), where he was transfused with two red blood cell concentrates and cryoprecipitated.

After stabilization measures, a fistulectomy was performed on the wound site and corticosteroid therapy was started. His general condition improved, his laboratory tests improved, the bleeding stopped and the wound closed. He was referred to the outpatient clinic for further follow-up and treatment.

On April 25, 2023, he returned to the same hospital complaining of asthenia, malaise, dyspnea on slight exertion, and an associated hyperglycemic peak of 300mg/dL. Tests again showed a drop in hemoglobin, with HB: 7.2, leukocytes of 9240 mm3 and a chest CT scan showing pneumonia. He was given 10 days of intravenous antibiotic therapy, ceftriaxone 2g a day. In addition, immunophenotyping was requested to assess the possibility of a recurrence of CLL, which showed a report of chronic lymphoproliferative B-KAPPA. On discharge, the patient was referred to a hematologist to start a new cycle of chemotherapy.

Due to previous use of chemotherapy drugs, treatment with Venetoclax was chosen. In 2018, he underwent chemotherapy with G-chlorambucil, with 6 cycles, without intercurrences and with regression of the disease. In 2020, he presented a subglottic lesion, with a biopsy confirming large B-cell non-Hodgkin's lymphoma, and opted for R-CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone). He is currently being treated with Venetoclax, with no complications, and is being monitored on an outpatient basis.

## 5. DISCUSSION:

Chronic lymphocytic leukemia is the most common type of leukemia in adults, diagnosed by immunophenotyping (IF), with a variable clinical course. The time of onset and first-line therapy remain debatable. Non-Hodgkin's lymphomas (NHL),[7] the most common neoplasm in the USA, usually present with lymphadenopathy and B symptoms.[10]

Adhesion molecules represent a group of families of receptors and counter-receptors that act in various biological processes, including cell migration. Since non-Hodgkin B lymphoma (NHL-B) cells are the malignant counterparts of B lymphocytes that have undergone one or more neoplastic transformation events at some stage of their development, it is possible that these cells use the same lymphocyte migration mechanisms as a method of dissemination from their tissue of origin, namely the lymph node, in the case of nodal NHL-B. [11]

As in the report in question, the patient diagnosed with CLL had significant complications from the disease over time, such as major bleeding episodes after a dental procedure. But what draws our attention is that in addition to the patient having CLL, the patient has myasthenia gravis and that the correlation of this disease has led to a change in

coagulation, leading to a change in interleukin 8 (IL-8), which is a cytokine produced by various cells, such as: monocytes, lymphocytes, endothelium or epithelium cells and fibroblasts, in response to different stimuli, with chemotactic functions and its primary function is to activate and attract neutrophils to the sites of inflammation. [12]

After starting corticosteroid therapy (pulse therapy), the patient showed an improvement in symptoms, clinical and laboratory improvement, and the bleeding stopped. He has been followed up as an outpatient, under treatment with Venetoclax, without any complications since then.[12]

Studies show that patients with CLL have an increased risk of bleeding due to various factors, including thrombocytopenia and alterations in platelet function and the immune system. CLL can cause a reduction in platelet production and quality, making the patient more susceptible to bleeding after invasive procedures such as tooth extractions. [12-13]

According to studies, bleeding complications in patients with CLL are common due to the hematological changes, especially when the patient is already undergoing active treatment, which may include chemotherapy or immunosuppressants, increasing the predisposition to bleeding and slowing down the healing process. [13]

Myasthenia gravis is an autoimmune disease characterized by muscle weakness, and treatment usually involves immunosuppressants, corticosteroids and, in some cases, plasmapheresis. Prolonged use of corticosteroids, such as prednisone, increases tissue fragility, which can compromise healing and predispose to post-surgical bleeding complications.[14] In addition, treatment for myasthenia gravis can include drugs such as azathioprine, which affect bone marrow function and can induce cytopenias, exacerbating the risk of bleeding. [15]

Studies suggest that immunosuppression can interfere with the body's ability to control the inflammatory response and regenerate damaged tissue. In patients with myasthenia gravis, the risk of bleeding complications may be even higher in cases where treatment is active and immunosuppression levels are high. [16]

According to recent research, CLL causes an increase in capillary fragility and a decrease in coagulation capacity, especially in patients using immunosuppressive therapies such as rituximab and corticosteroids, which inhibit the formation of new platelets and the function of coagulation factors. The rate of post-operative bleeding in patients with CLL can be up to 3 times higher than in patients without hematological alterations, especially if specific care is not taken with platelet levels and the use of local hemostatic agents. [17]

Treatment of myasthenia gravis with immunosuppressants and corticosteroids also increases the risk of bleeding in dental procedures. In patients with MG, the use of immunosuppressive agents, such as azathioprine, impairs coagulation capacity by reducing the synthesis of platelets and other components of the immune system that are essential for hemostasis. In addition, the generalized muscle weakness that characterizes MG can make it difficult to recover and control blood flow in the event of a hemorrhage. [18]

Research has highlighted the importance of adjusting the treatment plan for MG patients, including preoperative monitoring of platelet function and the use of local substitutes for clotting agents, in order to reduce the need for systemic medications that can exacerbate myasthenia. To minimize the risk of bleeding, it is essential to adjust medications preoperatively and constantly monitor the patient during the procedure. [19]

Patients with CLL may benefit from platelet transfusion in cases of significant thrombocytopenia, while those with MG should have their medications adjusted to minimize muscle weakness without compromising coagulation. According to studies, the use of topical hemostatic agents, such as collagens and hemostatic gels, has been shown to be effective in reducing the risk of postoperative bleeding, especially in patients with hematological conditions. It is important that the dental team works together with the doctor responsible for the patient's primary treatment for an integrated approach. [20]

The risk of bleeding after tooth extraction in patients with CLL and myasthenia gravis is a major concern due to the combination of hematological effects and immunosuppression. Invasive procedures in patients with CLL and on immunosuppressive treatment require a rigorous pre-surgical assessment protocol, including a complete blood count and, ideally, consultation with a hematologist. Clinical trials suggest that the use of local hemostatic agents and compressive suturing can help reduce post-operative bleeding in high-risk patients. [21]

To minimize the risk of bleeding in patients like this, joint follow-up between the dentist, hematologist and neurologist is recommended, assessing the possibility of temporarily adjusting immunosuppressive treatment or using alternative therapies, such as tranexamic, to promote local hemostasis. [22]

## 6. CONCLUSION:

In the case reported, the 64-year-old male patient, with chronic lymphoid leukemia and myasthenia gravis, under treatment, presented with wound hemorrhage after tooth extraction and IL-8 alterations.

Hemorrhage after tooth extraction is a significant risk in patients with CLL and MG, due to hematological alterations and the use of

immunosuppressive drugs. Preoperative management strategies, such as platelet monitoring and the use of local hemostatic agents, are recommended to minimize complications. More research is needed to develop specific clinical guidelines that integrate dental care and the management of systemic conditions in these patients.

This case highlights the complexity of managing patients with hematological and autoimmune diseases undergoing invasive dental procedures.

Multiprofessional coordination is essential to reduce risks and improve prognosis. The literature indicates that careful assessment of the hematological condition and immunosuppressive status is essential for preventing hemorrhagic complications.

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