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Research Article

Dementia in Epilepsy: A Clinical Contribution to the Metabesity of Epileptology, Geriatrics and Gerontology

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Abstract

Purpose: This paper discusses dementia in epilepsy with a rare case of an adult patient. The article, when published, will be followed by another one, to be published in another journal, in which I discuss "Brain plasticity and epilepsy in children and the aftermath of their epilepsy surgery", citing examples from a recent lecture given by Dr. Simon Harvey of Australia and the discussions that followed in March, 2017.

The patient who had survived three car accidents suffered intractable temporal lobe epilepsy (TLE) for which he underwent successful epilepsy surgery, viz., amygdalohippocampectomy. However, symptoms of dementia developed over a period of three years or so pre- and postoperatively. Although there is no postmortem evidence available of senile plaques and/or neurofibrillary tangles, I shall present clinical evidence to explore the relationships between dementia and epilepsy as a contribution to the connections between epileptology, geriatrics and gerontology heretofore avoided in the literatures. But note that neither dementia nor epilepsy is a disease, contrary to commonly so believed by many researchers.

Methods: The following methods were undertaken: Pre- and postoperative neurolinguistic testings over time; pre- and postoperative IQ tests, EEG and PET; surgical intervention performed by Dr. Yang-Hsin Shih, and interviews with the patient's family members by the author.

Results: The patient became seizure-free postoperatively without medication. He was tested preoperatively once and postoperatively twice. During each testing, he showed marked language disorders. However, symptoms of dementia developed progressively to the extent that he could no longer hold on to his job and was subsequently laid off.

Conclusions: The case fits the clinical description of dementia, which is not a disease any more than epilepsy is a disease. I therefore claim that epilepsy of any form is likely to cause apoptosis in the brain, with or without surgical intervention, on account of which dementia ensues.

In the present context, dementia is not synonymous with Alzheimer's Disease; it is re-defined as the differential manifestation of deteriorating brain functions in the form of language disorders over time due to apoptosis in the brain caused by brain damage of non-vascular or vascular factors.

Therefore, I believe that senile plaques may have started to form in his hippocampus, or elsewhere, which may be of vascular or non-vascular disorder in origin with neurodegenerative consequences. Even though he became seizure-free postoperatively, to the extent that he was followed up by me, in addition to the cooperation of his family members and on account of their careful observation, I believe that he may also have developed neurofibrillary tangles to result in Fischer's presbyophrenic dementia, owing to progressive glandular necrosis in his brain, albeit neurofibrillary tangles occur intracellularly.

I thus conclude that any damage to the brain that causes apoptosis, be it due to epilepsy of any form-- TLE, extra temporal epilepsy, among others – or to such neurological disorders like Parkinson's disease, Multiple Sclerosis, and the like, will ensue in dementia. I also stress that dementia in epilepsy is much more common than epileptologists or other neuroscientists would want to admit.

Keywords: *Dementia; Epilepsy; Epileptology; Geriatrics; Gerontology*

Introduction

Dementia is often believed to be synonymous with Alzheimer's disease (AD), and it is therefore regarded by many neurologists as a permanent, progressive disease that affects mostly the elderly [1-3]. As a result, most epileptologists would not want to even consider epilepsy in the context of dementia in the same way that experts dealing with AD would exclude epilepsy in the consideration of dementia.

During the Third World Congress on Vascular Factors in Alzheimer's Disease (April 7 - 10, 2002) held in Kyoto, Japan, for example, one of the keynote speakers presented "Criteria and Overview of Vascular Dementia" [4] in which he excluded all demented patients with epilepsy from the statistics of his overview. The reason is probably that dementia is considered a disease, and therefore both epileptologists and neurologists dealing with AD or vascular dementia are more inclined to handle only "pure" cases, aiming to find either genetic factors or environmental factors in the pathogenesis.

Such an inclination is unfortunate for the following reasons: (1) Dementia is misunderstood as a disease, when it is not, because it is traditionally equated with AD. when AD is now proven as a fiction [5], without distinguishing it from dementia which other brain diseases cause (2). Epilepsy, though it is not a disease to most epileptologists, but erroneously considered a disease by neuropsychologists, is a multifactorial neurological disorder or medical condition which is treatable in most cases by medication or surgical intervention, whereas AD or vascular dementia cannot be so treated for obvious reasons: AD is a fiction and vascular dementia ensues from wear and tear on a vascular cause.

Historically, however, such was not the case, because senile plaques as a neuropathology were first described in 1892 by Blocq and Marinesco in the brain of an elderly patient affected by epilepsy [6]. Since then, there have been very few cases reported, in either the literature on epilepsy or the literature on AD or vascular dementia, on account of territoriality. The scarcity is of course misleading precisely for the reason mentioned above, because cases of dementia and epilepsy are more numerous than neurologists would want to admit, owing probably to the fact that neuropsychiatrists or neuropsychologists use a different term, psychosis, when they examine epileptic patients. A detailed discussion of dementia and psychosis was presented in a keynote lecture entitled "Dementia Is Not A Disease: What Is It?" by me during the AAASPD (American Association for the Advancement of Science, Pacific Division) Annual Meeting at the Southern Oregon University, on June 15, 2005.

Purpose

The purpose of this presentation is therefore to report a case of dementia and epilepsy for the first time since 1892 from the point of view of language disorders and other behavioral alterations; dementia may be defined as the differential manifestation of deteriorating brain functions of memory in language behavior over time due to cell deaths in the brain caused by neurodegenerative disorders. Therefore, dementia in the present context is regarded as totality of the effects of wear and tear due to aging which is the ongoing process of wear and tear.

This case report is about a patient who had survived three car accidents and suffered from intractable temporal lobe epilepsy, for which he underwent successful anterior temporal lobectomy performed by Dr. Yang-Hsin Shin of the Taipei VGH. The cause-effect of car accidents and the onset of temporal lobe epilepsy is debatable. I am inclined to think the opposite; that is, mild seizure attack was the cause to car accident each time as the effect.

Notwithstanding, symptoms of dementia developed over a period of three years or so pre- and postoperatively. I presume that his dementia would perpetuate to his death since no longitudinal follow-up was conducted. Although there is no postmortem evidence available of senile plaques and/or neurofibrillary tangles, I shall present below clinical evidence to explore the relationships between dementia and epilepsy.

Methods

Preoperative neuropsychological testings, such as IQ tests, were conducted (FIQ117) as well as a preoperative neurolinguistic testing; also available were preoperative EEG and PET records; as a result, surgical intervention was performed (May 5, 1994) and interviews with the patient's family members were conducted. Postoperatively, three neurolinguistic testings were also conducted overtime (January 20, 1997, December 2, 1998, and April 15, 1999), as a follow-up, along with IQ tests. Detailed interviews with the patient's wife and daughter were then conducted on December 2, 1998) in the patient's presence.

Case Description

The patient with a college degree in engineering was a 47 year old male. He had a very unusual medical history, because he had survived three car accidents: The first car accident took place in Taiwan in 1980; in 1981 he was sent to Saudi Arabia by the Government of Taiwan as an engineer, and there he had the second car accident; the third time, however, took place in 1986, also in Saudi Arabia. As a result, he experienced the first complex partial seizure attack in 1987 in Saudi Arabia, and therefore he was sent back to Taiwan for epilepsy management.

Back in Taiwan, he underwent epilepsy treatment with AEDs, and so from 1987 to 1991 there was no seizure attack. However, in 1989, he experienced three episodes of "wandering" at night (i.e. sleep walk). A brain tumor in his left temporal lobe was discovered by a CT scan in 1991. Left anterior temporal lobectomy was then performed on May 5, 1994. The pathological finding was that the tumor was an astrocytoma. Postoperative MRI, taken on July 23, 1996 identified presence of residual atrophy of the posterior body and the tail of the left hippocampus involving the fornix.

He became seizure-free postoperatively, first with medication and then without medication from 1996 onward. However, from 1997 he began to experience behavioral alteration by asking his wife such weird questions repeatedly from day time to bed time as "What time is it?" "What is the date today?" "Where am I?" For this reason, his wife brought him back to VGH for observation in 1997 and was tested on January 20th, 1997 neurolinguistically; the results were very poor for word associations and sentence arrangement, indicating marked memory impairment, although his digital span maintained at 8 digits. However, CT scan found no more abnormality in his brain on October 28, 1997, as he was still able to go to work as usual and could also drive. Nevertheless, he said he was afraid to receive official documents from his superiors and to sign them for fear of making errors.

His behavioral alteration got worse and was tested again neurolinguistically on December 2, 1998, because his wife had observed more weird episodes. The results were just as bad. He was diagnosed to have TGA (Transient Global Amnesia) by the attending physician, but dementia was suspected by Peng. Thus, his wife and daughter were asked to accompany him for an interview the content of which will be presented further below. They were told that he might be suffering from dementia.

Because of his worsening condition, he was tested neurolinguistically for the third time on April 15, 1999; the results were as bad as or worse than before. He then told Peng that he had been laid off for reasons of serious memory impairment, as he could no longer handle his job. His statement verified the diagnosis of his condition as a form of dementia (i.e., differential manifestation of deteriorating brain functions in the form of language disorders over time due to cell deaths as a result of wear and tear).

Summary of Episodic Events

Car accidents: First, 1980 in Taiwan. Sent to Saudi Arabia in 1981.
Second, 1981 in Saudi Arabia. Third, 1986 in Saudi Arabia.

First complex partial seizure, 1987. Sent back to Taiwan for epilepsy management.
On AED medication: Seizure-free from 1987-1991.
Three episodes of wandering at night: 1989 experienced night walk.
Brain tumor: In 1991 a CT scan found a brain tumor in the left anterior temporal lobe.
Surgery: 1994, left anterior temporal lobectomy was performed to remove tumor
Brain tumor: Astrocytoma

Materials and Discussions

Contents of the Three Neurolinguistic Testings

The neurolinguistic test battery consists of ten test items: (1) Free Word Association Test; (2) Designated Phrase Association Test; (3) Backward Digital Span Test (from 4 digits to 8 digits); (4) Oral Description of a Complex Picture; (5) Arrangement of Phrase Cards to Form Short Paragraphs (three trials); (6) Oral Constructions of Short Sentences (two trials); (7) Oral Repetition of Long Sentences (two trials); (8) Arrangement of Word Cards to Form Short Sentences (three trials); (9) Dictation and Recall of 50 Words and Phrases (without warning); and (10) Dictation and Recall of 50 Words and Phrases (with warning).

Results of the First Testing:

1. Ten tasks all within normal range of semantic associations.
2. Ten tasks with none of them correct (0/10).
3. Better than average (with even seven of the ten 8 digit numbers right).
4. Worse than average.
5. Ten tasks with only three correct at first trial (but each correct task taking him at least five times longer to complete than the average control) (3/10).
6. Five tasks with only one correct at first trial (1/5).
7. Five tasks with only one correct at first trial (1/5).
8. Ten tasks with only three correct at first trial (but each correct task taking him three times longer to complete than the average control) (3/10).
9. Dictation 49/50; Recall 1/50.
10. Dictation 47/50; Recall 4/50

Results of the Second Testing

1. Same as before
2. One correct (Task 6 which is the easiest) (1/10)
3. Slightly improved
4. Same as before
5. Only two correct (each taking more than twice the time to complete) (2/10)
6. Two correct (2/5)
7. None correct at first trial (0/5)
8. Ten tasks with just three correct at first trial (two of the three correct tasks were the same tasks he did in the first testing, suggesting that he had some learning effect left).
9. and (10) were omitted, because they became two difficult for him

Results of the Third Testing

1. Same as before
2. None correct (0/10)
3. No longer able to repeat backward 8 digit numbers, with mistakes in 6 and 7 digit numbers
4. (4)-(10) omitted, for reasons of difficulty.

Reports from Family Members

Summary of the Report

On November 29, 1998, he took his daughter at about 5:00 p.m. on his motorcycle to a food fair being held in the park not far from his home. During the trip, many weird things happened. When they returned, his wife chatted with him and felt something wrong was going on in his brain, because he was not answering what was being asked of him. Later, they had dinner, and he took a bath and went to bed.

But the next morning, November 30th, when his wife told him that he acted funny and that their daughter had reported to her many weird episodes about him and asked what had happened, he could not remember a thing and was even unable to recall anything that had taken place within the 16 hours from 2:00 p.m. (Nov. 29) to the morning of Nov. 30. His wife got scared and took him back to VGH. It was on the basis of his wife's report that the attending physician diagnosed him to have TGA.

Details of the Reports from Wife and Daughter

Daughter: At about 5:00 p.m. (Nov. 29) he and his daughter left for the park. During the ride to the part, he kept asking his daughter "What time is it now?" at least more than three times. Upon arrival at a gasoline station near the park, shortly after 5:00, he stopped to get gas. He then went to the toilet. After that, they continued the ride in order to reach the park.

He parked the motorcycle at the front gate and told his daughter "not to forget where the vehicle was parked". Then they entered the park. Shortly after they entered the part, he asked her "where did I park the motorcycle?" She replied: "You parked it at the front gate". She thus asked: "How come you forgot it?" He then replied: "Take me back to the front gate where the motorcycle was parked". He also asked "Why isn't Mommy here with us?" She thus said: "Mother is not feeling well and taking a rest at home". She then took him to where the motorcycle was parked. He reminded her not to forget where it was parked. And they re-entered the park.

He then told her that he was only joking. She therefore put her mind to rest, and he went to the toilet at that time. When he came out of the toilet, he asked her: "Why is Mommy not here with us?" She then said: "You just asked the same question before?" He said: "I forgot". So, she told him again that mother was sick, resting at home. He nodded his head but asked: "What are we doing here?" She said: "We came here to eat supper. Afterward, we want to go to a department store and stroll a bit". In fact, it was he who had told her that they were going to the department store afterward, but he forgot the whole thing.

He then said "Where can we eat in the park? Nobody will feed us". She then pointed to the place where there were lights. He said: "How come we want to go there to eat?" She said: "There are people who will feed us". He said again: "How come Mommy is not here to eat with us?" She replied again that mother was resting at home. He then asked: "Have we finished eating yet?" At this time, the daughter became worried and lied to him that they had already finished eating and strolling, and coaxed him that they should go home. He asked: "Do you know how to get home? Which road do we take?" She replied: "Yes, I do". At the park entrance, he went to the toilet again, and stood aimlessly at the gate for about 20 minutes. During that period, he asked again: "How come Mommy and your sister didn't come and only you came?"

At that time he wore only a cap, so he asked: "How come I did not wear my helmet and only wear this cap?" She replied; "You did bring your helmet with you". He asked: "Did I?" and then said: "What are we doing here?" and repeatedly pointed to the street they had taken and asked three times: "Is this the street XYZ (name of the street)?"

They thus took to the road to head home. But on their way back he asked: "How do we go home?" She then told him how to get home. When they turned, they came to a temporary rest room, so he stopped in order to go to the toilet. When he re-appeared, he forgot which road to take to go home. She had to tell him again and direct him when to turn.. When they turned, he forgot which street would lead to his home, so she had to guide him. They finally arrived home way after 7:00 p.m. She then reported to her mother what had happened. As the mother had not eaten yet, she started to cook noodle soup for all, but appeared quite worried after hearing the daughter's report.

Wife: His wife's immediate reaction was that she thought he had had a stroke. So, after supper, she entered their bedroom and asked: "What had happened?" He replied: "I seem to be dreaming, My brain is empty". He asked back, while looking at his watch, "What time is it now? What date is today? What day is it, today?" She said: "Perhaps you are too tired. Go to sleep to take a rest, and you will feel better". He and the daughter had the noodle soup but his wife was too worried to eat anything.

Instead of going to bed, he watched TV but continued to ask about the time, the day and the date until 10:00 p.m. He then went to sleep. The next morning, Nov. 30, he did not get up at about 5:30 a.m. as usual, so his wife had to wake him up after 6:30 a.m. She then asked him: "Do you remember what happened yesterday?" He said: "No," She thus asked; "Do you know that you have to go to work today?" He said: "Yes, I do". She thus asked: "Which bus do you take to go to work?" He replied: "Bus 202". (which was correct). In the evening, 6:00 p.m. the wife brought him back to VGH. He was then hospitalized for further observation.

Discussions

Although there are no postmortem materials for his pathogenesis, as the patient is still living, the clinical materials and the longitudinal test results should indicate that the patient has the initial clinical symptoms of dementia (i.e. behavioral alterations due to apoptosis). It is clear that his memory impairment deteriorated gradually from 1987 when he had the first seizure attack in Saudi Arabia-or even earlier than 1987. Whether his epilepsy was caused by the formation of the brain tumor or by the three car accidents as risk factors is debatable but there is no denying that his epilepsy had a vascular component in origin.

Even though the astrocytoma was removed and the patient has become seizure-free postoperatively without medication, as a result, the vascular component (or risk factor) may have remained in his brain to cause further progressive apoptosis, as postoperatively his hippocampus was found to have residual atrophy. Thus, the vascular risk factor may have also formed senile plaques, as may be evidenced by his deteriorating language disorders caused by his progressive memory impairment, albeit not neurofibrillary tangles which are a neurodegenerative disorder rather than a vascular disorder. But I would not be surprised that he developed Fischer's Presbyophrenia, implying that its pathological substrate was glandular necrosis.

Conclusions

On the basis of the presentation above, I would like to draw the following conclusions as a contribution to the connections of epileptology, geriatrics, and gerontology.

1. It should be noted that the first case of senile plaques with the co-morbidity of epilepsy was published in 1892 by Blocq and Marinesco [6]. It could not have been the only case in the history of epileptology or senile dementia. I believe that cases of combined dementia and epilepsy are more numerous than epileptologists would want to admit because neither dementia nor epilepsy is a disease.
2. Although psychosis is a commonly known mental or psychiatric disorder in epilepsy, perhaps it should be regarded as a form of dementia. If and when cases of psychosis in epilepsy are followed up longitudinally on account of language disorders; as I did above, such patients with epilepsy (seizure-free or not postoperatively) and psychosis may have senile plaques gradually formed in their brains, leading to glandular necrosis, thus resulting in Fischer's presbyophrenia which is *de facto* a form of dementia.
3. The existence of mesial temporal tuberous sclerosis in TLE to cause intractable epilepsy may justify senile plaques as a sepa-

rate disease distinct from neurofibrillary tangles which were named erroneously after Alzheimer as Alzheimer's disease (AD) by Kraeplein in 1910.

Now that Alzheimer's Disease is a fiction {5}, it must follow that AD should not include senile plaques nor is it equivalent to dementia, although dozens of books and hundreds of articles in the literature have erroneously included both senile plaques and neurofibrillary tangles in AD which, oddly enough, is claimed to include both pre-senile and senile dementia in the literature [7].

4. Perhaps, it is time that Fischer is given proper credits, albeit belatedly, for his contributions on senile plaques and glandular necrosis (presbyophrenia); that is, he set up a dichotomy of simple dementia (without glandular necrosis) and presbyophrenic dementia (with glandular necrosis) both of which were most extensively described by him in 1907 and 1910, not by Alzheimer. His 1907 barely two-page article had nothing of that sort; and his 1911 article, after Kraepelin's invention of Alzheimer's Disease in 1910, simply echoed what Fischer had already described in great detail prior to 1911. I suggest that senile plaques and tangles be named after Fischer and called Fischer's disease (FD) which underlies his dichotomy of dementia; It is his dichotomy of dementia that pertains to the case I have described above. See also my detailed descriptions of Fischer's contributions [8] and the replacement of AD to FD in a vivid case of misdiagnosis of AD [9].

5. It should also be noted that Alzheimer called his inaugural case of Auguste D. in 1907, the same year as Fischer's extensive description of senile plaques, "Senile Psychosis" or "Atypical form of Senile Dementia," but that "Fischer called her dementia "Presbyophrenic dementia" in accordance with his dichotomy of simple dementia and presbyophrenic dementia. I am inclined to claim that the case reported above in detail falls in line with Fischer's dichotomy.

6. Since cases of dementia and epilepsy have been either avoided or ignored by both epileptologists and experts dealing with AD, perhaps it is time that care is taken to look seriously into dementia and epilepsy, from the point of view of language disorder which is a prominent form of memory impairment. I may add that dementia in epilepsy is not a one-to-one cause-effect correlation; it is caused by apoptosis in epilepsy ensuing from multiple pathological causes, as may be evidenced by this case report for the first time in the history of epileptology.

7. There is a possibility that psychosis in epilepsy is actually dementia (of whatever cause) in epilepsy if it becomes progressive over time when followed up carefully as presented above. Mental retardation in Rasmussen's encephalitis may also be a form of dementia and epilepsy in geriatrics and gerontology.

8. Where is the contribution to the connections between epileptology, geriatrics and gerontology, then? The answer is simple: The chief objective in epileptology is to treat the patient's epilepsy through medication and/or epilepsy surgery to make the patient seizure-free. This part was accomplished.

9. However, as the patient experienced numerous episodes of dementia, owing mostly to the progressive apoptosis on account of the residual atrophy in his brain resulting from the astrocytoma, the connections to geriatrics and gerontology may be seen in the rapid deterioration of his brain functions of memory and cognition, as evidenced by his statement to his wife: "I seem to be dreaming. My brain is empty".

10. Of course, there is no medical treatment of such progressive apoptosis resulting from brain tumor and epilepsy, because his dementia, as in all forms of dementia, ensues from totality of the effects of wear and tear. The difference is that the on-going process of wear and tear in his brain is accelerated by his epilepsy and brain tumor, many times faster than a normal aging without such complications.

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