



## A CASE REPORT OF LATE ONSET PRIMARY LYMPHEDEMA - FROM DIAGNOSIS TO SUCCESSFUL MANAGEMENT STRATEGIES

IVANA KLARIĆ KUKUZ<sup>1</sup>, JOSIPA GRANČIĆ<sup>2</sup>, MARTA PAVLOVIĆ<sup>3</sup>, ANA BARIĆ ŽIŽIĆ<sup>4</sup>, JURE ALJINOVIĆ<sup>3</sup>,  
IVANKA MARINOVIĆ<sup>3</sup>, ANA POLJIČANIN<sup>3</sup>

We present a case report of a 46-year-old nurse with lower limb, late onset, second degree primary lymphedema diagnosed thirty years after symptoms onset. Lack of specialised lymphedema clinics, lymphedema specialists, lymphedema management guidelines and lymphedema registry are main causes for prolonged diagnosis in Croatia. Primary lymphedema treatment was conducted through 45-minutes sessions three times a week in total 7 sessions. Treatment sessions consisted of limb circumference measurements and manual lymph drainage followed by Partsch compression therapy protocol and education. Instructions for physical activity were made likewise. Significant volume reduction was successful despite long primary lymphedema duration. Changes in quality of life and physical activity were noted by self-administered questionnaires. Compression garment specialist made measures for flat knitted stockings compression class III. that are indicated for lymphedema and have important role in the maintenance phase of limb volume. Despite the fact that primary lymphedema is chronic condition, and it has been left untreated for over thirty years in our patient. With proper lymphedema therapy management and teamwork it is possible to achieve and maintain satisfying treatment results especially if you have motivated and properly educated patient.

Keywords: PRIMARY LYMPHEDEMA, LYMPHOSCINTIGRAPHY, MANUAL LYMPH DRAINAGE, COMPRESSION BANDAGES

### INTRODUCTION

Primary lymphedema (PLE) is a rare disease that implies all developmental lymphatic abnormalities such as aplasia, dysplasia or rarely hyperplasia. These abnormalities lead to the absorption failure of the interstitial fluid which is manifested by characteristic swelling typically affecting the extremities but may involve other parts of the body. PLE is considered as a chronic disease when

symptoms last more than three months (1, 2). Unfortunately, a lot of time passes from first lymphedema (LE) symptoms onset until proper clinical assessment and diagnosis because it is often confused with other conditions. Difficult and prolonged diagnosis of PLE results in high number of undiagnosed and untreated individuals which leads to lifelong physical and psychological morbidity caused by limb deformities and tissue changes, increased infection risk, mobility reduction, sensitivity changes, joints overloads and trophic skin ulcers (3, 4). There are limited data on the PLE prevalence, but it is estimated that it affects 1.2 per 100,000 people under 20 years of age (5). Depending on the age of onset of swelling, the PLE was previously classified into three categories: congenital, praecox and tarda. Recently, a classification algorithm for the primary lymphatic anomalies has been developed to illustrate five main categories of PLE and individual subtypes within these categories. This classification has proved to be a useful clinical and research tool

to categorise PLE and to enhance proper PLE diagnosis (6). Patient that will be presented in this case report has congenital Meige's like LE that is developed at puberty, usually affects lower extremities and is unrelated with other congenital anomalies or family inheritance (6). Diagnosis of PLE should be made based on the clinical examination during which potential complications should be sought and evaluation of disease psychological and functional impact done. Positive Pitting test, Stemmer sign, difference in the limb circumference >2 cm or limb volume >200 ml indicates lymphedema (7-9). After the clinical examination patients may be referred to other significant testing to confirm diagnosis, such as: laboratory tests (albuminemia, protein electrophoresis, proteinuria), venous Color Doppler ultrasound, lymphoscintigraphy, magnetic resonance imaging (MRI) and genetic consultation (8). The primary goals in the lymphedema management are reduction and stabilization of the limb volume, prevention of complications and facilitation of patient se-

lf-management, favouring patient autonomy and improving patient's quality of life (9). The management of the primary lymphedema includes various physiotherapy techniques that are applied individually depending on the patient's condition and the lymphedema state. The most common management strategy is a Complete Decongestive Therapy (CDT). Other treatment possibilities include the intermittent pneumatic compression, kinesiotope, low level laser therapy, ra-

dial shock wave, cupping, acupuncture, liposuction, and other surgical procedures (10, 11). The CDT consists of reduction and maintenance phase. When using CDT for the primary lymphedema, a standard treatment in the reduction phase is comprised of manual lymphatic drainage (MLD), compression therapy using short stretch bandages, exercises, skin care, diet, and education (12, 13). Maintenance phase includes wearing individually made flat knit compression

garments on a daily basis to obtain the best volume stabilization. Other components of this phase include occasional compression bandaging, MLD or self lymphdrainage (SLD), skin care, physical activity, and weight maintenance. It is possible to apply compression nocturnal systems to improve compliance and promote autonomy (14). Self-management strategies must be implemented in everyday living to maintain best possible condition of lymphedema when the he-

Table 1.  
Detailed diagnosis workout pathway

Year	Symptoms	Clinical examination	Diagnosis	Lymphedema therapy
1986.	Swelling in right malleolus area in first year. Afterwards swelling is getting bigger and it is in whole foot area. Difficulties to find proper shoes.	General practitioner Nephrologist	No proper diagnosis	No proper treatment
2000.	Malleolar swelling on both legs	Plastic surgeon, Radiologist - Colour Doppler Ultrasound	No proper diagnosis, Varicose veins, postthrombotic syndrome	Recommendation to wear circular knit stockings. Bioflavonoid, varfarin
2004.	Malleolar swelling on both legs	Radiologist - Colour Doppler Ultrasound	No proper diagnosis, Varicose veins, postthrombotic syndrome	No proper treatment
2007.	Swelling of the foot, ankle and both lower legs, more pronounced on right side.	Internist, Vascular surgeon, Radiologist - Colour Doppler Ultrasound	No proper diagnosis (Suspect on deep Venous thrombosis)	Recommendation to wear circular knitted stockings. Self-initiated physical activity and exercises
2009.	Swelling of the foot, ankle and both lower legs, more pronounced on right side.	Radiologist - Colour Doppler Ultrasound	No proper diagnosis, No pathologic changes found	No proper treatment
2016.	Swelling of the foot, ankle and both lower legs, more pronounced on right side.	Radiologist - Colour Doppler Ultrasound	No proper diagnosis, No pathologic changes found	No proper treatment
2019.	Swelling of the foot, ankle and both legs, more pronounced on the right side.	General practitioner specialized in lymphedema practice in Mošćenička Draga (clinical examination, circumference measurements, Colour Doppler Ultrasound	PLE diagnosis	1 session of 24h compression therapy, supplied with circular knit stockings, referred to Clinical Hospital Split
2019.	Swelling of the foot, ankle and both legs, more pronounced the on right side.	Physical medicine and rehabilitation specialist specialized in LE, Vascular surgeon	PLE diagnosis	CDT, Instructions for muscle pump activities during therapy. Significant reduction in volume. Supplied with flat knit stockings
2020.	Swelling of the foot, ankle and both legs, more pronounced the on right side.	Radiologist - Colour Doppler Ultrasound	No proper diagnosis, No pathologic changes found	Supplied with flat knit stockings
2021.	Less swelling of the foot, ankle and whole lower limbs, more pronounced on the right side	Physical medicine and rehabilitation specialist specialized in LE, Vascular surgeon, Nuclear medicine specialist lymphoscintigraphy	PLE diagnosis confirmed	CDT, Instructions for muscle pump activities during therapy. Significant reduction in volume, visible anatomical structures of ankle and under knee area.
2022.	Stable limb volume	Physical medicine and rehabilitation specialist specialised in LE		Supplied with flat knitted stockings

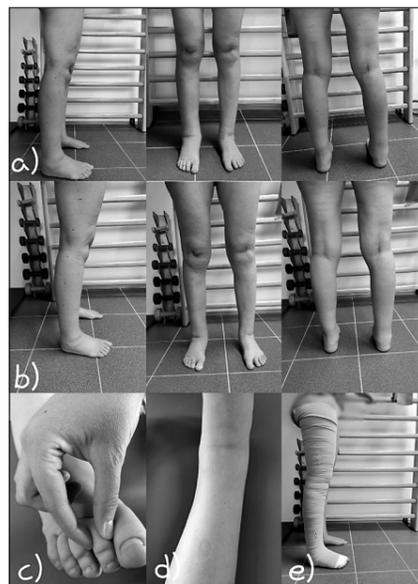


Figure 1. Clinical presentation of the second stage primary lymphedema before and after complete decongestive therapy. Figure 1a displays lymphedema state before the therapy from the anterior, lateral, and posterior side view. Figure 1b displays the lymphedema state after seven therapy sessions from the anterior, lateral, and posterior side view. Figure 1c displays Stemmer sign. Figure 1d displays Pitting sign. Figure 1e displays Compression therapy by doctor Partch.

alth care professionals and lymphedema treatment are unavailable (15, 16). The PLE patients face many difficulties and challenges on the personal, professional, and social level due to the chronicity of the illness. We hereby present a case of lower limb late onset, the second degree PLE diagnosed thirty years after the onset. A successful treatment for the reduction in volume of the lower limb using MLD and short stretch bandages was performed despite chronic nature of PLE. We wanted to highlight the positive impact that proper therapy can have on a patient's quality of life and the importance of early diagnosis to prevent complications.

CASE STUDY

A 46-year-old female with a long-standing history of the primary lymphedema affecting lower limbs was referred to our Physiotherapy Laboratory at the University Department of Health Studies, University of Split, Croatia for

lymphedema treatment during November 2021. Her path, from the first symptoms onset which manifested as right ankle swelling when she was 14 until PLE diagnosis when she was 46 years old, was not easy and it led to the formation of non-pitting, bilateral II. stage leg lymphoedema (Table 1.) (Figure 1.). The clinical diagnosis was finally confirmed by lymphoscintigraphy performed in December 2021. (Figure 2.). During 30-year period without proper diagnosis and management patient has developed some self-management strategies regarding her PLE e.g., bandaging, physical activity and wearing circular knitted compression garments. Cellulitis infections, which is common complication for lymphedema patients were prevented by regular skin care and avoiding cuts and heat sources (17).

Nevertheless, the lymphedema has slowly progressed over the years so patient had difficulties with finding shoes and clothes which has affected her professional, social, and everyday activities. After the diagnosis was established during 2019 the patient underwent CDT at the Clinical Hospital Centre Split. CTD was performed by a certified lymphtherapist for the first time in patient's life and flat knit compression garments compression grade III with accompanied toe caps compression grade I were applied. The patient is skilful in self- bandaging and donning of compression garments mostly because she is a nurse. Adherence to compression garments was full, as well as to the physical activity and skin care. Occasional intermittent pneumatic compression was performed at home. High level of everyday physical activity has been confirmed using IPAQ SF questionnaire (Table 2). A moderate adherence to the Mediterranean diet eating habits measured by MEDAS questionnaire (7 points) contributed to maintain healthy body weight and better PLE condition during the long maintenance phase without a proper therapy (18, 19). Everyday activities were performed using the stationary bicycle and trampoline for the regular aerobic exercises. Since she is not a driver, the long-distance walking routes were an everyday routine, as well as mountain climbing during the weekends. In

the summer period she included swimming activities for at least 30 min a day. Problems with PLE emerged during the summer 2021 due to the suspension of therapy in Clinical Hospital Centre Split during the COVID-19 pandemic. Access to the physician, the proper LE therapy and compression garments were difficult. PLE condition got worse also due to high summer temperatures and due to her personal and professional lifestyle changes like the prolonged standing and sitting period during the day. Her compression garment was out of date and no longer served its purpose. Her legs were heavy and more swollen which led to difficulties in performing everyday activities. Her quality of life got worse especially regarding her physical appearance such as difficulties in finding proper shoes and clothes (2.28 points) and her LE symptoms such as feeling of heavy,

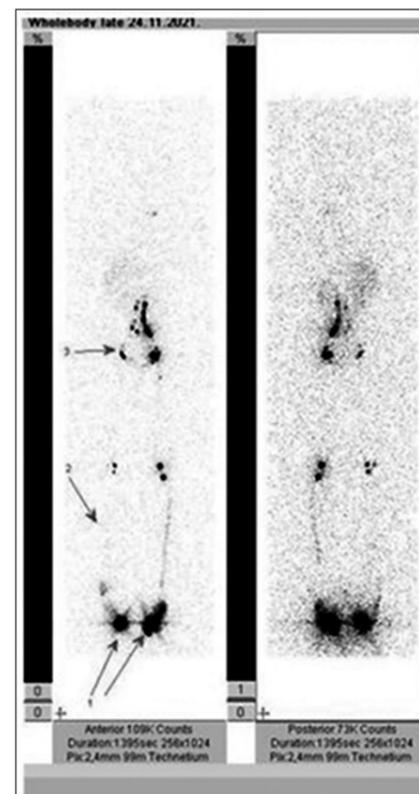


Figure 2. Lymphoscintigraphy. Whole body scan (AP projection) done with Tc-99m nanocolloid particles, 4h after injection. 1.) Site of subcutaneous injection of tracer in both feet. 2.) Absent display of right lower limb lymph pathway. 3.) Reduced number of regional lymph nodes (right inguinal region).

Table 2. Circumference measurement values on the first and seventh session of the compressive decongestive therapy. L left, R right, DIFF1 difference between L-R, DIFF2 difference between L 1. day therapy- L 7. day therapy, DIFF3 difference between R 1. day therapy - R 7. day therapy.

Leg measuring points (cm)	1st therapy session			7th therapy session			7th therapy session		
	L	R	DIFF1	L	L	DIFF2	R	R	DIFF3
10	23	25	2	23	21,5	1,5	25	22,2	2,8
20	25,5	29	3,5	25,5	25	0,5	29	27	2
30	25,5	27,5	2	25,5	25	0,5	27,5	26	1,5
40	32	34,5	2,5	32	30	2	34,5	30,7	3,8
50	36	36	0	36	34,5	1,5	36	35	1
60	38,5	39	0,5	38,5	35,5	3	39	35	4
70	41	43,5	2,5	41	40	1	43,5	40,5	3
80	47,5	50,5	3	47,5	46	1,5	50,5	47	3,5
90	57,5	61	3,5	57,5	54	3,5	61	56,5	4,5

old and weak legs (1.83 points) measured with LEQOL questionnaire. PLE therapy was conducted through sessions of 45 min three times a week in total seven sessions. Sessions consisted of Vodder method of MLD and compression bandaging according to dr. Partch with short stretch bandages (Figure 1. a, b, e). The patient was instructed to do the exercises for enhancement of muscle pump activity in lower limbs and everyday walking activities lasting at least for 30 minutes a day. Circumference measurements were performed, and photographs were taken before each session to follow success of LE therapy (Table 3., Figure 1b.). Also, the questionnaires (IPAQ, MEDAS, LEQOL) were filled out before beginning and three months after the therapy (Table 2). Reduction phase for

the PLE was conducted until circumference measurements were the same after two consecutive measurements (9). The most evident reduction in volume was accomplished in foot and ankle area so her shoes were better fitted. Overall reduction was on an average of 3 cm on her right limb, and 1,9 cm on her left limb. After the treatment Stemmer sign was no more positive (Figure 1. c.). At the beginning of treatment, her right lateral malleolus was not visible, which was not the case after the therapy. Tibia was also under the thick layer of oedema, and after the therapy was palpable and visible. Her skin was soft and elastic (Figure 1. b.). Quality of life measured with LEQOL questionnaire was improved especially regarding her symptoms (1.16 points) and physical appearance (1.85 points).

Immediately after the CDT she had an appointment with compression garments measurement specialist to get individually made flat knitted stockings compression class (ccl) III, for everyday use trough the maintenance phase of LE. She was fitted with a new pair of stockings three months after the measurement was performed. During the waiting period for a new pair of stockings the patient was advised to use self-management strategies of combining the compression therapy using the short-stretched bandages, regular physical activity, skin care and maintenance of body weight.

DISCUSSION

PLE is classified as a rare disease. Long waiting periods that can be longer than ten years from the first symptoms

Table 3. IPAQ SF results before and three months after the lymphedema treatment. MET min/week The Metabolic Equivalent of Task (MET) is a physiological measure expressing energy of specific physical activity to a reference metabolic rate, usually represented by metabolic resting rate. MET represent weekly metabolic engagement in walking, and moderate and vigorous physical activity.

IPAQ SF domains	IPAQ SF scoring			
	Before the treatment		Three months after the treatment	
	MET min/week	Kcl/week 1	MET min/week	Kcl/week
Low physical activity	1386	1819,13	2079	2728,69
Moderate physical activity	720	945	720	945
Vigorous physical activity	4800	6300	0	0
Total	6906	9064,13	2799	3673,69

onset to the correct diagnosis and adequate treatment plan make the condition of PLE chronic and difficult for treatment. Prolonged periods for establishing a proper diagnosis may occur because it is often confused with other diagnoses e.g., venous insufficiency, lipedema (2). Unfortunately, a Croatian patient presented here has waited 30 years for their diagnosis, which is unacceptable. We strongly believe that the main reason for the late diagnosis lays in the fact that there is no specialised lymphedema clinic, lymphedema specialist, lymphedema management guidelines and lymphedema registry in Croatia. Diagnostic possibilities for LE are either scarce (long waiting period for lymphoscintigraphy) or inadequate. Our patient has undergone venous Colour Doppler Ultrasound examination on several occasions but LE although clinically visible, was never recorded. Also due to the lack of proper LE education there is a low suspicion rate among the healthcare professionals. Although Clinical Hospital Centre Split has a long tradition in the LE therapy, the physiotherapists involved in the LE therapy differ in education and have different approaches in treating the LE I patients. Usually, the LE therapy is performed as a standalone MLD which has been proved insufficient for the proper treatment (9). Only the minority of patients have compression bandaging as part of the LE therapy. In our health system a patient is entitled for only ten sessions of the LE therapy every one to two years leading to only short-term results in the LE reduction. Prescription of compression garments as well as the patient adherence to wearing them is low. Besides that, reimbursement policy of compression garment in Croatia is inadequate as well as the provision of proper garment fitting. We still have not figured out the best possible way to ensure compression garments for our patients after the reduction phase. Unfortunately, a bridging period from the last CDT session and the acquirement of compression garments is one month and more depending on a supplier. In that period, there is a problem with maintaining the limb volume that mostly depends on the quality of the patient's self-management strategies. The already long waiting list for examination and treatment of the LE

has further increased during the COVID-19 pandemic. Therefore, our patient was forced to wear out of date compression garment that was not adequate for her LE and her condition got worse despite proper education and conducting LE self-management daily activities. Compression garments should be changed every three to six months to ensure the best effect (11). Considering the enduring nature of COVID-19, the published guidelines suggest imperative of having the LE services to provide suitable care for patients (20).

We must praise efforts of this patient that should serve as an example of how long-term struggling with the health system and chronic disease can eventually have great results. On the other hand, she has an advantage because as a nurse she has skills and knowledge that other patients do not have. In conclusion, it is our obligation to educate the healthcare professionals and patients to increase lymphedema awareness to improve the lymphedema management.

#### CONCLUSION

Although a primary lymphedema is a rare disease due to its chronicity and a late diagnosis it poses great problems for both patients and health care professionals. Lack of the specialised lymphedema clinics, lymphedema specialists, lymphedema management guidelines and lymphedema registry is one of the main causes for the prolonged diagnosis in Croatia. With presenting this case of the late onset lymphoedema we wanted to highlight the positive impact that proper therapy can have on a patient's quality of life and the importance of early diagnosis to prevent complications. It is our obligation to educate the healthcare professionals and patients to increase lymphedema awareness in order to improve the lymphedema management.

#### Abbreviations:

LE - Lymphedema  
CDT - Kompletna dekongestivna terapija  
PLE - Primary lymphedema  
MLD - Manual lymph drainage  
SLD - Simple lymph drainage  
ccl - compression class  
IPAQ-SF - International Physical Activity Questionnaire Short Form

MEDAS - Mediterranean Diet Adherence Screener  
LEQOL - Lymphedema Quality of Life

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SUKOB INTERESA/CONFLICT OF INTEREST  
Autori su popunili *the Unified Competing Interest form na www.icmje.org/coi\_disclosure.pdf (dostupno na zahtjev)* obrazac i izjavljuju: nemaju potporu niti jedne organizacije za objavljeni rad; nemaju financijsku potporu niti jedne organizacije koja bi mogla imati interes za objavu ovog rada u posljednje 3 godine; nemaju drugih veza ili aktivnosti koje bi mogle utjecati na objavljeni rad./ *All authors have completed the Unified Competing Interest form at www.icmje.org/coi\_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.*

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#### Sažetak

#### PRIKAZ SLUČAJA KASNOG TIPA PRIMARNOG LIMFEDEMA - OD DIJAGNOZE DO USPJEŠNE TERAPIJE

Ivana Klarić Kukuz, Josipa Grančić, Marta Pavlović, Ana Barić Žižić, Jure Aljinović, Ivanka Marinović, Ana Poljičanin

*Prikaz slučaja 46-godišnje medicinske sestre sa drugim stupnjem kasnog primarnog limfedema donjih ekstremiteta koji je dijagnosticiran 30 godina nakon pojave prvih simptoma. Nepostojanje ambulante za limfedem, liječnika specijalista koji se bavi limfedemom, smjernica za zbrinjavanje limfedema te registra za limfedem glavni su uzroci kašnjenja postavljanja dijagnoze limfedema u Hrvatskoj. Terapija limfedema provedena je u terminu od 45 minuta, tri puta tjedno ukupno sedam tretmana. Korišteni su fizioterapijski postupci: ručna limfna drenaža u kombinaciji s kompresivnom terapijom prema dr. Partchu i edukacija. Dane su upute o provođenju tjelesne aktivnosti. Postignuto je smanjenje volumena unatoč dugotrajnom trajanju limfedema. Promjene u kvaliteti života i razini tjelesne aktivnosti pratili smo uz pomoć validiranih upitnika. Po završetku terapije pacijentica je upućena ortotičarki radi uzimanja mjera za ravno tkanu kompresivnu odjeću kompresijske klase III. koja je prikladna za fazu održavanja volumena limfedema. Primarni LE je kronično stanje koje je u slučaju naše pacijentice bilo neliječeno preko trideset godina. Uz pomoć timskog rada i sveobuhvatnog terapijskog pristupa zbrinjavanju primarnog limfedema moguće je dobiti zadovoljavajuće rezultate terapije te iste održati, posebno ukoliko je pacijent motiviran i dobro educiran.*

Ključne riječi: PRIMARNI LIMFEDEM, LIMFOSCINTIGRAFIJA, RUČNA LIMFNA DRENAŽA, KOMPRESIVNO BANDAŽIRANJE

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