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Depression: A Risk Factor for Dementia

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Degree Master of Science

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Abstract

It is estimated one in five individuals will experience a depressive episode during their lifetime. The risk of dementia doubles every five years after age 65; approximately 40% of those with dementia will also be diagnosed with depression (Byers & Yaffe, 2011). The presenting case, and the premise of this project, was a 65 year old male with complaints of fatigue for a couple of months that has reportedly gotten worse over the past week, otherwise he was in his usual state of health. After a thorough interview, diagnostic labs to rule out differential diagnoses, and utilization of the PHQ-9 depression screening tool, the patient was found to have a "moderate" level of depression without any evidence of dementia. Through an extensive literature review including the most recent and relevant studies, this project will determine if there is sufficient evidence to support a link between the history of depression and the development of dementia. Depression is often misdiagnosed as dementia, the ability to distinguish the differences will allow the healthcare provider to choose more relevant, effective care that results in positive outcomes, thereby improving the quality of life of the elderly.

Keywords: dementia, depressive symptoms, prevalence, and vascular risk factors

Depression: A Risk Factor for Dementia

It is estimated that five million Americans have dementia, with this number expected to triple by the year 2050. The incidence of dementia increases with age; it is reported that 13% of patients greater than 65 and 43% of patients over the age of 85 have some form of dementia. It is further estimated that approximately 40% of those with dementia will also be diagnosed with depression, resulting in a poorer quality of life, greater disability in activities of daily living, higher nursing home placement, higher mortality rate, and a higher burden on caregivers (Byers & Yaffe, 2011).

Over the past decade numerous research studies have tested the hypothesis that depression is associated with the risk of developing dementia. The evidence suggests that "depression early in life is associated with more than a two-fold increased risk for development of dementia later in life and that there is some support for depression as a prodome of dementia" (Enache, Winblad, & Aarsland, 2011).

Case Report

Patient was a 65 year old male, who presents with complaints of fatigue and "no energy" over the past few months with symptoms worsening over the past week. Patient does not offer much for history, he does answer questions however, his answers are vague. The patient's past medical history and current medications were obtained; as chronic illnesses and specific medications have the potential to contribute to the patient's presenting complaints. The patient has no chronic illnesses, and currently does not take any prescription medications but does take an over- the- counter multivitamin and Metamucil daily. The patient's social and family structure is explored including supportive relationships outside of the family. Patient states he is married and lives with his wife, they have three adult children, eight grandchildren, and he works full

time outside the home. He does not smoke or drink alcohol. Prior to onset of symptoms, he had relations with co-workers outside of work, as well as with male friends who share common interests, that he would interact with weekly; his presenting symptoms have limited his outside interests. A full review of systems was conducted to screen for any acute medical problems that may be contributing to his complaints. Patient denies any fever, swollen glands, excessive thirst, feelings of hot or cold, easy bruising or bleeding. He has not had any vision loss, eye pain, or blurred vision. He does not report sore throat, runny nose, hearing loss, or any problems with his mouth or changes in his voice. He denies any chest pain or pressure, irregular heartbeat, cough, wheezing, or any breathing trouble. He has no reported rashes, changing moles, or changes in his hair, skin or nails. Neurologically he has no new onset of headaches, weakness, numbness or tingling. There has been no nausea, vomiting, heartburn, or diarrhea, he reports chronic constipation for which he takes Metamucil, he does not report any changes in bowel habits, and has had no unexplained weight loss. There are no complaints of difficulty starting or weak urinary stream, he does not have difficulty getting or maintaining an erection, no testicular pain, lumps or sexually transmitted diseases are noted. He does not have difficulty falling asleep or report frequent awakening other than once to use the bathroom, however he does report that he has increased sleep, he states, "I go to bed when I get home from work, and sleep until morning, I am wiped out." A review of the patients mood included the administration of the PHQ-9 that showed moderate depression with a score of 10/27; little interest or pleasure in doing things, sleeping too much, having little or no energy, and trouble concentrating on things such as reading the newspaper or watching television more than half the days or nearly every day.

A thorough focused physical exam was conducted. Patient is a 65 year-old Caucasian male, who appeared his stated age, he was dressed appropriate for the weather, his hygiene was

neat and clean, and his affect was variable and appropriate. Vital signs included blood pressure 134/74, pulse 68, respirations 20 and non-labored, with a temperature of 98.3 tympanic, denies any pain, he has no known drug allergies.

His skin is pink, warm, and dry with a smooth texture, no lesions noted; nails show no pallor, thickening, ridging, or cyanosis, capillary refill is less than three seconds. Facial features are symmetrical at rest and with smiling; no obvious asymmetry or drooping. Eye lids are firm and close in unison, palpebral fissure is of normal size, no lesions, erythema, or edema. No abnormalities noted with exam of the conjunctiva, sclera, cornea, or iris. Corneal light reflex is intact. Pupils are equally constricted to 3 mm, regular and symmetrical; pupils react to direct and consensual light, and accommodation. EOM are intact in all six fields of cardinal gaze. Fundoscopic exam of the eyes shows no abnormalities with lens, retina, arterioles, venules, or optic discs. Ears show no abnormalities, tympanic membrane is visible without perforation, bony landmarks are visible and the cone of light is at 6 o'clock on the left and 5 o'clock on the right, with a minimal amount of cereumen bilaterally in the outer canals. Sinuses, maxillary and frontal, are without overlying pain, erythema or edema. No abnormalities noted in the mouth, moderate amount of saliva is present, and mucosa is pink and moist. Lymph nodes are non-palpable and non-tender. Respiratory status is without abnormalities, regular rate and rhythm, non-labored and no accessory muscle use noted. Lungs are clear to auscultation in all lung fields. Heart sounds S1 and S2 present, no murmurs, S3, S4 or rubs identified. Peripheral pulses are 2+ and equal bilaterally, there is no edema noted. There is no abdominal abnormalities, the abdomen is symmetric without masses, tenderness, striae, or scarring. Liver, spleen, and kidneys are non-palpable and non-tender. Cranial nerves III, IV, VII, IX, and X are intact, testing of remaining

cranial nerves are deferred at this time. Musculoskeletal strength is 4-5+ and equal bilaterally in both upper and lower extremities with deep tendon reflexes 2+ bilaterally.

The data collected during the history and physical exam guided the determination for lab testing to rule out the following differential diagnoses: 1) anemia 2) hypothyroidism 3) electrolyte abnormalities 4) urinary tract infection in addition to *moderate depression* that was determined by the PHQ-9 screening tool. Lab studies to rule in or out potential diagnoses included a complete blood cell count, basic metabolic profile, TSH, and urinalysis all of which were within normal limits. It was concluded that the patient's symptoms were in fact related to the diagnosed depression and not due to another process. The patient was offered an antidepressant, in which he was willing to try. The patient was placed on Citalopram (Celexa) 10 mg tablet every morning. The benefits, risks and side effects were discussed, the patient's only concern was for the potential of further constipation on top of what he already has; he was advised that he could take Miralax daily. The patient will return in two weeks for follow-up or sooner if things are getting worse or there are additional symptoms. The follow-up appointment will also include a discussion, and possible referral to behavior health.

Literature Review

In order to determine if there is evidence to support depression as a risk factor for dementia a comprehensive literature review was conducted through CINAHL, Google Scholar, PubMed, and EBSCO Host using key terms such as *dementia, depressive symptoms, prevalence,* and *vascular risk factors*. The results of the search produced 28 articles that met the following criteria; full text, peer reviewed, published journals, English language, human subjects, as well as published dates 2006 to 2014. All 28 research articles were read for relevance and statistical validity; those studies whose participants did not meet the definition of depression and dementia

as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) were eliminated; resulting in 10 articles that were relevant to the case presentation.

The term depression as defined by DSM-IV is as follows:

> depressed mood and/or loss of interest or pleasure in life activities for at least 2 weeks and at least five of the following symptoms that cause clinically significant impairment in social, work, or other important areas of functioning almost every day: 1) depressed mood most of the day; 2) diminished interest or pleasure in all or most activities; 3) significant unintentional weight loss or gain; 4) insomnia or sleeping too much, 5) agitation or psychomotor retardation noticed by others; 6) fatigue or loss of energy; 7) feelings of worthlessness or excessive guilt; 8) diminished ability to think or concentrate, or indecisiveness; and 9) recurrent thoughts of death (American Psychiatric Association (APA), 2000, p. 356).

The term dementia as defined by DSM-IV, is as follows,

> the development of multiple cognitive deficits manifested by both 1) memory impairment (impaired ability to learn new information or to recall previously learned information) and one or more of the following cognitive disturbances: (a) aphasia (language disturbance); (b) apraxia (impaired ability to carry out motor activities despite intact motor function); (c) agnosia (failure to recognize or identify objects despite intact sensory function); and (d) disturbance in executive functioning such as planning, organizing, sequencing, and abstracting. The cognitive deficits listed above must cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning. The patient must also have focal neurological signs and symptoms such as exaggeration of deep tendon reflexes, extensor plantar response,

psuedobulbar palsy, gait abnormalities, or weakness of an extremity or have laboratory evidence indicative of cerebrovascular disease such as multiple infarctions involving cortex and underlying white matter on imaging studies that are judged to be etiologically related to the disturbance, these deficits cannot occur exclusively during the course of a delirium (APA 2000, p.350).

In review of the literature several studies showed evidence to make an association between depression and dementia. While the studies looked at depression as a potential risk factor for dementia, or a prodromal to dementia, they also looked to determine if there was a correlation between the time of onset of depression, early life or late life, and the increased risk of dementia, as well as vascular risk factors and their role in dementia. However, the interpretation of the statistical data among the studies was difficult to summarize due to several variables among the studies, such as length of follow up period, differences in interval between onset of depression (early versus late), the instruments used to measure depressive symptoms, the degree of depression, and the subtypes of dementia (AD, vascular dementia, Lewy body dementia, and mild to moderate cognitive impairment).

Some examples include, varying age parameters used to define early and late life; some used 50 years old while others used 60 years old as the cut-off between early and late. The length of the follow up period varied among studies from one to fifteen years, with an average of five years. In addition the studies used varying methods to determine depression; some used self-report tools such as the Geriatric Depression Scale (GDS) with varying number of questions (GDS-30, GDS-15, and GDS-5), and others used interview tools such as the Hamilton Depression Rating Scale (HDRS) and the Cornell Scale for Depression in Dementia (CSDD).

According to Watson and Pignone, (2003) self-rating of depressive symptoms with the GDS remain valid in patients with a Mini-Mental State Examination (MMSE) score of at least 15. The CSDD is the best established tool for screening depression in dementia, it has shown to have a sensitivity of 91.7%, with a specificity of 80% in mild dementia, and a 70% sensitivity with an 87% specificity in more advanced dementia (Lam et. al., 2004).

The studies concluded that depression symptoms were significantly associated with AD even when the onset of depression preceded the onset of AD by more than 25 years" (Li, et. al. 2011). It was also concluded that, "depressive symptoms in mid-life or late-life are associated with an increased risk of developing dementia. Depression that begins in late-life may be part of the AD prodrome, while recurrent depression may be etiologically associated with increased risk of Vascular Dementia" (Barnes, et. al., 2012).

Lastly, a meta-analysis found similar results. The purpose was to determine if there was a relationship between depression and AD, and also "to investigate the relationship of the interval between the diagnoses of depression and AD to observed risk for AD" (Ownby et. al. 2006, p.534). The studies that were included in the meta-analysis, had participants who had the risk for developing AD or "AD-like dementia" (emphasized gradual progression of cognitive deficits), also, they had to have a history of clinically diagnosed depressive disorder at some time before the clinical diagnosis of AD or dementia; the studies with data contrasting depressed versus nondepressed patients who did and did not later develop AD were included. The meta-analysis determined that "a history of depression may confer an increased risk of later development of AD; reflecting an independent risk factor for the disease" (Ownby, Crocco, Acevado, John, & Loewenstein 2006).

Other studies suggest that "depression is less a risk factor for, than a prodromal symptom of, vascular dementia" (Lenoir, et. al. 2011). These studies had "a high-level of depressive symptoms" either determined by self-report, lifetime treated depression, or the presence of current (within the past two weeks) or past (within lifetime) major depressive episodes (MDE) assessed by trained investigators through a face to face interview (. Results indicated subjects "with a high level of baseline depressive symptoms have a 50% increased risk of developing dementia within a few years" resulting in a "five-fold increased risk of vascular dementia, whereas there was no increased risk of Alzheimer's disease" (Luchsinger et. al. 2008, p. 925).

Another study in which the results were similar set out to determine a link between depression and dementia, but it also looked at the role of vascular risk factors such as diabetes, hypertension, heart disease, and stroke to determine a potential link to dementia. The study concluded that there was no relationship between depressive symptoms and AD, "the prospective relation between depressive symptoms and AD is not explained by a history of vascular risk factors and stroke, suggesting that other mechanisms may account for this association" (Luchsinger, Hong, Tang, & Devanand, 2008).

Relevance to Practice

Depression is often misdiagnosed as dementia, with up to 32% of those referred for dementia evaluation actually suffering from depression. It is estimated that approximately 30-40% of those with dementia will experience significant depression sometime during the course of the disease (Maynard 2003). "Depression not only adds to suffering, disability, suicide risk, and mortality rates, but is also associated with greater functional impairment in people of dementia" (Ownby, et. al., 2006, p. 538). As healthcare providers it is important for us to be able to distinguish the difference between depression and dementia. The ability to distinguish these

differences will allow the healthcare provider to choose more relevant, effective care that results in positive outcomes, thereby improving the quality of life of the elderly.

There are characteristic differences among depression and dementia that can assist the healthcare provider in differentiating depression from dementia as they relate to mental status, onset, course, affect, behavior, sleep, memory, attention, perception, and history.

A person who is depressed will be able to follow directions (although they may refuse), whereas in dementia they will tend to deny any memory problems by attempting to answer all questions and perform tasks. The onset of depression is relatively rapid, progressing from weeks to months, whereas dementia has an insidious and gradual onset. The course of depression is self-limiting, recurrent or chronic and often has periods of improvement, however in dementia there is a slow and continuous decline. Depression has a persistent sadness, which precedes dementia. In dementia, depression follows cognitive decline. Depression causes a person to be apathetic, fatigued, and they tend to complain more than the family. In dementia the person may be agitated, aggressive, or apathetic. The family, in dementia, is more concerned than the patient. Sleep is often affected during depressive episodes, the person awakens in the early morning, and either has excess sleep or insomnia. In dementia the sleep pattern has repeated awakenings that progress to day-night reversal. In depression cognitive impairment is inconsistent, whereas in dementia there is a short-term memory deficit early in the disease process progressing to long-term deficits. People who are depressed have problems with concentration, while in dementia concentration remains intact, they often focus on one idea for a long period of time. Perception remains intact in depression except in severe depression when hallucinations or delusions may be present, however someone with dementia will misperceive people and events as threatening.

Lastly, often in depression there is a history of prior episodes that were undiagnosed, whereas in dementia a psychiatric history is uncommon (Maynard, 2003).

Learning Points

- Depression is not a normal consequence of aging
- Consider other medical conditions and medications that are associated with depressive symptoms and cognitive impairment
- Successful treatment of depression is based on addressing comorbid conditions, tailoring pharmacological interventions to the individual, monitor therapy for side effects and effectiveness, and assuring close follow-up.

Conclusion

Further research is needed, as the number of people with dementia is set to double, and healthcare costs related to dementia are expected to triple, we need to determine if there is a link between depression and dementia. If there is a link, researchers need to conduct further studies to determine if the treatment of depression can decrease vascular changes, such as those caused by inflammation, which has been theorized to be the "pathological process leading to dementia," thereby potentially limiting the number of people who develop dementia (Manthorp & Iliffe 2006).

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