Complication of Chronic Lymphedema in an Elderly Achondroplasia Patient: A Case Report

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고령의 연골무형성증 환자에서 만성 림프부종에 의한 합병증과 치료: 증례보고

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Abstract

Chronic lymphedema can cause severe complications such as infection, pain, disability, and secondary malignancy. We introduce a case of neglected chronic lymphedema in an elderly achondroplasia patient. The patient visited the hospital for lymphedema and skin lesion suspected of malignancy, which had been neglected for more than 8 years after breast cancer treatment. The patient quickly confirmed chronic inflammation after biopsy of the suspected malignancy site. After that, taking into account the patient's underlying medical condition and social and economic status, a modified protocol of complete decongestion treatment (home-based) was established as a sustainable therapeutic strategy. Caregivers were educated to ensure proper home treatment, and thus, patient visits to institutions were minimized. At the same time, complete decongestion treatment was simplified to reduce the burden on caregivers and patient to ensure sustainable and appropriate treatment. As a result, successful lymphedema treatment was achieved without treatment abandonment.

Key Words

Lymphedema, Achondroplasia

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Introduction

Lymphedema is a chronic condition that significantly reduces the quality of life, especially in the elderly population with poor physical function. Lymphedema can cause additional psychological and social inactivity in the elderly.[1,2] This psychosocial inactivity lowers the adherence of lymphedema treatment, and the subsequent worsening of lymphedema creates a vicious cycle that aggravates psychosocial inactivity more.[3]

Currently, complete decongestion therapy (CDT) is known as the primary conservative treatment method,

which includes manual lymphatic drainage (MLD), compression bandaging, therapeutic exercise, and skin care.[3,4] CDT is conventionally progressed in two phases, a treatment phase (phase 1) for active reduction of lymphedema, and a maintenance phase (phase 2) to manage and maintain lymphedema, which was reduced during the treatment phase.[3] However, although the CDT protocol is known as the gold standard for conservative treatment of lymphedema, it is a relatively intensive treatment and requires frequent (daily) visits to medical institutions in phase.[1,3]

In order to prevent treatment abandonment (follow-up loss), the treatment must be appropriately adjusted according to various comorbidities such as the patient's behavioral restrictions, compliance, comorbidities, and age.[1,4] Since serious complications such as skin infection[3] or secondary malignancy[5] could occur, "sustainable" and "feasible" therapeutic strategy is needed so that these complications are not neglected.

Achondroplasia is a disease characterized by congenital short stature, also called dwarfism, and its dominant feature is proximal limb shortening (rhizomelic limbs).[6] To our best knowledge, there have been no case reports of achondroplasia with lymphedema. We present a case of achondroplasia patient with breast cancer related lymphedema (BCRL) uncontrolled for more than 8 years with pain and pigmented tumor-like lesion.

Case Report

A 81-year-old women with congenital achondroplasia was diagnosed with breast cancer 12 years ago and underwent local excision with axillary lymph node dissection. The

Table 1. Comparison of Pre-Post Treatment of Lymphedema

	Pre-treatment			Post-treatment		
Upper extremity circumference	Rt (aff) (mm)	Lt (unaff) (mm)	aff-unaff difference (mm)	Rt (aff) (mm)	Lt (unaff) (mm)	aff-unaff difference (mm)
MCP	185	167	18	160	160	0
Wrist	182	138	44	140	140	0
10 cm dist LE	240	157	83	190	170	20
Elbow	262	182	80	195	180	15
10 cm prox LE	262	182	80	200	185	15
Axilla	275	198	77	220	195	25
MBI		36			54	
VAS		5			2	
ISL stage		III			II	
APTA criteria		Severe (> 5 cm)			Mild (< 3 cm)	

Aff: affected side, APTA: American Physical Therapy Association girth difference, dist: distal, ISL: International Society of Lymphology, LE: Lateral Epicondyle of Elbow, MBI: Modified Barthel Index, MCP: Metacarpophalangeal Joint, prox: proximal, VAS: Visual Analogue Scale, unaff: unaffected side

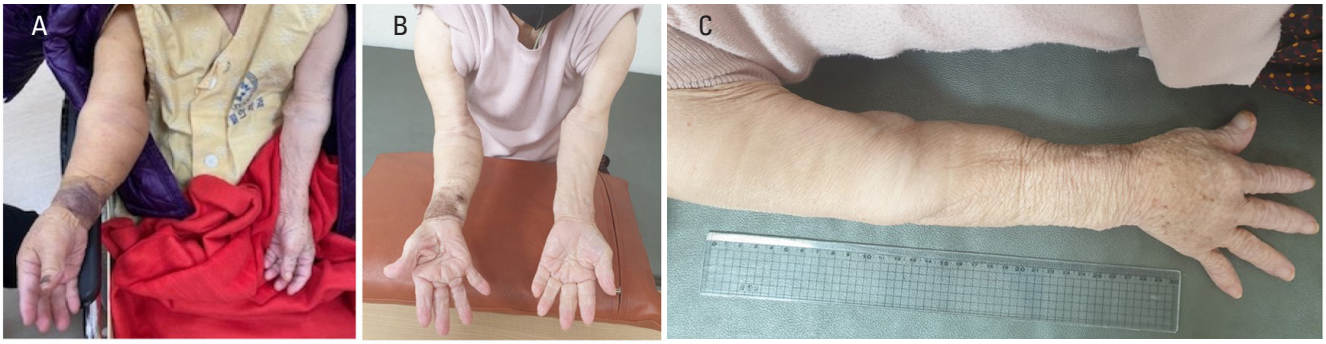

Fig. 1. Comparison before and after treatment of lymphedema. (A) photo of pre-treatment of lesion, (B) photo of post-treatment of lesion, (C) photo of short arms due to achondroplasia.

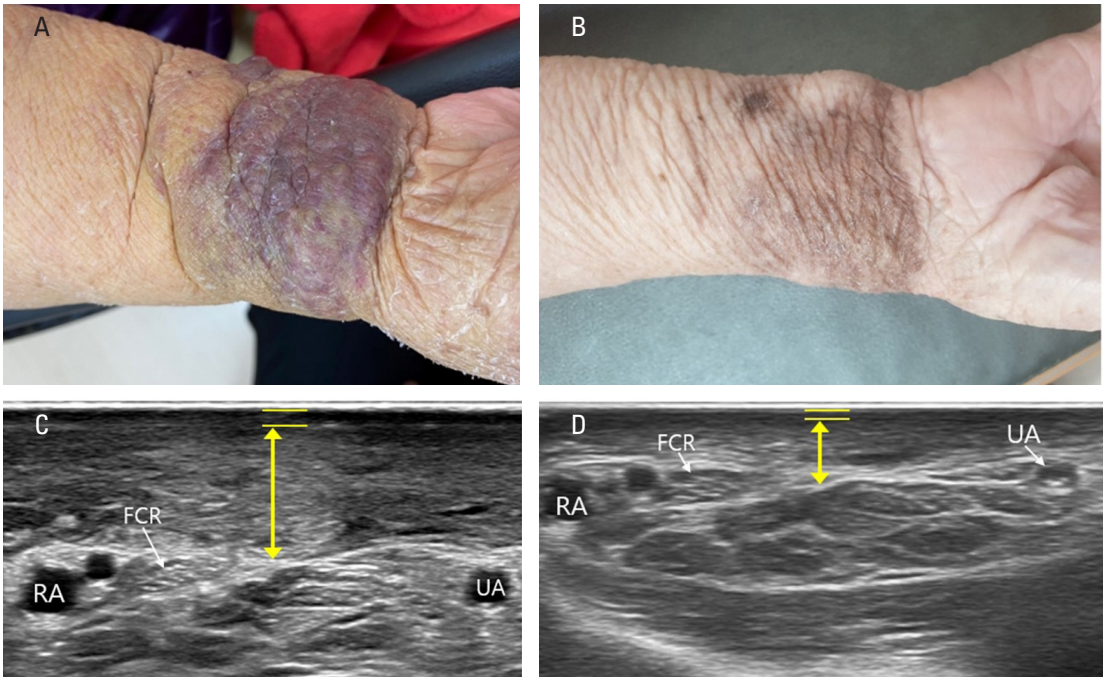

Fig. 2. Before and after treatment of pigmented tumor-like lesions in the wrist area. (A) photo of pre-treatment of lesion. Before treatment, non-pitting with trophic skin changes and warty overgrowth corresponding to ISL stage 3 were observed in the wrist, accompanied by purple color change. There were no signs of lymphostatic ulcerations with lymphorrhea or bleeding. (B) photo of post-treatment of lesion. After treatment, only mild pigmentation remained, darkened warty projections disappeared and the original skin texture was restored. (C) ultrasound transverse view of wrist with lesion of pre-treatment. (D) ultrasound transverse view of wrist with lesion of post-treatment. Yellow arrows in C and D indicate the thickness of the subcutaneous tissue corresponding to the region of interest in lymphedema (between the skin and fascia); The yellow parallel lines indicate the thickness of the skin layer. A decrease in subcutaneous layer thickness is seen along with the skin layer thickness, which is a characteristic finding in lymphedema.[9]
RA: Radial Artery, UA: Ulnar Artery, FCR: Flexor Carpi Radialis tendon

patient had no edema before surgery. But immediately after surgery, lymphedema of the right upper extremity detected, but the symptoms were mild, and the edema was reversible (International society of lymphology (ISL) stage 1). Four years later, the patient was treated for aggravated BCRL at hospital (ISL stage 2; partially reversible and no fibrosis). The patient started CDT phase 1 treatment (skin care, MLD, compression bandaging, and therapeutic exercise) at a medical institution, but because of the old age and congenital comorbidities, outpatient visits were difficult. As a result, follow-up was lost after 3 times of treatments.

Eight years after the last outpatient visit, she visited the hospital due to severe edema of right upper extremity (Table 1, Fig. 1A) and pigmentation with papillomatosis at wrist (Fig. 2A). It was reported that edema, pain, and pigmented tumorous lesion of the wrist occurred about 3 months ago and showed progressive deterioration. During the period of 8 years, no management of lymphedema had been performed at all. Although no signs of infection such as local heating sense or skin ulcers were observed, the patient needed to differentiate lymphangiosarcoma (Stewart-Treves syndrome)5 for the black discoloration of the wrist and tumor-like character (Fig. 2A). Immediately, ultrasound-guided excisional biopsy was performed, and only chronic inflammation with fibrosis was found, and there was no evidence of malignancy (Fig. 3). Then, appropriate strategy for BCRL established.

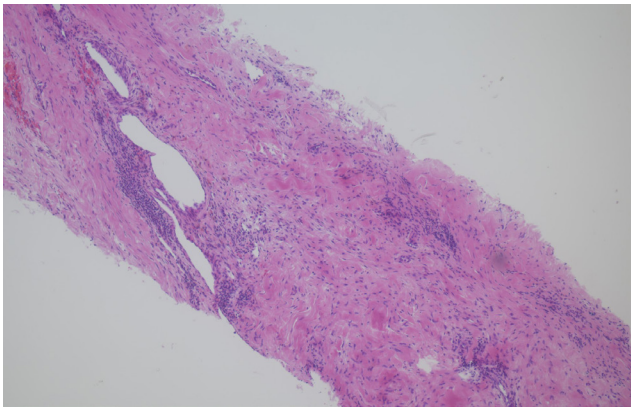

Fig. 3. Histopathological examination of pigmented tumorous lesion of patient's wrist. Inflammatory cells aggregation is identified in fibrotic tissue with H&E (Hematoxyline & Eosine) staining at 100x magnification.

1) Patient's underlying condition and functional status

The patient's height and weight were 131 cm and 36 kg, and the body mass index was 21.0, which did not require weight control. The patient was in a state of decreased activity, and became assist needed status with almost every activity of daily living (ADL) compared to 8 years ago. The patient needed wheelchair ambulation due to lower extremity function due to a left ankle fracture 3 years ago, and the function of the upper extremity was also deteriorated due to severe lymphedema of the right upper extremity which was her dominant hand, and pain in the right upper extremity of 5 points on the visual analog scale (VAS) due to worsening of lymphedema. As a result, the patient's overall ADL was dependent on the caregiver (Table 1).

2) Adjustment to sustainable lymphedema treatment protocol

Conventionally, as a phase 1 treatment for CDT, institution-based treatment should be performed. However, considering the condition of the patient who could not visit the hospital every day, a home-based modified phase 1 protocol of CDT was planned for a sustainable treatment. Modification of the CDT protocol was made for each component. First, in compression bandaging, which was considered the most important among the four components of CDT,[7] considering achondroplasia (short rhizomelic limb), it was impossible to apply easy-to-apply items such as garments or Autofit[8], so a multi-layer bandage known as the conventional gold standard was selected.[3]

During therapist-led treatment time, the caregivers were trained to be able to perform bandaging properly to the patient, and demonstrated to the expert to confirm proper performance. The caregiver was asked to perform

compression bandaging for more than 23 hours per day, as in the conventional phase 1 of CDT.[3] Second, for MLD and therapeutic exercise, simple repetitive motions that can be easily followed by patients and caregivers were educated. Third, regarding skin care, education was provided on applying an emollients and avoidance of sauna and skin puncture.[3] As compression bandaging was considered to be the most important component[7], the weight of the compression bandage was given more than the rest of the CDT components (MLD, therapeutic exercise, skin care), and caregivers were informed that not stopping the treatment is the top priority. After confirming that the caregiver performed it properly after about 2 days of training, a home-based modified phase 1 protocol of CDT was performed.

3) Treatment outcome of modified phase 1 of CDT

At follow-up after about 1 month, the caregiver performed compression bandaging appropriately as instructed without omission, and maintained skin care such as the use of moisturizer, but rarely performed therapeutic exercise or MLD. Edema was significantly improved, and pain in the right upper extremity was also relieved from VAS 5 to VAS 2 (Table 1). The tumor-like character in the wrist area disappeared and only the pigmentation remained (Fig. 2B). Additionally, the thickness of lymphedema (thickness of subcutaneous tissue; proportionately with the skin layer thickness9 was markedly decreased on the ultrasound of the wrist (Fig. 2C, 2D).

Modified Barthel Index (MBI), which reflects independent ADL, increased significantly, especially in ADL using the upper extremities (eating, washing, washing, and dressing items) after reduction of lymphedema on right arm. Additionally, as the frequency of patients' visits to medical institutions decreased, economic burdens such as transportation and hospital expenses were reduced. Furthermore, as the pain-free time increased, the depression improved and the reliability of treatment increased, and the treatment adherence also improved.

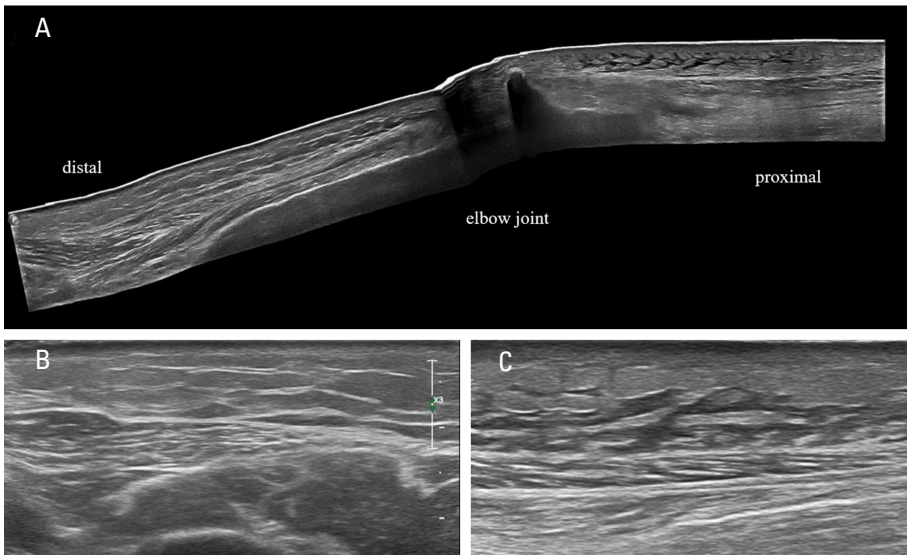

Fig. 4. Residual post-treatment lymphedema. After 1 month of phase 1 of CDT, there is still residual edema. An increase in the overall subcutaneous thickness is seen, but the echo free region is particularly prominent in the proximal area. (A) panoramic echo image of whole upper extremity, (B) mid forearm, (C) proximal upper arm.

4) Continuation of phase 2 of CDT

The patient still had mild remaining lymphedema (Fig. 4), so the lymphedema treatment corresponding to phase 2 of CDT has been maintained. For compression bandaging, it was difficult to apply garment or Autofit,[8] which were simplified substitutes, due to achondroplasia (rhizomelic limb), so multi-layered bandaging was maintained. However, instead of bandaging all day for 23-24 hours a day like in phase 1, the intensity was reduced to adjust according to the symptoms (10-20 hours a day). MLD and therapeutic exercise were educated to caregivers as in phase 1. As the pain relief and bandage free-time increased, it was encouraged to perform for as long as possible. Skin care was maintained as in phase 1, and caregivers were requested to monitor for skin changes reflecting infection, secondary tumors, and worsening of lymphedema. The patient checked the degree of lymphedema and skin condition at the outpatient clinic once every 2 months and maintained the improvement.

Discussion

This case emphasizes a patient-centered therapeutic approach for chronic lymphedema that has been neglected for a long time due to poor access to hospital derived from congenital comorbidity such as achondroplasia accompanied by acquired comorbidities such as ankle fracture and frailty from old age.

An appropriate surveillance approach was initially made for complications that could be caused by neglected BCRL, and then an appropriate treatment strategy was established in consideration of the patient's economic, social, personal, and medical situation. As a result, a sustainable and feasible treatment for lymphedema has been successfully achieved. Through this case, we consider various factors for lymphedema, suggest possible hypotheses, and suggest directions for future research.

1) Achondroplasia

Through this case of achondroplasia, we suggest a possible hypothesis and future research direction for lymphedema treatment.

First, the effect of arm length in the treatment of lymphedema. In measuring the severity of lymphedema, arm length is an often neglected factor. For the measurement of lymphedema, there is a volume-based method rather than a circumference-based method, but it requires special equipment,[2] so it is not easy to use in clinical practice conveniently. It seems that some correction is possible if the arm length is included in the classical circumference-based lymphedema measurement. Intuitively, the shorter the distance of lymphatic drainage, the greater the therapeutic effect can be expected. Considering that the patient with the short arm showed dramatic improvement in this case as well, a reasonable hypothesis can be established that the response to the treatment of lymphedema is greater with the short arm length.

Second, the relationship between achondroplasia and lymphedema. Achondroplasia is known to be caused by mutation of the fibroblast growth factor receptor gene (FGFR3).[10] Recent studies have revealed that the FGFR3 gene acts in the process of lymphangiogenesis,[11,12] and there are reports that lymphangiogenesis has potential as a new solution for lymphedema.[13] In light of these studies, it can be inferred that, after lymph node dissection, the patient had persistent (immediately after surgery) lymphatic retention (circulatory dysfunction) due to impaired lymphaniogenesis by genetic defects (mutation of FGFR3). In other words, it suggests the possibility that achondroplasia may have contributed in part to the occurrence of lymphedema. To reveal this, a large-scale investigation on lymphedema in patients with achondroplasia is needed in the future, and an analysis of the treatment effect according to arm length also would be helpful in predicting the treatment effect of lymphedema.

2) Surveillance of complications caused by neglected lymphedema; Exclusion diagnosis of lymphangiosarcoma

Screening of complications caused by neglected lymphedema and appropriate differential diagnosis are very important. In BCRL, there are reports that a tumor-like lesion with red-purple color change in the upper extremity is diagnosed as metastasis of a primary cancer,[14] or as lymphangiosarcoma.[15] Therefore, in this case, the process of differential diagnosis of the tumorous feature lesion seen in the upper extremity from malignancy is essential. Fortunately, only the findings of chronic inflammation and fibrosis were observed, and it was possible to proceed to the lymphedema treatment phase. The tumorous lesion of the patient's wrist can be regarded as a localized exophytic lesion called "Lymphostatic verrucosis" with wart-like skin accompanying chronic lymphedema. It is often accompanied by severe lymphedema of diffusely affected body parts (elephantiasis), but it could appear only in a limited area as localized lymphedema.[16] Since the localized lymphedema is common in the lower extremities and trunk, and there are few reports of upper extremities, this case report showing localized tumorous feature in upper extremity lymphedema is valuable. After localized unrecognized physical injury to the wrist, concomitant micro-lymphatic leakage or damage to lymphatic vessels may have contributed to localized hyperplasia.[16]

Therefore, the appearance of the skin on the wrist in this case appears to have a tumor-like shape due to the overlapping of the hyperpigmentation in chronic inflammation,[17] joint acanthosis in achondroplasia,[6,18] and papillomatosis by lymphedema. In addition, surveillance for infection is also important. There were no clinical features such as heating, and the blood test showed normal results, so infection was excluded in this case.

3) Patient-centered lymphedema treatment strategies

Patients with chronic lymphedema should be under continuous management by establishing a feasible and sustainable treatment strategy that reflects the patient's overall environment,[1] such as proximity to medical institutions, frailty and comorbidity that affects physical ability, social support, and economic situation, and should not be neglected. Especially in this case, Achondroplasia contributed to reduced mobility and participation, and likely led to treatment abandonment. Achondroplasia is likely to be accompanied by psychological and social shrinkage due to negative feeling of own congenital short stature, and may have lowered the aesthetic motivation for lymphedema treatment.[18,19] Therefore, we emphasized that adjusting the treatment protocol to be patient-centered should be a key consideration in the treatment of chronic lymphedema.

Although CDT is the gold standard for lymphedema treatment,[3] it might too intensive for vulnerable patients, so appropriate modification rather than strict insisting on all patients uniformly, can serve as a starting point for treatment success.[4,7] In this case as well, considering the patient's environment, performing all the elements of CDT would have had severe pressure on the caregiver to perform treatment and would have increased the probability of treatment abandonment. Therefore, treatment modifications should be considered to minimize the probability of treatment abandonment.

Recently, a study on the comparison between intensive CDT and compression bandaging (part of CDT) for elderly was conducted, and there was a report that compression bandaging showed similar effects to CDT, showing advantages in convenience and price.[7] Therefore, we argue that compression bandages should be weighted as a major component of CDT,[7] and that caregivers education on compression bandages should be focused on when establishing a adjusted protocol. And the therapeutic exercise and MLD, which are mainly performed by experts at medical institutions,[3] have been simplified in this case. And the frequency of visits was also minimized compared to routine protocol of CDT phase 1 (daily visits).[3]

However, a prerequisite for reducing the intensity of lymphedema treatment or the frequency of visits is good

caregiver compliance and careful treatment education for caregivers. Therefore, during treatment at a medical institution, intensive treatment education for caregivers was conducted so that the maximum treatment could be achieved at home. Caregiver education should include the process of demonstrating the treatment by the caregiver and monitoring and correcting it by the medical staff so that the treatment can be properly performed at home. In the subsequent phase 2, as an extension of phase 1, there should be continuous feedback and modification of patient-centered treatment.

In this case, after treatment, not only the lymphedema decreased, but also the pain and the upper extremity function improved. As such, improvement in the overall symptom cluster will have beneficial effects on quality of life improvement and emotional well-bing[2], and then recognizing the need for hospital visits through motivation for treatment, consequently increasing treatment compliance.[20] As the timing of intervention for the treatment of lymphedema is very important,[17] a sustainable and feasible treatment strategy for lymphedema according to the patient's condition is emphasized once again to improve the quality of life and prevent secondary complications for chronic lymphedema in the elderly.

In Conclusion, through this case, we emphasize a delicate evaluation of possible complications such as secondary malignancy or infection should be preceded prior to treatment in neglected lymphedema. In addition, we suggest to modify the lymphedema treatment protocol in consideration of aging related comorbidity and the patient's underlying medical and social condition for successful and sustainable BCRL management.

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