**Do you think Mr. C’s memory problems are stroke related? If so, how would the pathophysiology be different for Alzheimer dementia?**

Mr. C’s memory problems can be attributed to his stroke (vascular dementia), Alzheimer’s disease or a combination of both. Vascular dementia is caused by a narrowing or blockage in the blood flow to the brain (MayoClinic, 2007). These infarcts are caused by an alteration in blood supply to areas to the brain as result of emboli, thrombus or hemorrhage (McCance & Heuther, 2006). Depending on the area of brain involved different deficits may present. A single infarct in the thalamus, the anterior cerebral artery, the parietal lobes or the cingulated gyrus can cause vascular dementia. In Mr. C situation untreated diabetes may have resulted in small vessel disease. Small vessel disease occurs when there is an occlusion of small arteries and arterioles of the brain. It is most frequently associated with hypertension, diabetes and hypercholesterolemia (Rudd, 2002). Ischemia occurs as a result. Irreplaceable neurons are lost resulting in lesions in the brain. Patients often present with multi-infarct dementia rather than a defined area or focal stroke when this occurs (Hayashi, T., Shoji, M., & Abe, K., 2006).

Alzheimer’s disease (AD) can take several forms, familial early onset, late onset familial alzheimer’s dementia (FAD), nonhereditary and sporadic (McCance & Heuther 2006). At a molecular level this disease is characterized by the extracellular deposition of amyloid beta peptide (Abeta) in senile plaques, the appearance of neurofibrillary tangles (intracellular), cholinergic deficit, extensive neuronal loss and synaptic changes in the cerebral cortex,hippocampus and other areas associated with cognition and memory. The deposition of Abeta causes neuronal death by oxidative stress, inflammation and apoptosis. (Parihar & Hemnani, 2004).

 AD has a genetic component. The authors indicate four genes have been identified to autosomal dominant or FAD. These include:

* Amyloid precursor protein (APP)
* Presenilin 1 (PS1)
* Presenilin 2 (PS2)
* Apolipoprotein E (ApoE)

Parihar and Hemnani (2004) indicate that the mutations of these genes are responsible for an increase in Abeta formation and thus deposition of this peptide in senile plaques. These senile plaques disrupt nerve impulse transmission. The greater the numbers of plaques and neurofibrillary tangles in the cerebral cortex and hippocampus the more cognitive dysfunction is present. (McCance& Heuther, 2006).

The following table describes some of the differences in the presentation of AD and Vascular dementia.

**Differences between Alzheimer’s and infarct dementia**

 **Alzheimer’s Disease Vascular/Infarct Dementia**

|  |  |  |
| --- | --- | --- |
| **Etiology** | Can be familial, linked to chromosomes 14,19,21 | Related to Cardiovascular, Cerebrovascular disease and hypertension.  |
| **Risk Factors** | Advanced age, genetic factor | Pre-existing CV disease |
| **Occurrence** | Makes up 50-60% of all dementias | Makes up 20% of all dementias (the other 20% are related to delirium associated with hospitalization) |
| **Onset** | Slow | Often abrupt onset following a stroke or TIA |
| **Age of onset** | Early onset- 30yrs-65yrsLate onset- 65+Most commonly 85+ | Most commonly 50-70 yrs. |
| **Gender** | Affects males and females equally | Affects predominantly males |
| **Course** | Chronic, irreversible, regularly progressive | Chronic, irreversible, fluctuating, stepwise progression |
| **Duration** | 2-20 years | Variable, may be 5-10 years |
| **Symptom Progress** | Onset is insidious. In early form is mild and subtle but intensifies with progression to death r/t causes such as malnutrition and infection | Depends on location of infarct and success of treatment. Death more likely attributed to CV disease. |
| **Mood** | Early depression | Labile mood swings and inappropriate emotions |
| **Speech/Language** | Speech remains until late in the disease. Early in the disease pt may not be able to name objects (anomia). Deficits progress until speech lacks meaning. Pt may repeat words and sounds or may not speak at all. | May have speech/language deficits depending on location of infarct |
| **Physical signs** | Early in disease there are no motor deficits but as it progresses it becomes difficult to perform purposeful movement until there is loss of all voluntary movement. | Commonly exhibits motor deficits.Walking with rapid shuffling steps, wandering, getting lost in familiar place |
| **Orientation** | May exhibit Topographic disorientation (gets lost in a familiar place. Develops visual and spatial disorientation. With disease progression becomes disoriented to person, place, time | Same |
| **Memory** | Memory loss is an early sign. Loss of recent memory is soon followed by progressive decline in recent and remote memory. | Gradual, spotty memory loss. Most often affects recent memory |
| **Personality** | Apathetic(later stages), indifferent, irritable. Early on social behaviour remains intact as person is able to hide cognitive deficits. As the disease progresses person becomes disengaged from activities and relationships, becomes suspicious, paranoid delusions r/t memory loss, can be aggressive | Depression, Apathy present. Apathy early in the disease is more likely indicative of vascular dementia as usually only occurs late with AD. (Wikipedia, 2009). |
| **Functional Status/ADL’s** | Progressive decline in functional ability | A step wise progression |
| **Psychomotor Activity** | Distractable, short attention span | Same |
| **Sleep-Wake Cycle** | Often impaired, wandering and agitation at night | May also wander |

 **Unless otherwise indicated the above info is derived from:** (Smeltzer & Bare, 2000).

Recently, researchers have discovered evidence linking stroke and traumatic brain injury to Alzheimer’s disease (News-Medical.Net, 2007). After a stroke or TBI an increase in the protein-cleaving enzyme, BACE is noted. BACE snips a brain protein called amyloid precursor protein to form a shorter protein called A beta peptide that is a building block for amyloid plaques (News-Medical.Net, 2007). In the case of TBI, elevated BACE enzymes are attributed to enzymes produced during the assault on the brain, called caspases, which allows the BACE enzymes to linger in the brain cells. Caspases destroy cells that have been damaged by ischemia.

Given the above information, it is feasible to assume that multiple factors have affected Mr. C’s cognitive impairment

**Mr. C. states that he had at least one seizure while in hospital. He wants to know why this happened and what happened in his brain to cause this.**

McCance and Heuther (2006) define a seizure as a sudden rapid disorderly discharge of neurons that result in alterations in brain functioning. This results in physical manifestations and often a decrease in level of consciousness. Recurrent, unprovoked seizures are characteristic of epilepsy.  Seizures can also occur in the absence of epilepsy. Nowack (2009) indicates that non-epileptic seizures may occur as result of infection, stroke, brain trauma, medication toxicity, drug and alcohol withdrawal, and metabolic disturbances such as hypoglycemia.  Mr. C. presents with several of these risk factors.  He has recently suffered a stroke, a concussion while in hospital and is a Type 2 diabetic.  It is possible that he was hypoglycemic at the time of his fall. Seizures may also occur as result of space occupying lesions in the brain (Merck,2008).  It is possible that Mr. C. has brain metastases.

Other causes of seizure without epilepsy:

* Atrivenous malformation
* Drug intoxication
* Aminophylline or local anaesthetic toxicity
* Drugs that lower the seizure threshold such as TCA's
* Neurologic infections such as encephalitis, meningitis, AIDS, Malaria, Rabies, Syphilis, Tetanus, Toxoplasmosis
* Fever -common in children < 5 years
* Metabolic disturbances including hyponatremia, hypoxia, hypoglycemia, Kidney & Liver failure, underactive parathyroid gland, Vitamine B6 deficiency
* Drug withdrawal (anticonvulsants, sedatives, alcohol, barbituates, benzodiazepine)
* Space occupying lesions in the brain (abscess/tumour)
* During pregnancy, possibly associated with eclampsia
* Stroke- inadequate brain perfusion such as arrhythmia, carbon monoxide poisoning, near drowning/suffocation
* MS- rare
* Rapid light patters (video games)
* Structural damage to brain- tumours, hydrocephalus
* Birth abnormalities and hereditary disorders like Tay-Sachs disease and phenylketonuria
* Some prescription drugs
* Cocaine and Amphetamine use
* Exposure to toxins such as lead and strychnine

(Merck, 2008).

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