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Hiroshi Suzuki* Shigetoshi Kuroda[†] Hideki Ishizu[‡]
Yoshikatsu Fujisawa** Ken Sasaki^{††}

*Okayama University,

[†]Okayama University,

[‡]Okayama University,

**Kinoko-Espoir Hospital,

^{††}Kinoko-Espoir Hospital,

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Hiroshi Suzuki, Shigetoshi Kuroda, Hideki Ishizu, Yoshikatsu Fujisawa, and Ken Sasaki

Abstract

To better understand the nature of the symptoms of depression in the early stages of Pick's disease, we performed a retrospective study of the medical records of eight patients who were originally treated for major depressive disorders before being clinically diagnosed with Pick's disease. Six of the eight manifested psychomotor retardation and social withdrawal, seven of the eight were agitated and five of the eight showed hyperbulia too. However, only two of the eight showed melancholia or physical symptoms such as insomnia or loss of appetite. All patients were treated with antidepressants but these were not effective in relieving the symptoms of depression. The data we gathered in this study will be useful in the future for distinguishing between Pick's disease-related depression (in the early stages of the disease) and major depression.

KEYWORDS: pick's disease, depression, early stage

Depression in the Early Stages of Pick's Disease

Hiroshi SUZUKI^{a*}, Shigetoshi KURODA^a, Hideki ISHIZU^a, Yoshikatsu FUJISAWA^b and Ken SASAKI^b

^aDepartment of Neuropsychiatry, Okayama University Medical School, Okayama 700-8558, Japan and ^bKinoko-Espoir Hospital, Kasaoka, Okayama 714-0071, Japan

To better understand the nature of the symptoms of depression in the early stages of Pick's disease, we performed a retrospective study of the medical records of eight patients who were originally treated for major depressive disorders before being clinically diagnosed with Pick's disease. Six of the eight manifested psychomotor retardation and social withdrawal, seven of the eight were agitated and five of the eight showed hyperbulia too. However, only two of the eight showed melancholia or physical symptoms such as insomnia or loss of appetite. All patients were treated with antidepressants but these were not effective in relieving the symptoms of depression. The data we gathered in this study will be useful in the future for distinguishing between Pick's disease-related depression (in the early stages of the disease) and major depression.

Key words: Pick's disease, depression, early stage

Depression is a major psychopathological disorder in upper-middle age and elderly patients. It is important to treat individuals suffering from depression as soon as possible to prevent their condition from deteriorating to the point where they entertain thoughts of suicide. However, there are many disease that show some depressive symptoms, it is important to distinguish major depression and other disease-related depression.

While there have been many studies on depression in Alzheimer's disease (1-4), vascular dementia (5-7) and Parkinson's disease (8, 9), there have been no multi-patient studies on depression in Pick's disease focusing in particular on the aspects of the depressive symptoms. In this paper, we report on 8 patients all of whom were originally treated for major depression before being clinically diagnosed with Pick's disease. A better understanding of the symptoms in the early stages of Pick's

disease will make it easier to distinguish between this disease and major depression. Thus, in this paper, it is our intention to describe as accurately as possible the characteristics of the depressive symptoms in the early stages of Pick's disease.

Subjects and Methods

We studied the medical records of 8 patients (4 males and 4 females) who were originally diagnosed with major depression but, as their condition progressed, were eventually diagnosed with Pick's disease.

Case Presentation

Case 1. At age 58, this right-handed woman became unwilling to do housework, lost interest in watching television and was emotionally volatile, suffering frequent crying spells. In particular, she was concerned about her son's business. In a 6-month period, she lost 2 kg. She was referred to one of our hospitals and was diagnosed with depression and was treated with sulpiride (150 mg/day) and etizolam (1.5 mg/day) for 6 months with no positive effect. Hoping that a change of scenery would improve her condition, she moved to rural Nagano Prefecture in Japan but her symptoms continued. At age 59, she was again referred to our hospital. On examination, she showed psychomotor retardation and diagnosing physicians suspected some form of organic dementia. Her condition did not improve and she was hospitalized at age 64. While in the hospital, she was extremely apathetic and withdrawn. She also showed repetitive behavior, for example, continually following another patient about. This resulted in several beatings from the other patient who disliked her. Computed tomography (CT) showed bilateral frontal lobe atrophy. Less atrophy was observed

* To whom correspondence should be addressed.

in the temporal regions.

Case 2. This 68-year-old woman suffered from insomnia, heart palpitations and attacks of hyperventilation after being involved in a traffic accident. She was admitted to a psychiatric hospital and was treated for major depression with setiptiline (3 mg/day) and amoxapin (50 mg/day) for 5 months. The treatment was effective and she was released from the hospital. However, six months later, the hyperventilation attacks returned and she was readmitted. While she was in the hospital, she suffered from headaches and frequent attacks of hyperventilation. She was diagnosed with hysterical neurosis after which she was moved to a nursing home. There, she showed various behavioral disorders such as teacup throwing and stealing food and drugs. She was evaluated as having Pick's disease at age 71 by a psychiatrist. At this evaluation she displayed oral tendencies, roaming behavior and dementia. CT showed atrophy of the frontal and temporal regions.

Case 3. This 60-year-old woman was referred to one of our hospitals for evaluation of compulsive behavior. She had worked as an office worker for many years. At age 59, she started to repeat the same statements and questions over and over and had difficulty performing deskwork. As a result of this she was fired from her job. One year after this, her husband brought her to a psychiatric hospital. During her evaluation, she complained of cheerlessness and loneliness. She was treated with trazodone (maximum dosage: 75 mg/day) for 4 months with no positive results. During this time, she often bought the same items repeatedly; cooked the same dishes repeatedly; and suffered from irritability and restlessness. She was treated with tiapride (150 mg/day) for 2 months without any positive results. At age 60, an examination showed that she had lost interest in the world, wandered around all day long and said the same things over and over (perseveration). CT showed marked atrophy in the frontal lobes and less severe atrophy in the temporal lobes.

Case 4. At age 58, this hardware store employee was first evaluated for neurotic symptoms. He had become nervous and engaged in compulsive measuring behavior which made it difficult to continue his business. At age 59, his wife died and he became restless and agitated. On examination, he showed agitation and motor retardation as well as a mild loss of memory and orientation. He was treated with tiapride (125 mg/day) for 1 month with no positive effect. Following this, behavior

disturbances gradually started to appear. For example, he entered his neighbors' houses and ate their fruit. He ate large amounts of his own food and sometimes even ate flowers. After this, he became socially withdrawn and apathetic. CT revealed marked atrophy of the frontal and temporal lobes.

Case 5. At age 60, this man became concerned about the boundary between his and his neighbor's property. He quarreled with this neighbor then later reported to his family, 'I am ashamed of what I did.' Following this, he remained indoors and spoke few words. His family moved to a different place, in hopes that this would improve his condition but his symptoms continued. At age 64, an examination revealed that he was negative and withdrawn. He refused any communication with others. He was diagnosed as suffering from delusional depression and was hospitalized and treated with antidepressants (clomipramine [75 mg/day] trazadone [150 mg/day] mianserin [60 mg/day]) with no positive results. He lay in bed almost all day long, rising only to eat and go to the bathroom. He ate large amounts of food and stole candy from other patients. Magnetic resonance imaging (MRI) showed atrophy of the frontal and temporal lobes. Single photon emission computed tomography (SPECT) showed fronto-temporal hypoperfusion.

Case 6. At the age of 48, this factory worker had difficulty doing his work and was fired from his job, following this he was admitted to a hospital. On examination, he showed symptoms of depression, psychomotor retardation, anxiety, grief and reported thoughts of suicide. He was also hypochondriacal and complained of a loss of appetite. He was treated with clomipramine (75-225 mg/day) for 2 months with no positive results. While he was in the hospital, he showed flat affect and loss of initiative. As the initial diagnosis of depression was considered to be erroneous, clomipramine administration was stopped. At age 51, he was referred to our hospital for evaluation of possible dementia. On initial examination he showed laziness in thinking (Denkfaulheit), lack of initiative and compulsive behavior. MRI showed atrophy of both frontal lobes and, to a lesser degree, atrophy of the temporal lobes. SPECT showed extensive hypoperfusion of the frontal and temporal lobes.

Case 7. At the age of 52, this woman became very busy with housekeeping, because her mother had been admitted to a hospital. Her sister opposed their mother's admission and blamed the patient. The sudden death of her son-in-law made her more busy and she

became exhausted. She was admitted to a local hospital and complained of being depressed and having memory problems. She also suffered frequent attacks of hyperventilation and irritability. She was diagnosed as suffering from depression with an overlay of hysteria. She was treated with perphenazine (6 mg/day) for 1 month with some degree of improvement. However, 2 months later, she attempted suicide and was admitted to another hospital. She was given clomipramine (75 mg/day) and amitriptyline (75 mg/day) for 14 months without any positive effect. She was evaluated again at the age of 64 at which time she showed laziness in thinking, nominal aphasia, and poor cooperation and contact with other patients. CT revealed clear atrophy in the frontal and temporal lobes. The atrophy was more severe in the temporal lobes.

Case 8. At the age of 57, this office worker became irritable and restless due to concern over some leased land. His family took him to a neurology clinic where he reported having no problems with his mental state. Two years later, he showed difficulty remembering the names of friends and relatives and was socially withdrawn. He consulted a psychiatrist and was given antidepressants (details unknown) for 1 year with no positive results. He was transferred to one of our hospitals for evaluation of his mental status. He suffered difficulty with remembering words (nominal aphasia) and was withdrawn. An intelligence test revealed an IQ of 64, a performance IQ of 78 and a full-scale IQ of 68. MRI showed clear atrophy of the right temporal lobe. SPECT showed marked hypoperfusion of the same lobe. He was then transferred to a local hospital. Six years later he was extremely withdrawn and spoke very little. CT showed extensive atrophy of the frontal and temporal lobes.

Results and Discussion

Medical textbooks list depression as one of the personality changes that occur in the early stages of Pick's disease. However, the exact nature of this depression is not clear. In order to better understand the nature of this depression, we studied the medical records of 8 individuals diagnosed with Pick's disease, all of whom showed depressive symptoms in the early stages of their illness. These symptoms are summarized in Table 1.

We focused on 3 main aspects of the patients' clinical manifestations: a) mood and thinking, b) drive and behavior and c) somatic manifestations.

Mood and thinking. Melancholia was observed in only 3 of the patients, and these were mild in one of these patients. Grief was seen in three cases (mild in one). Anxiety and agitation were seen in 7 cases. A persecution complex was present in three cases (mild in one) and difficulty in thinking was seen in two cases.

Drive and behavior. Psychomotor retardation was seen in 6 cases. Social withdrawal eventually occurred in all 8 cases; this was recognized initially in 5 cases and later in 3 others.

Somatic manifestations. Autonomic nerve symptoms were seen in 3 cases, hyperventilation attacks in 2, loss of appetite in 2 and insomnia in one.

These findings demonstrate that the depression in the early stages of Pick's disease has some distinctive phenomenological features. Most of the patients suffered from motor retardation and social withdrawal. Agitation was frequently observed. Many patients showed *Tatendrung*. On the other hand, depressed moods, grief, and feelings of guilt were rarely observed. Common symptoms of major depression such as loss of appetite, insomnia and autonomic nerve symptoms were rare.

Clear environmental precipitating factors were present in 2 cases. Both involved the loss of a family member, in 1 case a wife and in the other case a son-in-law. Psychosocial stress may play some role in the development of depression in sufferers of Pick's disease. Thus, we cannot rule out Pick's disease simply because of the preexistence of a psychosocial trauma.

Table 1 Early symptoms of Pick's disease that were firstly misdiagnosed as major depression

Symptom/case	1	2	3	4	5	6	7	8
Depressed mood	—	—	○	—	—	○	△	—
Grief	○	—	△	—	—	—	—	—
Anxiety/agitation	—	○	○	○	○	○	○	○
Inhibition of thought	—	—	—	—	—	○	○	—
<i>Kleinheitswahn</i> *	—	—	—	—	○	○	△	—
Motor retardation	○	—	—	○	○	○	○	○
Social withdrawal	○	→	→	→	○	○	○	○
Confusion	—	○	○	○	○	—	○	△
Suicide attempt	—	—	—	—	—	—	○	—
Insomnia	—	○	—	—	—	—	—	—
Loss of appetite	○	—	—	—	—	○	—	—
Hyperventilation attack	—	○	—	—	—	—	○	—
Autonomic dysfunction	—	○	—	—	—	○	○	—

○: Definite; △: Probable; →: Appeared later; —: Absent.

**Kleinheitswahn*: Delusion of worthlessness or inability

Psychotropic agents had limited effects in the patients we studied. Drug treatment yielded mild and transient improvements in the symptoms of only 2 subjects (these symptoms were hyperventilation and agitation). This stands in contrast to the general effectiveness of antidepressants for treating major depression.

Recently, brain imaging techniques have been useful for the diagnosis of Pick's disease and findings for the patients we studied were prominent frontal and/or temporal lobe atrophy. However, it remains uncertain as to whether this atrophy is present in the earlier stages of the disease.

There have been many studies on the relationship between dementia and depression. In particular, these studies have focused on whether these conditions can be differentiated and whether they can coexist (10, 11). Some investigators have stated that depression is present at the beginning or in the course of primary dementia and may even precede the illness (12-15). Feinberg and Goodman (16) proposed a 4-category system for classifying different types of depression, dementia and pseudodementia. The depression found in the early stages of Pick's disease corresponds to their type III classification: Dementia manifested as depression. Likewise, Kendall (17) found 23 (2.6%) cases of dementia among 879 cases of that were diagnosed as depression. Liston (12) noted 13 cases (26%) of presenile dementia among 50 patients that had originally been diagnosed as having depression. He did not mention the diagnosis of dementia but most cases are thought to be Alzheimer's disease. A wide variety of depressive symptoms have been reported for Alzheimer's disease. This variability probably results from differences in sample population, diagnostic criteria and the severity of the dementia in question.

As for distinguishing between Pick's disease and Alzheimer's disease, some differences have been found in the cognition and behavior of the sufferers of these diseases (18-23). As for the nature of affective disorders or mood disorders in these diseases, opinions are divided. Miller *et al.* (24) found no difference between Alzheimer's disease and Pick's disease in this regard. Barber *et al.* (25) reported that patients with Alzheimer's disease showed anxiety and distress about the handicaps attendant to their disease, but patients with fronto-temporal dementia (FTD) such as Pick's disease were rarely concerned with their disabilities. Levy *et al.* (26) reported that patients with FTD are more apathetic, but less

depressive than they were predicted. We supposed that less melancholia is the feature of the depression in Pick's disease.

Depression in the early stages of Pick's disease proved to have some distinctive features. Retardation, social withdrawal and agitation were present in most cases. On the other hand, melancholia and somatic symptoms were rare. Antidepressants were not effective in treating the depressive symptoms of Pick's disease. We believe that the features of Pick's disease reported herein will be useful to physicians in differentiated depression associated with Pick's disease from other forms of depression.

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