Transmissible Dementias

Diagnosis
&
Management

A review article
Submitted for the Partial Fulfillment of
a Master Degree in Neuropsychiatry

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Cairo 2010

الخرف القابل للانتقال

"التشخيص والعلاج"

رسالـة مقدمــه من
الطبيب / شريف محمود احمد علي

تمهيداً للحصول على درجة الماجستير
في الأمراض العصبية والنفسية

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2010

Acknowledgement

No words will be sufficient to describe my faithful gratitude to my ***prof.Dr. Samia Ashour*** *, professor & head of Neurology Unit , Ain Shams University for her continuous support , wise helpful guidance and patience . It has been an honor to work under her supervision .*

Also , I would like to thank ***Prof.Dr. Azza Abd El Naser*** *, Professor of Neurology , Ain Shams University who supported me a lot in doing this work .*

And I would like to thank ***Prof.Dr. Ahmed Gaber*** *, Assitant Professor of Neurology , Ain Shams University for his warm encouragement and kind support .*

Also , I have to thank all my ***Senior Staff*** *of Neuropsychiatry Department , Ain Shams University who teach us , me & my colleagues , how to be kind & careful about all the patients .*

Finally , I would like to thank my family who did their best for this study to be completed , specially my beloved wife ***Dr. Marwa*** *, my great* ***Mother & Father*** *.*

Table of contents	*pages*

List of Figures		pages
Figure 1	Human prion protein dimerStereo	12
Figure 2	Interaction between PrPc & PrPsc	16
Figure 3	Proposed mechanism of prion propagation	17
Figure 4	pathology of prion diseases (EM) brain biobsy	18
Figure 5	Nissl-Stained Specimens of Brain Tissue from the One of Jakob's Patients	57
Figure 6	Electroencephalogram (EEG) in patient with SSPE	124
Figure 7	Brain MRI in patient with SSPE	126

INTRODUCTION

Dementia is defined as a decline in a person's ability to think and learn . To distinguish true dementia from more limited difficulties due to localized brain damage , the strict medical definition requires that this decline affects at least two distinct spheres of mental activity , Examples of such spheres include memory , verbal fluency , calculating ability and understanding of time and location .

Some definitions of dementia also require that it interfere with a person's work and social life . However , this may be difficult to show when a person's work and social life is already limited , either by choice or by another mental or physical disorder . As a result , the most recent and most authoritative definition, that developed by the National Institute for Neurological and Communicative Disorders and Stroke (NINCDS) part of National Institute for Health , does not include this criterion . The NINCDS definition focuses strictly on a decline from a previously higher level of mental functions .

(Whitehouse and Peter, 1993).

The term dementia goes back to antiquity , but was originally used in the general sense of being “ out of one’s mind” . Identification specifically with difficulties in thinking and learning occurred in the late eighteenth and early nineteenth centuries . Even then , however , the term was used for almost any sort of thinking , learning, or memory problem, whether temporary or permanent and without regard the cause . The most typical picture was of young adult suffering insanity or a disease affecting the brain .

The first step in diagnosing dementia is to show that the person’s ability to think and learn has , in fact , declined from its earlier level . His or her current ability in different spheres of mental activity can be measured by any of a variety of mental status tests. The difficulty comes in comparing these current ability levels with those at earlier times . A patient’s own reports cannot be relied upon , since memory loss is typically part of dementia . Frequently , however , family members` descriptions of what the person once could do , will establish that a decline has occurred . In other cases , comparison with what a person has accomplished throughout his or her life is enough to show that a decline has occurred . If neither sources of information provides a clear

answer , it may be necessary to read minister the mental status test several months later and compare the two results . **(Hyman, 2000).**

Any decline is not sufficient to establish a diagnosis of dementia . Research has shown that the mast older people suffer a small but measurable decrease in their mental abilities . For example , One resent study followed 5,000 people , some for as many as 35 years . This study found that scores on tests of mental abilities did not changes between ages 25 and 60 , but declined about 10 percent ; between ages 60 and 70 . Moore significantly , people in their late eighties had scores more than 25 percent ; below those seen earlier .

Since none of the people tested were considered demented , one might assume that assume that these declines are normal . It is still possible , however , that some tests individuals were in the early stages of dementia ; these people's results may then have pulled down the averages scores for the group as a whole and created a false impression of a sizable "normal" drop in IQ . This ambiguity is particularly unfortunate because it has significant implications at the individual level : No one knows whether , if an older person's mental sharpness starts to decline , this a

normal part of aging or a possible signal of approaching dementia .

Once the existence of dementia has been established , the next question is ; what is causing the condition ? Alzheimer's disease is by far the most common cause of dementia , especially in older adults . One resent study found that it directly caused 54%of dementias in people over 65 , and may have been partially responsible for up to 12% &more .

Unfortunately , there is no direct way to diagnose Alzheimer's disease in a living person ; only microscopic examination of the brain after death can conclusively establish that a person had a disorder . The same is true for the second most common cause , multi-infarct dementia . Both diagnoses are made by excluding other causes of dementia .

Primary Causes of Dementia

Alzheimer's disease (most common cause of dementia) , **Vascular dementia** , **pick's disease** , **Lewy-Body** dementia , **Huntington's disease** and **Parkinson's disease** .

Secondary Causes of Dementia:

Infectious diseases (this will be discussed later) , **Vitamin deficiency** (as in vitamin E , B vitamins or folic acid deficiency) , **Metabolic disorders** (as in D.M , cortisole hormone imbalance , electrolyte levels disturbance , kidney failure , liver disease & thyroid disorders) , **Medications** (as anti diarrhea , anti epileptic , antihistamines , lithium , sleeping pills & tricyclic antidepressants) , **Brain tumors** , **Alcohol** and **substance abuse**.

Pseudodementia

Depression can result in dementia symptoms . In any case , effective treatment of the depression will relieve the dementia it has produced .

(Canadian Broadcasting Corporation, 2003).

Researches have established a link between infectious diseases such as **Prion Diseases** e.g Creutzfeldt-Jakob Disease (CJD) and **HIV** and the onset of dementia . Dementia may also be caused by a number of other infectious **Viruses** (as in progressive multifocal leukoencephalopathy & measles) , **Bacteria** (as in

General Paresis of insane , encephalitis & Lyme Disease) , disease-carrying **Parasites** and **Fungi** .

Infectious diseases can cause neurological damage with symptoms such as confusion , delirium , memory loss and other dementia-related symptoms . **(Beers and Berkow, 1999).**

Aim of The Work

Since the infectious or transmissible dementias represent an important cause of presenile dementias ,

This review aims to highlight the current state of knowledge about the possible role of infectious agents in dementia , the possible ways for diagnosis , and the available lines of treatment .

Prion Diseases

Prions are infectious pathogens principally composed of abnormal forms of a protein encoded in the host genome . Prion diseases are a newly discovered type of disease caused by prion protien . The best known disease is "mad cow disease" but there are in fact several diseases that appear to be caused by prions . Almost all of these diseases affect the brain . **(Huntley, 2008).**

The protein that prions are made of (PrP) is found throughout the body , even in healthy people and animals . However , PrP found in infectious material has a different structure and is resistant to proteases , the enzymes in the body that can normally break down proteins . **(Aguzzi, 2008).**

Functions of Normal Prion Protien

The function of the prion protein remains controversial , but there is evidence that it serves as a copper-dependent antioxidant .

PrP and long-term memory

There is evidence that PrP may have a normal function in maintenance of long term memory .

PrP and stem cell renewal

PrP expression on stem cells is necessary for an organism's self-renewal of bone marrow . **(Aguzzi, 2008).**

Properties of Normal Prion Protien

➢ Physical Properties

1. Filterable to 25 to 50nm average pore diameter.
2. Stable at 90C for 30 minutes, but effectively inactivated by autoclaving. However, cases of CJD had been transmitted through the use of autoclaved instruments.
3. Hydrophobic with a strong tendency for aggregation of the infectious unit with itself and with cellular elements.
4. Continuum of size ranges from 40S->500S on rate-zonal sucrose gradients.
5. Target size determined by ionizing radiation ranges from 64000-150,000 daltons.
6. Gel filtration after zwitterionic detergent treatment gives <= 50,000 mol wt.
7. Density range 1.08-1.30 g/ml

The above physical properties suggest that the monomeric form of the agent is very small, but they must be interpreted