EDITORIAL

Depression Secondary To Medical Illness

By : A . Okasha

By definition, depression is secondary to medical illness when it appears after the medical illness has been diagnosed.

Depression secondary to psychiatric disorders :

The symptom picture in secondary depression (depression secondary to another psychiatric disorder) is clinically indistinguishable from that of primary depression-the insomnia, anhedonia, psychomotor, and other symptoms look to the examiner the way they look in primary depression. In general, in every five patients with a diagnosis of depression, two have a secondary depression. The secondary depressive patient is more likely to be younger at the time of study, with an earlier onset of depression, and more likely to be male . The most likely primary diagnosis is alcoholism, with hysteria, sociopathy, drug abuse, and anxiety neurosis also common preexisting syndromes. It was initially believed that biological markers could distinguish primary from secondary depressives; but when secondary depressives were matched with primary depressives for age and severity, sleep electroencephalogram (EEG) measurements revealed decreased rapid eye movement (REM) latency and increased REM density to be present in both groups.

No adequate prevalence studies of depression secondary to medical illness have been done. Depression is often seen in general medical practice, and studies estimate that of all medical inpatients, between 20 and 32 percent show at least mild depression.

There were six symptoms for depressive severity that successfully discriminated both medically ill depressives and psychiatric depressive from normals and hence may not be confounded by the physical illness or its

attendant distress; sense of failure, loss of social interest, feeling punished, suicidal ideation, dissatisfaction, and indecision. Although crying did not discriminate depressive severity in the psychiatric population, it was significant in discriminating depressive severity in the medical sample.

States commonly mislabeled "Depression":

Up to one-third of patients referred for depression will, on clinical examination, have neither major nor minor depression. By far the most common diagnosis found among these mislabeled patients has been an organic mental syndrome. A quietly confused patient often looks depressed. The patient with dementia or with a frontal lobe syndrome due to brain injury can lack spontaneous initiative and thus appear depressed. Sleep apnea, which may occur in as many as one-third of elderly men, is commonly associated with depressive symptoms, but is easily diagnosed by asking the patient and spouse about insomnia, excessive daytime sleepiness, and snoring . Male patients with prolactin-secreting tumors of the pituitary commonly present with apathy as a clinical feature, mental retardation may also be mistaken for depression.

Excluding organic causes of depression:

Throughout the evaluation, it is helpful to have in mind a systematic schema for the exclusion of organic disorder. Ludwing (1980) has provided an excellent comprehensive list that has been expanded somewhat in Table 1.

Table 1. Differential Diagnosis of Medical Illnesses Capable of Causing Depressive Symptoms*

General Etiology	Specific Etiologies
Vascular	Hypertensive encephalopathy; cerebral arteriosclerosis; intracranial hemorrhage or thromboses; circulatory collapse(shock); systemic lupus erythematosis; polyarteritis odosa; thrombotic thrombocytopenic purpura
Infectious	Encephalitis; meningitis; general paresis
Neoplastic	Space-occupying lesions such as gliomas; meningiomas, abscesses
Degenerative	Senile and presenile dementias such as Alzheimer's or Pick's dementia, Huntington's chorea
Intoxication	Chronic intoxication or withdrawal effect of sedative - hypnotic drugs such as bromides, opiates, tranquilizers, anticholinergics, dissociative anesthetics, anticonvulsants
Congenital	Epilepsy; postictal states; aneurysm
Traumatic	Subdural and epidural hematomas; contusion; laceration; postoperative trauma; heat stroke
Intraventricular	Normal pressure hydrocephalus
Vitamin	Deficiencies of thiamine (Wernicke-Korsakoff), niacin(pellagra), B_{12}(pernicious anemia)
Endocrine-Metabolic	Diabetic coma shock; uremia; myxedema; hyperthyroid dysfunction; hypoglycemia; hepatic failure; porphyria; severe electrolyte or acid/base disturbance; remote side-effect of carcinoma; Cushing's or Addison's syndrome; sleep apnea
Metals	Heavy metals (lead, manganese, mercury); carbon monoxide toxins
Anoxia	Hypoxia and anoxia secondary to pulmonary or cardiac failure, anaesthesia, anaemia
Depression-Other	Depressive pseudodementia; hysteria; catatonia

*Ludwing's differential diagnosis of the confusion-delirium-dementia-coma complex

Table 2. Drugs Associated with Depressive Syndromes

Antihypertensives	Cimetidine, ranitidine
reserpine	Barbiturates
methyldopa	Benzodiazepines
thiazides	Beta-blockers
spironolactone	especially propranolol
clonidine	Metoclopramide
Oral contraceptives	Cocaine
Steroids and adrenocorticotropin hormone (ACTH)	Amphetamine

Table 2 presents drugs most commonly associated with the production of a depressive syndrome.

A check on the medications that the patient is currently receiving will generally tell the physcian whether or not the patient is receiving something that might cause a change in mood.

Abnormal laboratory values should never be missed and may provide the clues to an undiagnosed abnormality responsible for the depressive symptoms. A workup is not complete if the evaluation of thyroid and parathyroid function is not included.

Medical illnesses specifically linked to depression:

For more than 50 years carcinoma of the pancreas has been noted to show frequent association with psychiatric symptoms, especially depression, which in some cases seems to be the first manifestation of the disease.

Whether the increase in psychiatric symptoms is due to the grim prognosis of pancreatic cancer (though depression has often been demonstraied before the patient or physician knew the diagnosis) or to a humoral process initiated by the malignancy is unclear.

Stroke; Direct injury to the brain can produce regular changes of affect full syndrome of major depression. One model for this is the cerebrovascular accident (CVA), now shown by Robinson and co-workers (Robinson et al.,1985; Lipsey et al., 1984) and others to be followed often by major depression. According to these studies, when the stroke is unilateral, major depression will occur in approximately 60 per cent of the patients with a left hemisphere lesion and in approximately 15 per cent of patients with a right hemisphere lesion. The depression will appear within the acute period in approximately two thirds of the patients destined to suffer it, with the remainder developing depression by the sixth month. Moreover, the severity of the depression is directly related to the distance of the injury from the frontal pole. That is, the closer the insult to the left frontal pole, the more depressed the patients will be. Further work by the same group established the same relationship between location of injury and severity of depression in patients with traumatic brain injury other than stroke, patients with bilateral brain injury, and even in left-handed patients with similar lesions.

Right hemisphere lesions deserve special diagnostic attention. As noted above, the closer the lesion is to the occipital pole, the more likely the patients is to be depressed . But when the lesion is in the right anterior location, the mood disorder tends to be an apathetic, indifferent state associated with "inappropriate cheerfulness."

When depressed stroke patients are treated with appropriate drugs, they respond well.

Multi-infarct dementia; Cummings and associates (1987)applied DSM-III diagnostic criteria to 45 consecutive patients referred for dementia, 30 with Alzheimer's dementia and 15 with multi-infarct dementia(MID). Four of 15 MID patients, as opposed to none of 30 Alzheimer's patients, were diagnosed as having had major depressive disorder.

The subcortical dementias. Parkinson's disease and Huntington's disease commonly include major depression within their symptomatology. In as many as one-half of the cases of Huntington's disease, a major depression

prior to the onset of either chorea or dementia may represent the first appearance of the disease (Folstein et al, 1983).Diagnosis is made clinically, as described above.

In Parkinson's disease depression is the most frequent mental change, and major depressive episodes occur in 40 per cent more of patients. Antidepressants are required and are beneficial . Some reports note that as depression is treated in the patient with Parkinson's disease, the Parkinsonian symptoms will also improve. This is especially striking in case reports in which ECT was used (Holcomb et al., 1983), although the same improvement has been reported after tricyclic antidepressants.

Another subcortical dementia that has drawn increased interest recently is Binswanger's encephalopathy, a state of white matter demyelination presumably based on arteriosclerosis, presenting with an abulic withdrawn state and a paucity of focal neurologic findings. Antidepressant medication has produced striking relief for depressive symptoms in this supposedly rare condition (Summergrad, 1985).

In multiple sclerosis, Joffe and associates (1987) found a lifetime prevalence of 38 per cent with unipolar major depression and 13 per cent with bipolar disorder.

Human immunodeficiency virus (HIV). The encephalopathy caused by HIV, particularly in its earlier manifestations, produces a syndrome that verges on and often becomes a major affective disorder. Depression can exist, as can mania or hypomania, in more advanced stages of the infection or with some of the opportunistic infections suffered by patients with AIDS-related complex.

Cushing's syndrome. Careful prospective studies had shown a strikingly high incidence of major affective disturbance in patients with Cushing's syndrome.

Investigators have evidence that there are other medical illnesses that regularly produce depressive symptoms, such as temporal lobe epilepsy or complex partial seizures (Schiffer and Babigian, 1984; Mendez et al., 1986).

Choosing appropriate antidepressant treatment :

Although there has been concern that medically ill depressed patients will not respond well to antidepressants, our experience is encouraging. Whenever major depression is diagnosed, effort to alleviate the clinical symptoms almost always includes somatic treatments. The consultant who understands the interactions of the antidepressants with illness and other drugs is best prepared to prescribe these agents effectively.

Electroconvulsive therapy remains the single most effective somatic treatment for depression, often the treatment of choice for medically ill patients with severe depression.

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