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VIEWPOINT

An English Translation of Alzheimer's 1907 Paper, "Über eine eigenartige Erkankung der Hirnrinde"

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INTRODUCTION

Although "Alzheimer's disease" (AD) has become the subject of innumerable publications with broad scientific, economic, and social ramifications, the original 1907 article is not readily available in English and probably has never been read by more than a handful of authors who discuss AD every year. It seemed appropriate that a translation of Alzheimer's original paper with a brief comment on its historical perspective might be appropriate and useful to those involved in the neuroanatomy of dementia, especially since the story of dementias continues to advance on all fronts and since a large number of investigators are fast approaching an age when they will be expected to be increasingly concerned with dementia.

TRANSLATION

Alzheimer—Munich: On an Unusual Illness of the Cerebral Cortex

A. relates a case which had been observed in the insane asylum of Frankfurt am Main. The specimen of the patient's central nervous system was given to him for clinical analysis by Mr. Sioli, the director of the asylum.

Clinical observation alone made the case appear so unusual that it could not be classified as one of the recognized illnesses; it showed anatomical characteristics which set it apart from all recognized cases.

The first symptom the 51-year-old woman showed was the idea that she was jealous of her husband. Soon she developed a rapid loss of memory. She was disoriented in her home, carried things from one place to another and hid them, sometimes she thought somebody was trying to kill her and started to cry loudly.

In the institution her behavior showed all the signs of complete helplessness. She is completely disoriented in time and space. Sometimes she says that she does not understand anything and that everything is strange to her. Sometimes she greets the attending physician like company and asks to be excused for not having completed the household chores, sometimes she protests loudly that he intends to cut her, or she rebukes him vehemently with expressions which imply that she suspects him of dishonorable intentions. Then again she is completely delirious, drags around her bedding, calls her husband and daughter and seems to suffer from auditory hallucinations. Often she screamed for many hours.

Unable to understand the situation, she starts screaming as soon as an attempt is made to examine her. Some more detailed observations were possible only after repeated efforts.

Her memory is seriously impaired. If objects are shown to her, she names them correctly, but almost immediately afterwards she has forgotten everything. When reading a test, she skips from line to line or reads by spelling the words individually, or by making them meaningless through her pronunciation. In writing, she repeats separate syllables many times, omits others, and quickly breaks down completely. In speaking, she uses gap-fills and a few paraphrased expressions ("milk-pourer" instead of cup); sometimes it is obvious that she cannot go on. Plainly, she does not understand certain questions. She does no longer remember the use of some objects. Her walk is unimpeded, she uses her hands equally well. Her patellar reflexes are normal. Her pupils react normally. There is a slight hard-

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ening of the radial arteries, no noticeable prolongation of the systolic pulse, no albumen.

As the illness progressed, these phenomena which are to be interpreted as complex symptoms appear sometimes stronger, sometimes weaker. But they are never severe. On the other hand, the imbecility of the patient increased in general. Her death occurred after four and a half years of illness. At the end, the patient was lying in bed in a fetal position completely pathetic, incontinent. In spite of all nursing care, she had developed bedsores.

The post-mortem showed an evenly atrophic brain without macroscopic focal degeneration. The larger vascular tissues show arteriosclerotic change.

Specimens which were prepared according to Bielschowsky's silver method show very striking changes of the neurofibrils. Inside of a cell which appears to be quite normal, one or several fibrils can be distinguished by their unique thickness and capacity for impregnation. Further examination shows many fibrils located next to each other which have been changed in the same way. Next, combined in thick bundles, they appear one by one at the surface of the cell. Finally, the nucleus and the cell itself disintegrate and only a tangle of fibrils indicates the place where a neuron was previously located.

Since these fibrils can be colored with dyes to which normal neurofibrils do not react, a chemical change of the substance of the fibrils must have taken place. This fact may be the reason why the fibrils outlast the disintegration of the cell itself. The change of the fibrils seems to be a parallel process to the deposition of a pathological metabolic substance in the neuron whose closer examination is still pending. Approximately 1/4 to 1/3 of all neurons of the cortex show these changes. Many neurons, especially the ones in the upper layer, have completely disappeared.

Distributed all over the cortex, but especially numerous in the upper layers, there are minute miliary foci which are caused by the deposition of a special substance in the cortex. This substance can be observed without dye, but it is very refractory to dyeing.

The glia have developed numerous fibers, moreover, many glial cells show adipose saccules. There is no infiltration of the vessels, however, a growth appears on the endothelia, in some places also a proliferation of vessels.

Considering everything, it seems we are dealing here with a special illness. An increasing number of similar cases have been observed during the last years. This fact should persuade us not to be satisfied with classifying clinically undetermined cases by forcing them into the categories of recognized illnesses. There are certainly more psychiatric illnesses than are listed in our textbooks. A histological examination will enable us to determine the characteristics of some of these cases. This process will gradually lead to a clinical distinction of specific illnesses from the more general categories of our textbooks and it will enable us to define them clinically in greater detail.

No discussion.

COMMENT

The 51-year-old patient Alzheimer described had a progressive presenile dementia with general cortical atrophy. This disease is similar to Pick's disease (Wisniewski et al., 1972) in which progressive bilateral degeneration of the cortical association areas begins in the third and fourth decades. Widened sulci and narrowed gyri are frequently observed with MRI in the elderly, with or without dementia (Hart and Nelson, 1993).

The advent of silver impregnation technics around the turn of the century opened a new era for microscopic study of the nervous system. When Alzheimer gave his report in 1907, these methods (Alzheimer probably used the 1902 method of Bielschowsky) were new and the function of neurofibrils were of special interest (Ramon y Cajal, 1910). The introduction of electron microscopy half a century later demonstrated that neurofibrils were an artifact of fixation (Peters et al., 1976) with formalin or alcohol.

It is now recognized that it is common to find neurofibrillary tangles and neuritic plaques within the cerebral cortex of the elderly. These neurofibrillary tangles develop in relation to degenerating neurons and invariably occur in some degree as a result of the normal aging process (Walton, 1981). Amyloid forms the core of senile plaques, a characteristic of AD. Cerebrovascular amyloid containing the beta/A4 protein is frequently found in the cortex in AD (Hart and Nelson, 1993).

The current inclusion of patients with onset of dementia after age 65 as having AD has resulted in an overlap with senile dementias and is not what Alzheimer described. Considering the paucity of autopsies performed in the current medical-economic environment, it is therefore virtually impossible to provide a differential diagnosis of the redefined (Khachaturian, 1985) AD at autopsy.

Perhaps Alzheimer's conclusions are as appropriate today as they were in 1907. Certainly Alzheimer was ahead of his time in his interest in this phenomenon and his powers of observation and deduction have not been disproved over time.

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