



Clinical Case Report: Lymphedema Rehabilitation in a breast cancer patient treated with Palbociclib (Ibrance)[®]

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ABSTRACT

This case report describes a 64-year-old woman with a history of breast cancer who underwent a mastectomy, axillary lymph node removal, chemotherapy, and radiotherapy, and subsequently developed persistent lymphedema in her left arm. The patient received, pharmaceutical drug, Palbociclib (Ibrance[®]) for hormone receptor–positive breast cancer and experienced episodes of infection during follow-up. Circometry was performed to monitor changes in limb volume, and underwent complete decongestive therapy including manual lymphatic drainage, compression bandages, pressotherapy, and therapeutic exercises. Despite adherence to treatment, lymphedema was persistent and showed limited improvement over a six-month period. This case highlights the challenges of managing secondary lymphedema in breast cancer survivors and discusses the potential role of Palbociclib side effects in chronic inflammation and their possible relationship with persistent lymphedema.

Key words: lymphedema; breast cancer; palbociclib; ibrance[®]; decongestive therapy; case report.

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RESUMEN

El reporte de caso describe a una mujer de 64 años con antecedentes de cáncer de mama, tratada con mastectomía, extirpación de ganglios linfáticos axilares, quimioterapia y radioterapia, que posteriormente desarrolló linfedema crónico en su brazo izquierdo. La paciente estaba recibiendo Palbociclib (Ibrance®) para cáncer de mama con receptores hormonales positivos y presentó episodios de infección durante el seguimiento. Se realizó circometría para monitorear los cambios en el volumen del miembro. La paciente recibió terapia descongestiva completa, que incluyó drenaje linfático manual, vendajes compresivos, presoterapia y ejercicios terapéuticos. A pesar de la adherencia al tratamiento, el linfedema no mostró mejoría durante un período de seis meses. Este caso resalta los desafíos en el manejo del linfedema secundario en sobrevivientes de cáncer de mama y discute el posible papel de los efectos secundarios del Palbociclib en la inflamación crónica y su relación potencial con el linfedema persistente.

Palabras clave: linfedema; cáncer de mama; palbociclib; ibrance®; terapia descongestiva; caso clínico.

INTRODUCTION

Lymphedema is “a disorder of lymphostasis with protein-rich edema in which the lymph transport capacity and the proteolytic capacity of the tissues are less than normal, while the lymphatic load remains unaltered. Lymphedema is considered an evolutionary process caused by an excess of proteins, tissue edema, chronic inflammation, and excessive fibrosis”.¹ “It can present as soft edema with pitting or can evolve into non-pitting edema that transforms into progressive fibrosis”.¹

Primary lymphedema is characterized by congenital or hereditary abnormalities of the lymphatic system, whereas secondary lymphedema is acquired, caused by damage to lymphatic vessels, such as trauma, cancer, or surgical interventions.² Lymphatic fibrosis refers to the chronic thickening of soft tissues caused by the accumulation of protein-rich lymph and the subsequent remodeling processes it triggers.² The lymphatic system performs two essential functions: an immunological function, involving the formation, transport, and filtration of lymphoid cells and antibodies within the lymph nodes, and a circulatory function, responsible for reabsorbing, transporting, and returning plasma proteins —such as albumins, globulins, lipoproteins, and fibrinogen— back into the bloodstream.³

Breast cancer treatment often involves mastectomy, axillary lymph node dissection, chemotherapy and radiotherapy. These procedures are most common to treat breast cancer, but also are very important risk factors for the development of secondary lymphedema.⁴ The incidence of lymphedema among breast cancer survivor varies but it is estimated that 40% of survivors will experience lymphedema to some degree.⁵ Lymphedema after breast cancer treatment is a

well-recognized complication, primarily caused by axillary surgery and radiotherapy.⁵ Radiotherapy can impair lymphatic endothelial integrity and function, leading to chronic disruption of drainage pathways in the lymphatic system.⁵

Palbociclib is a selective CDK4/6 protein kinase inhibitor. This protein is widely used in hormone receptor-positive breast cancer. This halts the cell cycle, stopping cells from replicating. This is important because the drug's main purpose is to block tumor growth.⁶ One of its most frequent adverse effects is neutropenia, which reduces the patient's ability to control infections. Neutrophils are key regulators of the inflammatory response, and their dysfunction increases susceptibility to infectious episodes that can exacerbate lymphatic inflammation, aggravate fibrosis, and reduce responsiveness to conventional lymphedema therapies.⁷

In the clinical case presented, the patient showed impaired lymphatic function because of oncologic surgery —which included the removal of 17 axillary lymph nodes— and subsequent radiotherapy. These interventions disrupted lymphatic circulation and substantially increased the risk of secondary lymphedema. In this case, lymphedema was ultimately triggered by a mosquito bite on the affected arm, which led to local infection, chronic inflammation, and fibrotic tissue changes.

A 64-year-old female patient with a history of breast cancer, underwent a left mastectomy, axillary lymph node dissection (17 nodes removed), chemotherapy, and 30 sessions of radiotherapy. The patient subsequently underwent breast reconstruction with an expander and placement of a prosthesis. According to the patient, after five years she developed liver metastasis and was prescribed Palbociclib





(Ibrance®) on a schedule of 15 days on treatment followed by 7 days off, which she continued at the time of evaluation. She reported that her last PET-CT scan was described as “controlled,” although the official oncology report was not available.

Her medical history included reactive hypertension, hysterectomy, an ovarian cyst removed three years prior, and three cesarean sections. Her family history was relevant for a father with lung cancer. Following her last radiotherapy session, she presented with shoulder discomfort and neuropathy. At the time of physiotherapy evaluation in 2019, her weight was 55 kg, height 1.60 m, and BMI 21.5.

The patient was first evaluated in physiotherapy on September 3, 2019, by a specialist in oncology and lymphedema rehabilitation. During this visit, she was instructed on lymphedema care, correct use of a compression sleeve, and post-radiotherapy stretching. She did not return to follow-up until August 13, 2024, when she presented with an edematous left arm after a mosquito bite that evolved into infection and chronic inflammation. At that time, she reported a sensation of heaviness and functional discomfort in the left arm.

Clinical examination confirmed secondary lymphedema of the left upper limb, with circumetry showing increased limb volume compared to the contralateral side. Despite maintaining full range of motion, persistent edema and fibrosis were evident. Complete decongestive therapy was prescribed, consisting of manual lymphatic drainage, pressotherapy, compression bandages, and therapeutic exercises.

Between August 2024 and January 2025, the patient attended physiotherapy sessions once per week, which were

temporarily increased to twice per week during exacerbations. On December 30, 2024, she confirmed continued use of Palbociclib. Despite adherence to therapy, the lymphedema showed limited improvement. On January 29, 2025, the patient expressed fatigue with the treatment and lack of significant progress. She was advised to use a compression sleeve and glove until 2:00 p.m., wear the glove alone in the afternoon, and apply nocturnal compression and self-manual lymphatic drainage as part of fibrosis management. follow-up consult was scheduled for ten days later.

In terms of lifestyle, the patient continued to engage in physical activity, with regular practice of Pilates (three to four times per week), stationary cycling, and daily domestic activities. It was also reported that the subject was carrying her two young granddaughters and walking her dogs. The clinical relevance of these activities lies in their capacity to induce repetitive physical exertion, thereby augmenting venous return in the upper limbs. It is evident that there is a close interaction between the venous and lymphatic systems. Consequently, an increased blood flow can result in an elevated lymphatic load. It is evident that, given the lymphatic system’s comparatively diminished drainage capacity, this overload may precipitate the accumulation of interstitial fluid and thereby exacerbate lymphedema.

DISCUSSION

For this clinical case, the patient was assessed using circumetry (see Appendix) to monitor changes in limb volume. Circumetry was performed at the beginning of each session, comparing the affected arm with the contralateral side (Table 1-3).

APPENDIX A. Table 1 – Circometry Measurements (2019–2024)

Measurement point (cm)	R	L	L	L	L	L	L	L	L	L	L	R	R
1	16	15.5	15.6	15	15	15.4	15.3	15.4	16.2	16.4	17	15.1	15
2	17.9	17.3	16.9	16.5	16.2	16	16.4	17.7	18.3	18.7	19	15.6	16
3	20	19.9	19.8	18	19	18.4	18.5	21.1	20.7	22.5	22.5	18	17.5
4	23	22.9	22.5	21	21	21.8	22.1	22.9	24	25.5	26	20.6	21
5	25.5	14.4	24	23	23	24	23.7	25.5	26.3	27.7	28	22.8	22
*6	25.6	25.3	24.5	24	24	26	24.7	26.7	26.8	28.4	28.5	23.8	23
7	24.5	25.9	24.6	24	24	24	23.8	25.4	26.2	28.1	28	23.7	23.5
8	28.5	29	27	26	26.5	27	26.9	28	29	30.9	31	24.7	24
9	29.3	29.4	28.5	27	27	27	27.4	29.5	29.4	30.8	31	26.5	25
10	30	30.5	28.6	26.5	28	26.5	27.1	28.5	28.4	29.1	29	26.1	26.5
11	31.9	31.7	30.2	28	28	27.5	28.1	28.6	28.2	29.4	28	26.7	27
12	32.4	34.5	31	30	30	29	29.1	29.4	28.8	29.7	30	27.8	29
Hand	19	18.5	18.2	17	17.5	18	17.9	17.1	18.2	18.7	18.5	17.8	17.5
knuckles	18.2	18	17.9	16.5	16.5	16.5	18.2	17.2	17.7	18.3	18	17.1	17
fingers	5.7	5.9	5.6	5.5	5.7	5.7	6.1	6	6	6.2	6	6	6
date	3/08/19	3/08/19	7/08/19	30/08/24	9/9/24	23/09/24	30/09/24	28/11/24	3/12/24	9/12/24	9/12/24	28/11/24	9/09/24

*The highlighted data indicates when the measurements are out of range (two centimeters or more higher compared to the last session or the opposite arm)

Circometry Method:

For upper-limb measurements, 12 standardized anatomical points were used. Point 6 corresponds to the elbow crease and serves as the central reference. Measurements were taken every 6 cm proximally (toward the arm) and distally (toward the forearm) from this point. The first column of Tables 1–3 indicates these measurement points.” 1 is the most distal measurement; 12 is the most proximal measurement.



APPENDIX B. Table 2 – Circumetry Measurements (Dec 2024–Jan 2025)

Measurement point (cm)	R	L	L	L	L	L	L	L	L	L	L	L	R
1	15.1	16.7	16.8	16.5	17.3	16.8	16.5	16	16.4	16	16.1	16.3	15.3
2	16	18.6	18.6	18.8	18.9	18.8	18.3	17.8	18.5	20	18.3	19	16.3
3	18.1	21.3	21.2	20.6	22.4	21.4	20.3	20.8	21	21.5	21.3	21.5	18
4	20.4	24.7	25.3	24.5	25.3	24.6	23.5	24.2	25	25	24.5	25.5	20.8
5	22.5	27	27.3	26.7	27.6	26.8	26.3	27.3	26.8	27.5	26.5	27.5	22.5
*6	23.5	27.5	27.8	27.7	28	27.6	27.2	27.4	27.8	28	27.6	27	23.5
7	23.	26.8	27.2	27.4	27.3	27.2	27	26.7	26.7	28	27.2	28	23
8	24.4	29.8	30	29.1	29.6	29.2	28.2	29.3	29.8	31	29.7	31.2	24.5
9	25.5	31	29.4	29.4	30.1	30	28.8	29.4	30.6	31	30	31	25.5
10	25.6	30.1	28.8	28.9	28.7	28.8	28.5	28.5	29.3	29	29.5	29.5	26
11	26.3	29.8	29	29.5	29.5	28.8	29.2	29.3	29	30.5	30.7	29.7	27
12	27	29.9	30.1	30.4	29	30.2	30	30.2	29	31	31	30	27.5
hand	17.5	18.8	17.7	18	17.4	18.1	17.5	18	17.5	18.5	18.1	18.4	18
knuckles	17.6	18.3	17.6	17.3	17.2	17.7	17.7	17.3	17.4	17.5	17.5	17.3	17
Middle finger	5.8	6.3	6.2	6.1	5.9	6.1	6.2	5.8	5.7	5.8	5.8	5.8	6
Index finger	6.1	6.6	6.4	6.3	6.2	6.2	6	6	6	6	6	6	6
thumb	6	6.4	6.2	6.5	6.2	6.3	6.1	5.9	6	6	6.7	6	6
Ring finger	-	6	5.8	5.8	5.7	5.8	5.7	5.7	5.6	5.5	5.5	5.2	5.7
Little finger	5.2	5.4	5.2	5.1	5.2	5.3	5	5	5	5.2	5	5	5.2
date	10/12/24	11/12/24	12/12/24	13/12/24	16/12/24	18/12/24	19/12/24	20/12/24	30/12/24	2/01/25	3/01/25	6/01/25	2/01/25

*R= right, L=left

APPENDIX C. Table 3 – Circometry Measurements (Jan 2025 final sessions)

Measurement point (cm)	R	L	L	L	L	L	L	L	L	L	L	L	RSI
1	15.3	16.5	16.1	16.3	16	16	16.3	16.5	16.5	16.8	16.5	17	15.1
2	15.5	18	18.1	18.6	18.3	19	18.3	19	17.7	17	18	17.5	16
3	20	21	21.4	21.3	20.7	22	21	22	20.3	20.1	20.7	20	19
4	22.3	23.8	24.2	24.7	24.2	24.7	24	25	23.7	23.4	24	24	21.7
5	23	27	26	26.6	26.3	26.2	25.9	27	26.1	25.9	26	26	23.2
6	23	27.5	26.8	27	26.5	26.7	26.8	27.5	26.9	26.8	27	27	23.3
7	23	27	26.8	26.5	26.5	27.3	26.7	28	26	26.6	27	26	23.4
8	24	31	30.4	29.3	30.4	30.3	30	31	29.5	29.8	30	30	26
9	25.5	20	31	30.6	31	30.7	30.2	31	30.8	30.5	30.5	29.5	27.2
10	25	31	29.5	30.1	29.8	31	29.3	30.5	29.8	30.1	29.8	30	27.1
11	27	31	30.1	31.1	29.3	31.5	30.6	31	30	31	30.6	31	25.8
12	29.5	31	30.9	30.8	29.4	33	31.2	31.5	30.8	31.7	30.4	32.5	28.7
Hand	17	16.5	17.6	17.8	17.5	17	17.7	17.5	17.8		17.5	17.5	17.2
knuckle	17	17.5	17.1	17.6	16.8	16.5	17.4	17	17.3		17.4	17	17.5
Middle finger	6	5.5	5.6	5.7	5.6	5.7	5.7	6	5.7		5.8	6	5.8
indice	6	6	6.1	6	5.9	6	6	6	6.1		6	6	5.6
thumb	5.5	5.5	5.6	5.8	5.8	6	6	6	6		6	6	5.9
Ring finger	5.5	6.5	5.4	5.4	5.4	5	5.5	5.5	5.4		5.4	5.5	6
Little finger	5	5	5.1	5	5	5	5.2	5.5	5.1		5.1	5.2	5.4
date	8/01/24	8/01/25	9/01/25	13/01/25	13/01/25	15/01/25	17/01/25	20/01/25	24/01/25	Final de session	29/01/25	30/01/25	15/01/25

*The underlined data indicates when the measurements are out of range (two centimeters or more higher compared to the last session or the opposite arm).



Given the persistence of lymphedema, the potential contribution of the patient's pharmacological treatment was considered. Palbociclib (Ibrance®), a CDK4/6 inhibitor used for hormone receptor-positive breast cancer, has been shown in preclinical studies to inhibit the growth of estrogen receptor-positive breast cancer cells.⁸ The most common adverse events reported in randomized clinical trials include neutropenia, leukopenia, fatigue, nausea, stomatitis, alopecia, and diarrhea.⁸ Neutropenia, in particular, may predispose patients to recurrent infections, which could worsen pre-existing lymphatic dysfunction. However, in this case, no laboratory data were available to confirm neutropenia at the time of lymphedema evaluation. No additional adverse effects typically associated with palbociclib—such as fatigue, alopecia, or stomatitis—were reported by the patient.

Beyond mechanical obstruction caused by radiotherapy treatment, lymphatic dysfunction significantly alters both local and systemic immunity. It disrupts immune cell trafficking and antigen transport, increasing susceptibility to recurrent infections and perpetuating chronic inflammation.⁹ Persistent lymphostasis promotes fibrosis and adipose tissue deposition, further impairing drainage and creating a cycle of immune dysregulation.⁹

In this particular case, the onset of oedema was triggered by a local infection after a mosquito bite. It is well established that recurrent infection of lymphedematous tissue is a known complication, including cellulitis and other types of infection. These have been shown to exacerbate lymphatic injury and inflammation.⁹ While it is established that neutrophils play a key role in host defense and tissue repair, the literature does not support a direct causal link between Palbociclib-induced neutropenia and the development of lymphedema. It is an established fact that breast cancer survivors who receive systemic therapies may experience immunosuppression and an increased susceptibility to infections. This has the potential to exacerbate existing treatment-related complications. Although there is no established correlation between neutropenia induced by systemic cancer therapies and lymphedema, impaired neutrophil function has been demonstrated to increase susceptibility to infection and may amplify local inflammatory responses.¹⁰ This assertion is supported by immunological evidence.

CONCLUSION

To our knowledge, no studies have directly linked persistent upper limb lymphedema and fibrosis with the use of Palbociclib (Ibrance®). While Palbociclib-induced neutropenia may increase the risk of infections in lymphedematous tissues, there is no evidence to suggest that this drug initiates lymphedema or explains resistance to conventional physiotherapy. In this case, surgery and radiotherapy remain the primary contributing factors to the patient's chronic lymphedema and fibrosis. Nevertheless, immunosuppression associated with Palbociclib may contribute to a cycle of recurrent infection and inflammation, potentially aggravating the condition.

LIMITATIONS

The absence of laboratory tests and oncological records, including inflammatory markers, receptor status, and staging, is a limitation to this clinical case.

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