



Case Report

Lymphoma as a Complication of Recurrent COVID-19 Infection in Patients with Rheumatic Disease

Urbano Solis Cartas^{1*}, Jorge Luis Valdés González², Wilmar Hernandez³, Cecilia Alejandra Garcia Ríos⁴

¹Rheumatology Specialist, Universidad Nacional de Chimborazo, Escuela Superior Politécnica de Chimborazo, Ecuador

²Dermatology Specialist, Escuela Superior Politécnica de Chimborazo, Ecuador

³Ph.D. in Electronic Engineering, Universidad de las Americas, Quito, Ecuador

⁴Pediatrics, Escuela Superior Politécnica de Chimborazo, Ecuador

***Corresponding author:** Urbano Solis Cartas, Rheumatology Specialist, Universidad Nacional de Chimborazo, Escuela Superior Politécnica de Chimborazo, Ecuador

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Abstract

Introduction: Rheumatic diseases and lymphomas have as common elements the involvement of the immune system, specifically T and B-lymphocytes, and the presence of viral infections as a possible triggering factor for these diseases. The presence of rheumatic diseases increases the risk of developing lymphomas. COVID-19 is a viral disease that affects the immune system, so it could be the trigger for the appearance of lymphomas in patients with rheumatic diseases. **Material and method:** Two patients diagnosed with rheumatic diseases and COVID-19 infection are presented on three occasions each. One year after the last respiratory symptoms, they began with clinical manifestations that led to the diagnosis of Hodgkin's lymphoma in a 27-year-old male patient with rheumatoid arthritis and non-Hodgkin's lymphoma in a 58-year-old female patient with a history of rheumatoid arthritis and Sjogren's syndrome. **Discussion:** The affectation of the immune system that COVID-19 generates, in patients with previous rheumatic disease, increases the risk of the appearance of neoplastic complications.

Keyword: Rheumatoid arthritis; COVID-19; Rheumatic Disease; Hodgkin lymphoma; Non-Hodgkin lymphoma; Sjogren's syndrome

Introduction

Lymphomas are described as malignant diseases characterized by neoplastic proliferation of the lymphoreticular portion of the immune system; with B cells being the most frequently affected. They are not frequent diseases; an incidence between 5 and 8 people per 100,000 inhabitants is described. In

the vast majority of cases, a history of viral infection is reported as an etiopathogenic element of the disease; although radiation, male sex and advanced age are also conditions that increase the risk of these diseases [1].

Despite being hematological diseases and presenting manifestations common to both diseases, there are clinical, laboratory and pathological features that distinguish them. Among the common elements, the presence of tiredness, fatigue, decay, adenomegaly, splenomegaly, fever and anemia stand out. In the case of Hodgkin's disease, a single involvement of B cells,

greater lymph node involvement, less extranodal involvement, sparing Waldeyer's ring and the presence of Reed Sternberg cells is described. Non-Hodgkin's lymphomas affect B and T cells, express greater extranodal involvement, mainly at the level of the intestine, and do not present Reed Sternberg cells [2-4].

Despite the existence of some clinical and laboratory elements that guide towards the clinical suspicion of these conditions; the definitive diagnosis is made by histopathological study. Therapeutic schemes for both conditions include the use of chemotherapy, radiotherapy and biological therapy. The evolution and prognosis of both diseases is variable and depends on many factors such as age, the presence of chronic diseases and complications of the disease, among others [2, 3].

On the other hand, rheumatic diseases (RD) are a group of chronic diseases that are characterized etiopathogenic by alterations of the immune system that generate a sustained inflammatory process and affectation of T and B cells, respectively. These diseases are clinically characterized by presenting articular and extra-articular manifestations due to the involvement of other organs and organ systems [5, 6]. In conditions such as rheumatoid arthritis (RA) and Sjogren's syndrome (SS), an increase in risk of the presence of neoplastic diseases that is associated with the etiopathogenic process of these diseases [7, 8].

At present, the exact cause that generates the appearance of RD is unknown; however, viral infections are also pointed out as one of the possible triggering factors of these conditions [5]. Therefore, viral infections have been pointed out as a factor that increases the risk of the appearance of both lymphomas and RD.

In this sense, it is important to highlight that since the end of 2019 the world has experienced the globalized impact of COVID-19. This viral disease, caused by a specific type of coronavirus, is characterized by affecting the immune system, generating an inflammatory process with local and systemic expression accompanied by coagulation disorders [9-11].

Material and Methods

It is decided to present the following report of two patients with RD, a history of involvement by COVI-19 on three occasions and that one year after the last respiratory symptoms they begin with clinical manifestations that allow the definitive diagnosis of lymphoma.

Result

Clinical Case 1

Male patient, 27 years old, with a diagnosis of RA of 6 years of evolution for which he was treated with 10 mg weekly

of methotrexate, 5 mg weekly of folic acid and 10 mg daily of prednisone. He reports that during the last 3 years he has maintained a favorable evolution of the activity of the disease. He reports that he presented, since April 2020, 3 cases confirmed by the results of the COVID-19 polymerase chain reaction (PCR) test, despite maintaining the complete vaccination schedule. On none of the three occasions has he required hospitalization, the last respiratory condition was 13 months ago.

She went to the consultation referring for about 5 months the presence of tiredness, marked decay and fatigue that have been exacerbated during the last month; For about a month he has been feeling discomfort and abdominal heaviness and has had a prolonged fever of 23 days, in the evening or at night, which ranges from low-grade fever to fever of up to 38.6 degrees Celsius.

On physical examination, the presence of pale mucosal skin, slight pain on superficial and deep palpation at the level of the epigastrium and both hypochondria, and the presence of bilateral cervical [6] and axillary [8] adenopathies, with little pain and consistency, are collected as significant data. Indeterminate. Laboratory tests show hemoglobin levels of 10.4 gr/l and left lobe hepatomegaly of 3 cm.

Clinical Case 2

Female patient, 58 years old, diagnosed with RA and SS of 11 years of evolution, treatment with 10 mg weekly methotrexate, 5 mg weekly folic acid, 10 mg daily prednisone and 8 mg daily bromhexine. Refers favorable evolution of rheumatic disease. During 2020 and the first semester of 2021, he presented 3 cases confirmed by PCR of COVID-19, for which he needed hospitalization during the second infection without severe complications. He currently maintains a complete vaccination schedule with a first booster dose.

She went to consultation referring general manifestations (tiredness, fatigue and weakness) for several months, of variable intensity and frequency of presentation. Increased volume of the cervical chain for about 4 months and abdominal discomfort given by abdominal heaviness and occasional diarrhea that lasts about 2 or 3 days with between 3 and 5 semi-pasty stools daily. In the last one, he has presented evening fever for 18 days, without improvement with the use of antipyretics. Physical examination revealed the presence of cervical lymphadenopathies and pale skin mucosa. The results of the laboratory tests showed hemoglobin of 11.2 gr/l and hepatosplenomegaly of 3 and 3.5 cm, respectively (Table 1).

Clinical, epidemiological and laboratory characteristics	Patients with rheumatic disease, COVID-19 and lymphoma	
	Case 1	Case 2
Age (years)	27	58
Gender	Male	Female
Rheumatic disease	AR	AR + SS
Evolution time of ER	6 years	11 years
History of COVID-19 before diagnosis	13 months	15 months
General manifestations (tiredness, fatigue, decay)	Yes	Yes
Fever (days)	febrile illness 23 days	febrile illness 18 days
Night sweats	Yes	Yes
Enlarged lymph nodes (affected chain)	Cervical and axillary	Cervical
Extra nodal involvement	No	No
Hepatosplenomegaly	Hepatosplenomegaly 3 cm	Hepatosplenomegaly 3 and 3.5 cm, respectively
Hematological alterations	Mild anemia (10.4 gr/L)	Mild anemia (11.2 gr/L)
Histopathological findings	Presence of Reed Sternberg cells	Absence of Reed Sternberg cells
Definitive diagnosis	Hodgkin lymphoma	Non-Hodgkin lymphoma

Table 1: Summarizes the main clinical and epidemiological characteristics of both cases.

Clinometry was applied for rheumatic diseases, finding, in both cases, control of the clinical activity of the RD. Both cases were evaluated by the oncohematology subspecialty and a histopathological study of the lymph nodes was requested. In both cases, the presence of findings compatible with lymphoma is reported and in the case of the male patient with RA, the presence of Reed Sternberg cells is reported, so it is concluded as Hodgkin's lymphoma, in the other patient the definitive diagnosis was non-Hodgkin's lymphoma. They are currently on a Rituximab therapeutic regimen at a dose of 375 mg/m² of body surface area per cycle, until completing 8 cycles, and regular clinical and laboratory monitoring; the evolution, up to the moment of the next report, has been favorable.

Discussion

There are several elements of coincidence in both cases; the first of these is related to the diagnosis of RD, which has been described as a factor that increases the risk of the appearance of neoplastic diseases, specifically lymphomas [7, 8]. The second element to highlight is the history of viral involvement, in this case, a reiterative picture of COVID-19. It is described that in both types of lymphomas the presence of a history of viral involvement

is a common finding among patients with this disease [4].

The clinical, epidemiological and laboratory characteristics coincide with those described in the literature, although one of the cases is female, which is not the sex in which the disease occurs most frequently; however, it does not mean that lymphomas cannot be diagnosed in female patients. The diagnosis of Hodgkin's lymphoma was centered on the presence of Reed Sternberg and the patient's age (27 years), coinciding with one of the incidence peaks of the condition [5]. After the initial evaluation and staging of the tumor disease, it was decided, in both cases, to start treatment with biological therapy (Rituximab) at the dose described for the treatment of this type of disease [6].

One of the most important elements of this report focuses on the fact that both patients, with RD in control of their clinical activity, have suffered on several occasions, despite having a complete vaccination schedule, from COVID-19 and that around one year after their last picture begin with manifestations that lead to the diagnosis of lymphomas. From a clinical point of view, repeated infection by COVID-19 could be established as the trigger for the appearance of lymphomas in patients with an increased risk of this disease, such as rheumatic patients.

Conclusion

COVID-19 infection, being a viral disease that affects the proper functioning of the immune system, could be considered as an element that favors the appearance of lymphomas in patients with predisposing diseases. More studies are needed to confirm this hypothesis.

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Authors' contribution

Conceptualization: Urbano Solis Cartas, Jorge Luis Valdés González

Formal analysis: Cecilia Alejandra García Ríos

Research: Urbano Solis Cartas, Jorge Luis Valdés González, Wilmar Hernandez

Methodology: Cecilia Alejandra García Ríos

Project management: Urbano Solis Cartas

Resources: Jorge Luis Valdés González, Wilmar Hernandez

Supervision: Urbano Solis Cartas

Visualization: Cecilia Alejandra García Ríos

Writing - original draft: Jorge Luis Valdés González, Wilmar Hernandez

Writing - revision and edition: Urbano Solis Cartas, Wilmar Hernandez

Conflicts of interest

The authors report no conflicts of interest

References

1. Gálvez Paz CN, Mendoza Goycochea ME, Espíritu N, Paz Carrillo EM (2021) Características clínicas, epidemiológicas y patológicas de los linfomas en pacientes del Instituto Nacional de Salud del Niño de Breña - Perú, 2015-2019. *An. Fac. med.*, 82: 27-33.
2. Calderín Miranda JM, de Castro Suárez N, Fernández GR (2022) Linfomas no Hodgkin indolentes y terapia anti-CD20: una revisión de la literatura. *Rev Cubana Hematol Inmunol Hemoter.* 38: e1583.
3. Benítez YS, Fernández YN, Llorente MP (2019) OncoHodgk: Aplicación interactiva para el aprendizaje del diagnóstico y tratamiento de los Linfomas. *RCIM*, 11: 75-87.
4. Martín-Domínguez V, Mendoza J, Díaz-Menéndez A, Agrados M, Moreno-Monteagudo JA, Santander C. (2018) Linfomas de colon: análisis de nuestra experiencia en los últimos 23 años. *Rev. esp. enferm. dig.*, 110: 762-767.
5. Cartas US, Batista SDLAC, Moldón YR, Lara AE (2022) Enfermedades reumáticas e inmunosupresión, mitos y realidades desde la perspectiva etiopatogénica de la enfermedad. *Revista Cubana de Reumatología*, 24: 38-46.
6. Cartas US, González JV (2022) Actividad del sistema inmune en pacientes reumáticos. *Revista Cubana de Medicina Militar*, 51: 23-29.
7. Benítez Falero Y, Solis Cartas U, Armas Hernández A, Armas Hernández Y (2016) Asociación entre Síndrome de Sjögren y enfermedad tumoral: a propósito de un caso. *AMC.* 20: 219-227.
8. Solís Cartas U, Benítez Calero Y, Calvopiña Bejarano SJ, Aguirre Saimeda GL, de Armas Hernández A (2018) Uncommon combination of hepatocarcinoma with Sjögren's syndrome. *Rev Cub Med Mil.* 47: 1-9.
9. Martínez Avila DR, Gracia Medina E, Benítez Caballero B, Archer-Austin K, González Madruga T, Jiménez Galaimena J, et al. (2021) Características clínicas de pacientes con Linfomas de Células del Manto. *Rev Cub Oncol.* 19:
10. Hernández DLR, Martínez LB, Cruz RG (2022) Metástasis ósea como presentación del linfoma de Hodgkin. *Reporte de un caso. Revista Finlay.* 12: 6.
11. Miranda JLC, de Castro SN, Fernández RG (2022) Linfomas no Hodgkin indolentes y terapia anti-CD20: una revisión de la literatura. *Revista Cubana de Hematología, Inmunología y Hemoterapia.* 38: 34-42.