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Six Month Study of Therapeutic Effects of Deep Cervical Lymphaticovenular Anastomosis in an Alzheimer's Disease Patient: A Case Report

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Highlights

Obstruction was observed in a lymph node in the district 3 of deep cervical area on both sides of a AD patient.

A super-microsurgical technique was established to improve the drainage function of central lymphatic system by deep cervical lymphaticovenular anastomosis (LVA) in the AD patient.

The deep cervical lymphatic system was dysfunctional in the AD patient due to obstruction of a lymph node in the district 3.

Fixing the obstruction by surgery generated a consistent therapeutic effect in AD patient during the six-month follow-up.

1. Abstract

1.1. Introduction and Importance

Degeneration of the central lymphatic system is reported to account for pathogenesis of aging-associated Alzheimer's disease (AD) through accumulation of metabolic waste of large molecules in the mouse brain. The findings remain to be translated into a clinic therapy of AD.

1.2. Methods

Fluorescence dye of indocyanine green was used to identify blockage of deep cervical lymphatic system in an AD patient. Lymphaticovenular anastomosis (LVA), a super- microsurgical technique, was conducted to connect the influx lymphatics of obstructed lymph nodes into the jugular vein to fix the blockage.

1.3. Outcomes

Obstruction was found in lymph nodes of the district 3 (area III) of deep cervical area on both sides of the AD patients. The surgery resolved the obstruction and improved behaviour, memory and psychiatry of the AD patient. The improvement was confirmed in the follow-up studies at 1st, 4th and 6th months. p-tau181 level was decreased in the peripheral blood from 4.26 pg/ml before surgery to 0.64 pg/ml at 6th month post surgery. The PET-CT image of glucose utilization demonstrated that the neuronal functions were increased in multiple areas of the brain.

1.4. Conclusion: The deep cervical lymphatic system was dysfunctional in the AD patient due to obstruction of lymph nodes in the district 3. The LVA surgery fixed the obstruction and generated a consistent therapeutic effect independent of anaesthetics in the patient for months.

2. Introduction

The central lymphatic system is merging as a promising target in the treatment of AD for clearance of metabolic wastes of the brain [1]. The system drains central lymph fluid generated in the glial lymphatic (glymphatic) in clearance of large molecular metabolic wastes (Lipids and amyloid-beta, Aβ) [2]. The lymph fluid flows through the meningeal lymphatic [3], nasopharyngeal lymphatic plexus and deep cervical lymphatic and lymph nodes eventually into the blood system to move the metabolic wastes away [4]. Many elegant studies have reported that dysfunction of the central lymphatic system 1 is an important risk factor of AD [5]. In mice, disruption of meningeal lymphatics accelerates Aβ deposition, promoting the progression of AD [6]. Animal studies have found that AD mice exhibited significant impairment in cerebrospinal fluid outflow from the submandibular lymph nodes with a reduced contraction frequency of peripheral lymphatic [7]. Blocking the deep cervical lymphatic system by ligation exacerbated the AD-like phenotype in APP/PS1 transgenic mice, resulting in more severe brain Aβ accumulation, neuroinflammation, synaptic protein loss, impaired aquaporin-4 polarization, and cognitive and exploratory behaviour deficits [8]. The dysfunction is responsible for accumulation of lipids and amyloid-beta (Aβ) proteins in the neuronal microenvironment and cerebrospinal fluid in the brain [2]. The central lymph fluid enters the medial cervical lymphatic vessels and then into the deep cervical lymph nodes in the route of efflux. This lymphatic network connects to the deep cervical lymphatics, rather than the lateral lymphatics [2]. Based on these finding, Xie, et al. generated a "cervical lymph venous anastomosis (CLVA)" protocol to treat AD patient [9]. The surgery was done with super-microsurgical techniques to drain the brain lymph fluid into the jugular vein in the neck for clearance of metabolic wastes from the brain. Compared to the existing AD drugs, the innovative surgery technique exhibited rapid therapeutic effect in the treatment of AD patients. However, the efficacy remains to be tested in AD patient as the diagnosis of AD disease was not well conducted in the study [9]. In current study, the patient was diagnosed with AD through a strict examination before the surgery. The therapeutic efficacy was observed within days post-surgery and confirmed in six-month follow-up by assessments of the cognitive function, peripheral blood AD biomarkers, and brain 18F FDG-PETCT test. All of the parameters were improved in the AD patients in the six-month follow-up. The improvement in cognitive function was demonstrated in the mini-mental state examination (MMSE), Montreal cognitive assessment (MOCA), auditory verbal learning test, activity of daily living (ADL), and neuropsychiatric inventory (NPI) over the pre-surgery. The effects were 2 observed within days of the surgery and the improvements were consistent during the follow-up. The peripheral blood AD biomarkers showed a significant decrease in p- tau181 as early as the second day post-surgery with a continued downward trend in the six-month follow-up. These data provide clinical evidence of therapeutic efficacy of the surgery. The follow-up is ongoing to assess the efficacy beyond six months. The patient did not experience any surgery-related complications. This report is prepared in reference to the PROCESS 2020 Guideline [10].

3. Methods

3.1. Study Design

This is a prospective study at single centre with one AD patient. The follow-up was six months post-surgery by examination of behaviour, brain function and blood samples of the patient.

3.2. Medical History

The patient, a 57-year-old female with a high school education, was admitted on November 14, 2023, due to progressive memory decline for 1 year. She began experiencing memory decline without any apparent brain trauma or other diseases, characterized by forgetting recent events and repeatedly asking the same questions. One month before admission, the patient's memory function was declined significantly after her mother’s death. She suddenly lost ability to do daily work, such as picking up her grandson at school as she could not remember the school address. Additionally, she could not operate TV or do other household work. She became lazy, irritable, lost her sense of geographic direction and security, and frequently called her husband by phone every few minutes.

3.3. Initial Consultation and Treatment

The patient visited our memory clinic and received a diagnosis of Alzheimer's disease in combination with anxiety and depression on September 21th, 2023. She was prescribed Donepezil 5 mg qn, Memantine 10 mg qd, and Escitalopram 10 mg qd to 3 take care of the symptoms. After two months of treatment, her symptoms were not significantly improved. Then, Sodium Oligoamine Capsules 0.45 g bid were added to the medicine treatment. The treatment improved her ability in recording daily activities, but failed to correct her memory loss. She became severe irritable every afternoon leading to her hospital admission.

3.4. Physical Examination

The patient had no history of hypertension, diabetes, stroke, traumatic brain injury, infectious diseases, or substance abuse. Denies smoking, alcohol consumption, and family medical history. No significant abnormalities in heart, lung, and abdominal examinations. Neurological: Clear consciousness, poor mental state, fluent speech, indifferent facial expression, poor concentration, decreased recent memory, impaired temporal and spatial orientation, normal cranial nerve examination, normal motor and sensory systems, negative meningeal signs. Auxiliary examinations: The patient exhibited normal parameters in the standard tests of blood, urine, stool, liver and kidney functions, electrolytes, fasting blood glucose, thyroid function, and glycated haemoglobin and was negative for the eight infectious diseases. The parameters of blood lipids include total cholesterol 6.28 mmol/L, triglycerides 2.36 mmol/L, high-density lipoprotein 1.79 mmol/L, low-density lipoprotein

3.98 mmol/L, homocysteine 20.2 μmol/L, electrocardiography (ECG) Sinus rhythm. Imaging computed tomography (CT) and ultrasound showed no significant abnormalities in the neck vascular vessels.

3.5. AD-Specific Examination

The neuropsychological assessments were conducted before surgery with parameters including MMSE 22 points, MOCA 20 points, digit span forward was 6 points, backward was 4 points. Trail making test: Part A 39 seconds, Part B not completed. Auditory verbal learning test: Immediate recall 12 points, delayed recall and cued recall both 0 points. ADL 21 points, NPI 8 points, Hamilton anxiety scale 10 points, Hamilton depression scale 5 points, Athen's insomnia scale 1 point, and 4 clinical dementia rating (CDR) 1 point. In the blood AD biomarkers, p-tau181 was 4.26 pg/ml (≥1.82 pg/ml); Aβ42 was 15.37 pg/ml (≥10.37 pg/ml); Aβ40 was 129.86 pg/ml; Aβ42/Aβ40 ratio was 0.12 (≥0.09); APOE genotype was APOE3/4. The 18F FDG-PETCT test was conducted in the patient at the first- and sixth-month post-surgery, respectively.

3.6. Diagnosis and Treatment

The patient was diagnosed with Alzheimer's disease, hyperlipidaemia, Hyperhomocysteinemia. The treatment plan was adjusted to: Donepezil 10 mg qn., Memantine 20 mg qd., Sodium oligoamine capsules 0.45 g bid. and Escitalopram 10 mg qd. Despite the medication treatment, the patient continued to experience a significant memory loss and irritability.

3.7. Surgical Intervention

With the consent of the patient and her families, ethical approval by our hospital's ethics committee (ZXYY202472), and exclusion of surgical contraindications in presurgical evaluation, we conducted the bilateral deep cervical lymphaticovenular anastomosis in the patient under general anaesthesia. In the procedure, the patient had a flat face-up position and surgery was performed under a ZEISS fluorescence surgical microscope (model KINEVO900). In the right-side surgery, the patient's head was slightly tilted back and to the left, a vertical incision approximately 5 cm long was made along the anterior border of the right sternocleidomastoid muscle. In the pre-operative assessment, colour Doppler ultrasound was used to detect the lymph nodes in the cervical Va area. Using the midpoint of the Va area as a surface projection, indocyanine green (25 mg/0.2 ml, produced by Dandong Yichang Pharmaceuticals) was injected at three points: below the bilateral mastoid processes, angle of the mandible, and the occipital bone to assess the lymphatic flux function of the deep cervical lymph nodes. The injections were made at 3 cm in depth under the skin to avoid staining of the skin lymphatics. A fluorescence imaging system (ARGOS NIR-300PTB) was used to track 5 the deep cervical lymphatic fluid flow, which was used to identify the obstructed lymph node. The obstructed lymph node had fluorescence in the influx lymphatic, but not in the efflux lymphatic. Under the fluorescent microscope, the influx lymphatic was identified by the fluorescence and the efflux lymphatic was not visible at the position below the obstructed lymph node. The influx lymphatics were dissected to form a lymphatic bundle that was inserted into the jugular vein for anastomosis. The vein was isolated and cut at the end nearby the obstructed lymph nodes. The influx lymphatics were anastomosed with the proximal end of jugular vein in the anastomosis. The efficacy of lymphatic drainage was confirmed by observation of fluorescent lymph flowing into the jugular vein under the fluorescent microscope. The same procedure was done for the left-side surgery of deep cervical lymphaticovenular anastomosis. In the wound closure, the subcutaneous tissue was sutured with 5-0 collagen sutures, and the incision was closed with 5-0 Prolene sutures. A sterile dressing was applied, and an external cervical collar was used for neck stabilization. The operators are senior surgeons with more than 20 years of experience in surgical operation.

3.8. Checklist

This case report has been prepared in line with the PROCESS Guideline [10].

4. Outcomes

4.1. Obstructed Lymph Node

Blockage of the central lymphatic system is expected to increase the risk of metabolic waste accumulation in the brain in the pathogenesis of AD. However, it is not clear how the drainage block happens in AD patients. In the surgery, the blockage was observed in a lymph node of deep cervical district 3 (Figure 1). To observe this, a fluorescence imaging system (ARGOS NIR-300PTB) was used to track the deep cervical lymphatic fluid flow, which contained the fluorescence of indocyanine green (Figure 1). The obstructed lymph node had bright fluorescence with visible fluorescence in the influx lymphatic, but not in the efflux lymphatic under the fluorescent microscope. The fluorescent influx lymphatic was identified in the surgical field at the position above the lymph node, and the efflux lymphatic was not visible at the position below the lymph node. The influx lymphatics were dissected to form a lymphatic bundle that 6 was inserted into the jugular vein for anastomosis. The result suggests that the district 3 lymph node obstruction is responsible for the impaired drainage function of central lymphatic system in the AD patients.

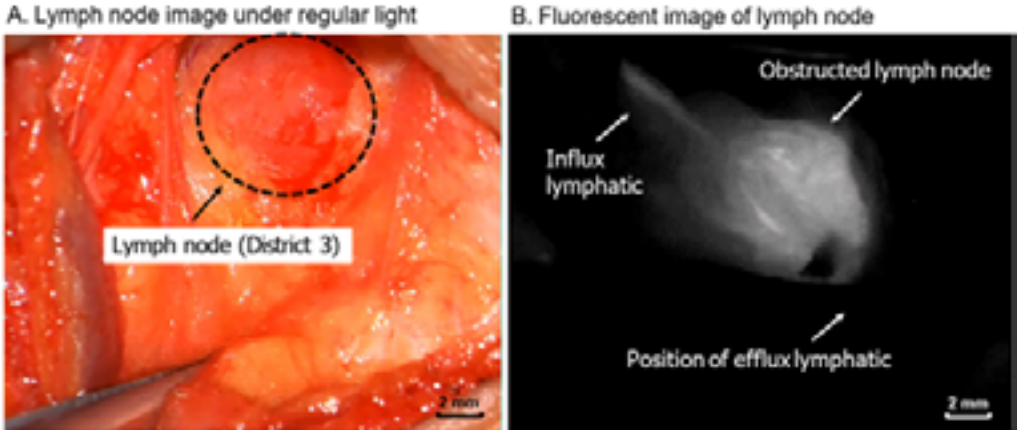

Figure 1: Images of obstructed lymph node in the tissue of deep cervical area.

4.2. Effect of the Surgery

The AD patient exhibited a mild demyelination of white matter, and the left hippocampus showed a mild atrophy (MTA visual rating scale score of 2 for medial temporal lobe atrophy) in the magnetic resonance imaging (MRI) (Figure 2, A and B). The PET-CT image demonstrated that the neuronal glucose consumption was increased in multiple areas of the brain by the surgery (Figure 2C), suggesting improvement of neuronal functions in multiple regions of the brain. On the second day post-operation, the patient exhibited improvement in behaviour, such as stopping calling her spouse repeatedly and exhibiting no more irritable behaviour. She could recall what she had for breakfast in the evening. In the neuropsychological assessments on the days 2 and 10, and at 1st, 4th and 6th months post-surgery, a significant improvement was recorded in cognitive and memory functions along absence of abnormal behaviours relatively to the preoperative (Table 1). The patient showed improvement in memory and emotional stability in the entire follow-up of six months. She regained the ability to send and pick up her grandchild to and from the school, and able to complete complex household activities. The ability to perform daily living activities was improved significantly. In AD biomarkers, p-tau181 was monitored in the peripheral blood and the level was decreased consistently by the surgery from 4.26 pg/ml before surgery to 0.64 pg/ml at the sixth month post-surgery (Table 2). The Aβ42/Aβ40 ratio was not changed in the peripheral blood by the surgery (Table 2).

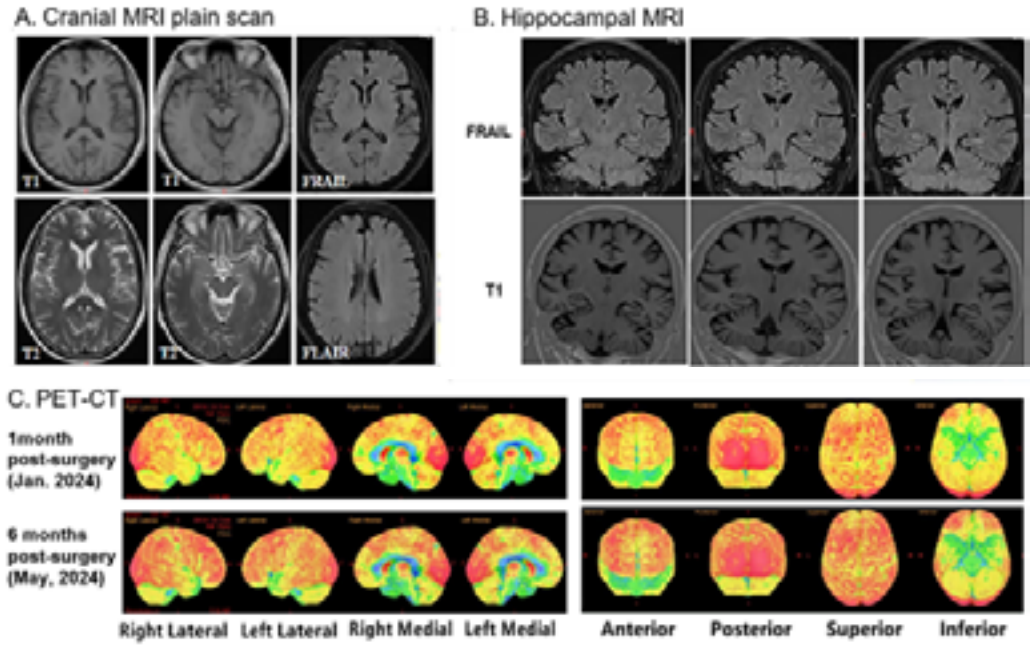

Figure 2: NRI and PET-CT imaging of AD patient brain.

PROCESS 2020 Checklist			
Topic	**Item**	**Checklist Item Description**	**Page Number**
Title	**1**	- The phrase 'case series' and the area of focus should appear in the title (e.g. patient population, diagnosis, intervention or outcome).	1
Key Words	**2**	- Include three to six keywords that identify what is covered in the case series (e.g. patient population, diagnosis, intervention or outcome). - Include 'case series' as one of the keywords.	1
Abstract	**3a**	Introduction and Importance - Describe what is unique or educational. - What is the overarching theme of the case series?	1
	3b	Methods - Describe what was done, how and when was it done and by whom.	1
	3c	Outcomes - Describe the outcomes ofthe intervention and management strategy.	1
	3d	Conclusion - Describe the take home message(s), including what has been learnt? - How will this impact future clinical practice?	1
Introduction	**4**	- Describe the background of the case series and specify the overarching theme (e.g. common disease, intervention, or outcome). - The introduction should explain what is unique or educational about the case series. - Relevant scientific literature should be referenced. - Introduction should be 1-2 paragraphs in length.	1-3
Methods	**5a**	Registration - State the research registry number in accordance with the Declaration of Helsinki - "Every research study involving human subjects must be registered in a publicly accessible database". This can be obtained from, for example, ResearchRegistry.com, ClinicalTrials. gov, or ISRCTN. - If a protocol already exists, state the corresponding registration number and access directions (e.g. website or journal, and include a hyperlink that is publicly accessible). It must be written in the English language.	9
	5b	Study Design - State that the study is a case series. - State whether the case series is: (1) prospective/ retrospective, (2) single/multi-centre, and if (3) cases are consecutive/non-consecutive.	3
	5c	Settings and Time-Frames - Describe the setting(s) in which the patient was managed (e.g. research institution, teaching/ district general hospital, community, or private practice). - Document any relevant dates (e.g. recruitment, intervention, follow-up, and data collection time-frames).	3-4
	5d	Participants - Describe the relevant characteristics (e.g. demographics, comorbidities, tumour staging, smoking status) and if relevant, exposure(s) of the participants. - Describe the method of participant recruitment, if relevant. - State any subsequent inclusion or exclusion criteria, and how the participants were selected. - Methods used to ensure the de-identification of patient information.	3

	5e	Pre-Intervention Patient Optimisation - Lifestyle (e.g. weight loss). - Medication review (e.g. anticoagulation, oral hypoglycemics/insulin). - Pre-surgical stabilisation/ preparation (e.g. treating hypothermia/ hypovolemia/ hypotension, ICU care for sepsis, nil by mouth, or enema). - Other (e.g. psychological support).	3-4
	5f	Interventions - Describe the type(s) of intervention(s) used (e.g. pharmacological, surgical, physiotherapy, psychological, preventative). - Describe any concurrent treatments (e.g. antibiotics, analgesia, antiemetics, venous thromboembolism prophylaxis).	5
	5g	Intervention Details - Describe the rationale behind the treatment offered, how it was performed and time to intervention. - For pharmacological therapies, include information on the formulation, dosage, strength, route, and duration. - For surgery, include details such as anaesthesia, patient position, preparation used, use of other relevant equipment, sutures, devices, and surgical stage. - The degree of novelty for a surgical technique/device should be mentioned (e.g. 'first in human' or 'first in this context'). - Medical devices should have manufacturer and model specifically mentioned.	5-6
	5h	Operator Details - Where applicable, include operator experience and position on the learning curve, any relevant training, and specialisation (e.g. ‘junior trainee with three years of surgical specialty training in Plastic Surgery and seven similar cases completed previously under direct supervision’).	5-6
	5i	Quality Control - What measures were taken to reduce inter- or intra- operator/operation variation, to ensure quality, and to maintain consistency between cases (e.g. independent observers, lymph node counts, standard surgical technique). - State any specific disparities between cases.	5-6
	5j	Follow-Up - When (e.g. how long after discharge, frequency, maximum follow-up length at the time of submission). - Where (e.g. home via video consultation, primary care, secondary care). - How (e.g. telephone consultation, clinical examination, blood tests, imaging). - Any specific long-term surveillance requirements (e.g. imaging surveillance of endovascular aneurysm repair or clinical exam/ultrasound of regional lymph nodes for skin cancer). - Any specific post-operative instructions (e.g. post- operative medications, targeted physiotherapy, psychological therapy). - State if any participants were lost to follow-up and why.	3
Results	**6a**	Participants - Please state the number of patients involved, the patient characteristics (e.g. demographics, comorbidities, smoking status, and if applicable, tumour staging (e.g. TNM)).	3
	6b	Deviation from the Initial Management Plan - State if there were any changes in the planned intervention(s) (e.g. what was changed and why). - Please include a suitable schematic diagram if appropriate.	3

	6c	Outcomes and Follow-Up - Expected versus attained clinical outcome as assessed by the clinician. Reference literature used to inform expected outcomes. - When appropriate, include patient-reported measures (e.g. questionnaires including quality-of-life scales). - Describe and explain the percentage of patients lost to follow-up.	6-7
	6d	Intervention Adherence and Compliance - Where relevant, detail how well the patient adhered to and tolerated the advice provided (e.g. avoiding heavy lifting for abdominal surgery, or tolerance of chemotherapy and pharmacological agents). - Explain how adherence and tolerance were measured.	6-7
	6e	Complications and Adverse Events - Precautionary measures taken to prevent complications (e.g. antibiotic or venous thromboembolism prophylaxis). - All complications and adverse or unanticipated events should be described in detail and ideally categorised in accordance with the Clavien-Dindo Classification (e.g. blood loss, length of operative time, wound complications, re-exploration or revision surgery, impact on length of stay). - If relevant, was the complication reported to the relevant national agency or pharmaceutical company. - Specify the duration of time between completion of the intervention and discharge, and whether this was within the expected timeframe (if not, why not). - Where applicable, the 30-day post-operative and long- term morbidity/mortality may need to be specified. - State if there were no complications or adverse outcomes.	6-7
Discussion	**7a**	- Summarise the key results.	7-9
	7b	Relevant Literature and Placing the Results in Context	7-9

Informed Consent	**10**	- The authors must provide evidence of consent, where applicable, and if requested by the journal. - State the method of consent at the end of the article (e.g. verbal or written). - If not provided by the patients, explain why (e.g. death of patient and consent provided by next of kin). If the patients or family members were untraceable then document the tracing efforts undertaken.	5
Additional Information	**11a**	- State any conflicts of interest.	9
	11b	- State any sources of funding.	Title page
	11c	Other Relevant Disclosures - Please state any author contributions, acknowledgments, and where required, institutional review board and ethical committee approval. - Disclose whether the case has been presented at a conference or regional meeting.	Title page
Clinical Images and Videos	**12**	- Where relevant and available, include clinical images to help demonstrate the cases pre-, peri-, and post- intervention (e.g. radiological, histopathological, patient photographs, intraoperative images). - Where relevant and available, include a link (e.g. Google Drive, YouTube) to the narrated operative video to highlight specific techniques or operative findings. - Ensure all media files are appropriately captioned and indicate points of interest to allow for easy interpretation.	Fig. 1-2
Referencing the Checklist	**13**	- Include reference to the PROCESS 2020 publication by stating: 'This case series has been reported in line with the PROCESS Guideline' at the end of the methods section (and include citation in the references section).	6

Table 1: Neuropsychological assessment of the patient before and after the surgery.

		Pre-surgery	Post-surgery				
Items \ Date		2023-11-14 (1 day)	2024-1-7 (2 days)	2024-1-16 (10 days)	2024-2-5 (1 month)	2024-5-11 (4 months)	2024-7-10 (6 months)
MMSE		22	24	26	24	24	24
MOCA		20	23	24	23	19	20
Digit span		6/4	7/5	9/5	9/4	8/5	8/5
Trail Making Test A		39s	28s	27s	46s	143s	46s
Trail Making Test B		Incomplete	33s	48s	60s	163s	60s
AVLT	Immediate Memory	12	19	19	19	17	17
	Delayed Memory	0	2	4	0	4	4
	Cued Memory	0	5	9	3	5	16
ADL		21	18	18	16	14	14
NPI		8	2	0	0	0	0
HAMD		5	1	1	2	0	2
HNMA		10	1	1	2	0	0
AIS		2	2	2	2	0	0
CDR		1	1	1	1	1	1

Note: MMSE: Mini-Mental State Examination; MOCA: Montreal Cognitive Assessment; AVLT: Auditory Verbal Learning Test; NPI: Neuropsychiatric Inventory; ADL: Activities of Daily Living Scale; HAMD: Hamilton Depression Rating Scale; HAMA: Hamilton Anxiety Rating Scale; AIS: Athens Insomnia Scale; CDR-SB: Clinical Dementia Rating-Sum of Boxes. s: seconds.

Table 2: Changes in blood AD biomarkers in response to the surgery.

AD biomarker	Surgery					
	1 Day before	1 Day after	3 Days after	10 Days after	4 Months after	6 Months after
Aβ42 (pg/ml)	15.37	22.08	20.69	20.83	31.12	11.20
Aβ40 (pg/ml)	129.86	140.77	117.03	114.32	161.89	72.55
Aβ42/ Aβ40	0.12	0.16	0.18	0.18	0.192	0.154
p-tau181 (pg/ml)	4.26	2.26	2.32	2.54	1.51	0.64

5. Conclusion

In this study, the lymphaticovenular anastomosis surgery provided a long-term effect in the treatment of AD patient in the six-month follow-up. The lymphaticovenular anastomosis surgery is often used in the treatment of limb lymphedema for reconstruction of efflux of local lymph fluid. The LVA surgery has been adapted to the treatment of AD patients in the clinical settings by Xie's group [9]. During the period of 7 current study, another group reported that a similar surgery protocol had a therapeutic effect on an AD patients with a follow-up of 5 weeks [11]. In the two published studies, the therapeutic effects were examined for days or weeks all in single patient, respectively, in the absence of long-term follow-up. Therefore, the long-term therapeutic effect remains to be tested for the surgery in the AD patients for a lack of relevant report in the literature. In the current report, the surgery effect was tested for six months in the AD patient and sustained therapeutic outcomes were observed. The three independent studies by the different groups consistently suggest that the surgery is a reliable therapeutic method in the treatment of AD patient. The long-term effect in our study excludes the possibility of anaesthetics effect that are reported in some studies to improve the glymphatic function in clearance of Aβ protein [12]. Current study demonstrated that the lymph node in the district 3 of deep cervical area was obstructed for congestion of the central lymph fluid in the AD patient. The central lymphatic system drains the lymph fluid through the deep cervical lymphatic [4], and ligation of the cervical lymphatic increases the risk of AD in mice [8]. It is believed that waste accumulation from the drainage dysfunction of central lymphatic system contributes to AD in the Aβ deposition, tau protein over phosphorylation, lipid droplet formation and chronic inflammation in animal models [12,13]. In the study of aging mice, the dysfunction was associated with atrophy of nasopharyngeal lymphatic plexus [4]. However, it is not clear if the dysfunctional occurs in AD patients. In the AD patient, we observed that the lymph node obstruction was responsible for the lymphatic dysfunction as the fluorescent dye failed to flow through the lymph node in the district 3 of deep cervical area. To resolve the drainage problem, we isolated multiple vessels of influx lymphatics of the obstructed lymph node and anastomosed them into the jugular vein to bypass the blocked lymph node. This led to a quick improvement in the cognitive and memory functions on the second day post-surgery (Table 1). The improvement was companied by a continuous decline of p-tau181 level in the peripheral blood (Table 2) and improvement in glucose consumption in the brain by the 18F FDG-PETCT test (Figure 2C). The data suggest that the lymph node obstruction in the district 3 of deep cervical area is a potential cause of drainage dysfunction of the central lymphatic system in the AD patient. The therapeutic effect of surgery is likely dependent on restoration of the drainage function of the deep cervical lymphatics 8 system. This study suggests that lymph node of deep cervical area is likely a potential target in the surgical treatment of AD in this new therapy. Drug development by targeting the Aβ protein, phosphorylated tau protein and chronic inflammation has been ongoing for decades. However, the attempts have received very limited success in the clinical treatment of AD as the clinical benefit is modest for the anti-Aβ therapy [14]. This surgery opens a new avenue in the clinical treatment of AD patients. The therapy has shed light on the lymph node of deep neck area although the mechanism of lymph node obstruction remains unknown. In terms of limitation of this study, the study was done in one patient and the mechanism of lymph node obstruction was unknown. In the future, the surgical therapy is deserved to be tested in more patients at multiple centres. The mechanism of lymph node obstruction should be investigated to support the therapy.

6. Consent

Consent to publish the case report was obtained from the patient and her family. The report does not contain any personal information that could lead to the identification of the patient.

7. Funding

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