Marked Improvement of Neuropsychological Impairment in a Patient with Chronic Obstructive Pulmonary Disease after Lung Volume Reduction Surgery

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This paper reports a case of a 71-year-old pulmonary emphysema patient with neuropsychological impairments that were markedly improved 6 months after he underwent lung volume reduction surgery (LVRS). He also underwent pulmonary rehabilitation before and after surgery. He was suspected of having memory impairment and attention disorder when he was referred for rehabilitation. The neuropsychologic test showed a general cognitive impairment, attention disorder, and verbal memory impairment. Magnetic resonance imaging showed moderate atrophy of the left hippocampal area, cortex, and lacunae infarction in the periventricular area. Interestingly, scores of the neuropsychologic test, as well as severity of dyspnea and lung function, remarkably improved 6 months after LVRS. These results suggested that the neuropsychological impairments in pulmonary emphysema patients can be improved after lung reduction surgery.

——— pulmonary rehabilitation; pulmonary emphysema; lung volume reduction surgery (LVRS); hypoxemia; neuropsychological impairment

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It has been reported that neuropsychologic disorders, in particular verbal disorders, are seen in patients with chronic obstructive pulmonary disease (COPD) (Incalzi et al. 1993, 1997; Stuss et al. 1997). However, few detailed studies have been made on improvement of neuropsychologic disorder in patients with COPD and the results are still controversial (Emery et al. 1991; Incalzi et al. 1993; Zielinski et al. 1999). Exercise rehabilitation of older adults with COPD enhanced cognitive functioning (Emery et al. 1991) and domiciliary long-term oxygen therapy was reported to improve cognitive functions (Zielinski 1999). However, Incalzi et al. (1993) reported that continuous oxygen therapy did not provide a complete protection against deteriorating cognition. We have been conducting comprehensive pulmonary rehabilitation, including the assessment of exercise tolerance, quality of life (QOL), psychological well-being, exercise therapy, and patient education, for patients with COPD (mainly pulmonary emphysema) (Kohzuki and Yajima 1998). We have observed a number of pulmonary rehabilitation patients suffering from neuropsychologic disorders, and thus have been assessing the neuropsychological function of these patients in detail using various neuropsychological function tests (Lezak 1995).

Lung volume reduction surgery (LVRS) has been reported to improve lung function, exercise performance, and quality of life in patients with severe emphysema (Cooper and Patterson 1995). So far, no reports have been published whether LVRS improves cognitive functions. Here, we report a case of a COPD patient who had been suffering from various neuropsychologic disorders which markedly improved 6 months after LVRS.

CASE REPORT

The patient

The patient was a 71-year-old man. In August of 1988, he was admitted to Yamagata

City Hospital due to pneumothorax and was diagnosed as having pulmonary emphysema. He had smoked 35 cigarettes a day for 30 years prior to admission. In September of 1993, the patient's feeling of respiratory distress exacerbated, and as a result he began oxygen therapy at home (1.0 liter/minutes). In January of 1997, his symptoms had exacerbated further, and even after the flow rate of oxygen was increased to 1.5 liter/minutes, the severity of exertional dyspnea worsened to Class V according to the Fletcher-Hugh-Jones classification. The patient began to experience shortness of breath when changing clothes, and was later admitted to our hospital in September of the same year to undergo LVRS. At this point, pulmonary rehabilitation was initiated. The patient was very thin (height: 165 cm, body weight: 51 kg, body mass index [BMI]: 18.7, and a respiratory function test confirmed severe mixed ventilatory disorders (VC: 1.5 liter, %VC: 43.6%, FEV_{1.0}: 0.39 liter, FEV_{1.0}/VC: 26%). An arterial blood gas analysis (room air) revealed hypoxemia and hypercapnia (pH: 7.443, PaO₂: 51.0 mmHg, PaCO₂: 50.7 mmHg, HCO₃⁻: 31.7 mEq/liter, and SaO₂: 86.6%). No abnormalities were detected in the peripheral blood cells of the patient, and a blood biochemical test did not reveal any notable abnormalities.

The depressive status was measured by using a self-rating questionnaire for depression called SRQ-D (Rockliff 1969). The patient was not depressed (SRQ-D 8/36 points), but was instead rather euphoric. However, attention and memory disorders became apparent soon after the start of pulmonary rehabilitation (the patient had difficulty in following directions, and quickly forgot instructions).

The patient underwent LVRS (left side) in January 20, 1998 and was again placed in pulmonary rehabilitation. At this point, various neuropsychologic tests and brain MRI in February 19, 1998 were performed. The patient underwent electro encephalogram

(EEG) in April 24, 1998. The subjective symptoms subsequently improved, and the patient was discharged. While at home, home oxygentherapy (HOT) was continued and the patient began consulting a physician in Yamagata City Hospital on an outpatient basis. Six months after the discharge, brain MRI and the same neuropsychologic tests were again performed. As shown below, marked improve-

ments in neuropsychological functions were confirmed.

Results of laboratory tests including respiratory function tests

The distance of 6-minute walking tests (6 MD) improved slightly from 140 to 160 m. BMI, which is an indicator of the nutritional status, did not change markedly (18.7→18.5).

Fig. 1. Brain MRI scan image of the patient.

An axial scan image (Fig. 1a) and an image parallel to the long axis of the hippocampus, (Fig. 1b). Arrow; atrophy of the left hippocampus.

In addition, all the parameters showed that the patient's respiratory function had improved (VC: 2.01 L, %VC: 58.4%, FEV_{1.0}: 0.73 L, FEV_{1.0}/VC: 36%). The results of the arterial blood gas analyses (room air) showed an improvement in hypercapnia (PaO₂ 51.0→50.2 mmHg, and PaCO₂ 50.7→43.3 mmHg). Brain MRI scan performed in February 19, 1998 yielded the following results: an axial scan showed a lacunae infarction in the periventricular area and atrophy of the cortex, including the frontal lobe. The severity of this change was greater than that normally seen in people of the patient's age group (Fig. 1a). On an image taken parallel to the long axis of the hippocampus, atrophy of the left hippocampus was detected (Fig. 1b). The MRI scan performed approximately six months later revealed similar findings, and thus no changes were detectable.

Results of neuropsychological function tests

Table 1 summarizes the results of the various neuropsychologic tests. We primarily investigated whether the test results improved 6 months after LVRS. These neuropsychologic tests underwent February 19, 1998 on the first time, 1 month after LVRS. A mini-mental-state (MMS) score, an indicator of overall

cognitive function, was 19 points on the first time, whereup on it improved to 24 points 6 months after LVRS. Digit span was used as an indicator of attention. His digit span score improved from 4 to 6 digits.

To further investigate this reduced verbal memory score, an auditory-verbal learning test (AVLT) was conducted. AVLT was used as a verbal test. In AVLT, the subject reads 15 unrelated words (list A) and is then asked to repeat them verbally. This is repeated five times. Then, the subject reads another set of 15 unrelated words (list B) and is asked to repeat the second set of words verbally (interference). Next, the test subject is asked to recite the first set of words (list A). The subject is then shown a piece of paper listing 30 words, and is asked to identify the first set of words (list A). The total points for reciting (a total of 5 tries) improved markedly from 11 to 28 points 6 months after VRS, and the point for recognition improved slightly from 12 to 14 points.

DISCUSSION

This is a report that describes the neuropsychologic disorders that exist in COPD patients in detail, and the first report that describes the finding that such disorders improved when the

TABLE 1. *Results of neuropsychological function tests*

	Feb 19 1998 (1st time)	Jul 3 1998 (2nd time)	Reference value; mean±s.d.
MMS	19	24	26.0±1.8 (age: 70-74 and education level: 5 to 8 years) ^a
Digit span (Forward)	4	6	5.25±1.29 (age 60-79) ^b
AVLT (Trials A1-5, List B, Trial A6)	0-2-3-3-3-0-0	3-5-6-6-8-4-4	3-5-6-8-8-3-6
AVLT (Recognition)	12/15	14/15	11.5±2.6
(Total)	11/75	28/75	32.6±8.3 (age>70) ^b

^aCrum et al. (1993); ^bLezak et al. (1995)

MMS; Mini-Mental-State; AVLT; Auditory-Verbal Learning Test.

TABLE 2. *Results of pulmonary function tests and arterial blood gas analyses*

	Oct 1, 1997 before LVRS before rehabilitation	Jan 14, 1998 before LVRS after rehabilitation	Feb 19, 1998 after LVRS (1 months)	Apr 22, 1998 after LVRS (3 months)
VC (liter)	1.36	1.5	–	2.01
%VC (%)	39.5	43.6	–	58.4
FEV _{1.0} (%)	0.43	0.39	–	0.73
%FEV _{1.0} (%)	18	16.3	–	30.5
FEV _{1.0} /VC (%)	31.6	26	–	36
%TLC (%)	97.5	–	–	74
RV/TLC (%)	73	–	–	58.9
DLCO/VA (ml/min/mmHg/liter)	1.03	–	–	0.9
PaO ₂ (mmHG)	50.8	51	46.9	50.2
PaCO ₂ (mmHG)	57.5	50.7	52.9	43.3

respiratory functions improved 6 months after LVRS. We confirmed a reduced general cognitive function, attention, and verbal memory in this COPD patient. Interestingly, the results for the present patient on the second set of neuropsychologic tests (6 months after LVRS) were better than those on the first set of tests, suggesting that neuropsychologic disorders are to some extent reversible, once the respiratory functions improve.

Description by Incalzi et al. (1993) that continuous oxygen therapy did not prevent or only partly prevents cognitive decline in COPD is not surprising since several COPD-related factors other than hypoxemia (hypercapnea, acidosis, and hypocapnea-induced hyperventilation) are known to affect cognition. An improvement in hypercapnia after LVRS was found in our case suggests that the improvement of the neuropsychologic disorders is associated with PaCO₂ decrease 3 months after LVRS. Stuss et al. (1997) reported that the severity of hypercapnia correlated to that of memory and attention disorders in patients with COPD. We speculate that the following factors also contributed to the improvement of the neuropsychologic disorders in the present patient: the improvement in subjective symptoms brought about by LVRS; effective usage of HOT (appropriately adjusted O₂ flow rate); and the

improvement in somatic and psychological activities resulting from regular and safe physical exercise.

General cognitive impairment, attention disorder and verbal memory impairment improved when the respiratory functions improved 6 months after LVRS. Moreover, the Rey-Osterrieth complex figure test (a non-verbal test) (Lezak et al. 1995) underwent only second time in this study, achieved a score of 32 points for copying and 18 points for immediate recall, which were higher than the average scores for his age group (21 points and 13 points, respectively). In this test, a meaningless complex figure is shown to a test subject, and he is then asked to look at the figure and copy it. Next, the subject is asked to draw the figure again from memory.

The MRI scan, taken parallel to the long axis of the hippocampus, showed atrophy of the left hippocampus and the cortex, including the frontal lobe. It has been reported that the hippocampus is likely to be damaged during hypoxia (Graham 1992), and damage to the left hippocampus leads to verbal memory impairment (Soininen et al. 1994). Additionally, the observed tendency is that an increase in the severity of respiratory disturbances is accompanied by an increase in the severity of cortical atrophy (Scheltens et al. 1992; Stuss et

al. 1997). Such disorders are often associated with the abnormal findings of MRI imaging. However, in some patients with COPD, such characteristic findings could not be seen by diagnostic imaging even when similar neuropsychologic disorders were apparent (unpublished observations). Thus, other factors may be involved in the onset of neuropsychologic disorders. Further research is needed to draw definitive conclusions on the factors that contribute to the improvement of neuropsychologic disorders.

We are currently investigating the following issues in a large number of patients: the relationship between neuropsychologic disorders and hypoxemia in COPD patients with chronic respiratory insufficiency, and the factors that contribute to improvement of the neuropsychologic disorders.

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