Sadness: Diagnosis, Evaluation, and Treatment

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LESSONS LEARNED AT THE INTERFACE OF MEDICINE AND PSYCHIATRY

The Psychiatric Consultation Service at Massachusetts General Hospital (MGH) sees medical and surgical inpatients with comorbid psychiatric symptoms and conditions. During their twice-weekly rounds, Dr Stern and other members of the Consultation Service discuss diagnosis and management of hospitalized patients with complex medical or surgical problems who also demonstrate psychiatric symptoms or conditions. These discussions have given rise to rounds reports that will prove useful for clinicians practicing at the interface of medicine and psychiatry.

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Have you ever been challenged when caring for a profoundly sad patient? Have you wondered why you felt sad while interacting with him or her? Have you ever considered sadness to be a harbinger of a more serious medical problem or the result of a medical or psychiatric problem? Is depression typically the first thing that comes to your mind when one of your patients appears sad? Have you thought about how you could (or should) respond to your patient's sadness or tears and wondered whose role (eg, internist, psychiatrist, nurse, family member) it was to explore the patient's sadness? If you have, then this article should prove useful regarding the importance of exploring and evaluating sadness in patients, the potential etiologies for sadness, and approaches to the management of sadness that are based on an underlying etiology.

CASE VIGNETTE

Mr A, a 63-year-old retired community hospital office manager with a history of coronary artery disease, paroxysmal atrial fibrillation, aortic stenosis (coronary artery bypass graft and aortic valve repair 7 months earlier), and polycystic kidney disease (that resulted in a kidney transplant 5 years earlier), came to the emergency department after experiencing 5 to 6 weeks of persistent lethargy, myalgias, back pain, poor appetite, decreased energy, depressed mood, and an inability to perform activities of daily living.

Mr A attributed his malaise to grief over the unexpected death of his son. However, he had dark malodorous urine and a temperature of 101.2° F. Mr A was started on empiric antibiotic treatment (with vancomycin and zosyn) and was admitted to the transplant service.

His workup revealed blood cultures positive for *Streptococcus sanguinis*, a white blood cell count of $15.9/\times10^9$/L (with 94% neutrophilia), and a nondiagnostic computerized tomographic study of the chest, abdomen, and pelvis. Psychiatric consultation was requested to assess his depression. He was anhedonic, lacked energy, and had impaired concentration ability, but he denied having thoughts of suicide or using alcohol or illicit drugs. During the psychiatric examination, he became nauseated, started to vomit, developed headache and blurry vision, and felt pressure behind his right eye. A noncontrast computed tomographic study of the head revealed a large right parietotemporo-occipital intraparenchymal hematoma for which the neurosurgery service performed an emergent hemicraniotomy (to evacuate the hematoma). Following surgery, Mr A's depressed mood continued to improve, and he was transferred to a rehabilitation facility.

WHAT IS SADNESS?

Ekman and Friesen,[1] psychologists and researchers on the relationship of emotion and facial expressions, described sadness as an emotional expression of grief, unhappiness, loss, hopelessness, helplessness, or sorrow. Sadness can also be experienced as loneliness, discouragement, rejection, and dissatisfaction with oneself.[2] The facial expression of sadness is typically created by the raised and pulled together inner portion of the eyebrows, pulled down corner of the lips, and pushed up chin, sometimes accompanied by tears.[3] Although sadness is considered a negative emotion, it plays a crucial role in adaptation[4]; it may elicit empathic responses,

Clinical Points

- Although sadness is a normal emotional expression, it can be a harbinger of serious medical and surgical conditions, which are easily missed by most clinicians.
- Sadness is prevalent among hospitalized medical and surgical patients and should be evaluated by any clinician who recognizes or suspects that a patient is sad.
- Always explore why your patient is sad and consider a broad differential diagnosis including medical, neurologic, and psychiatric problems in your assessment.
- Physicians of all disciplines can conduct the initial evaluation of sadness, while psychiatric consultation can be obtained when a more extensive psychiatric assessment is needed.

Table 1. Differential Diagnosis of Sadness

Adjustment disorder
Grief
Major depressive disorder
Mood disorder secondary to a general medical illness
Delirium
Cerebrovascular accident
Difficulty coping
Demoralization

and it facilitates group attachments.[2] Ekman and Friesen[1] further noted that sadness is ubiquitous and transcultural; people from different cultures can recognize sad facial features regardless of the culture of the person displaying the emotion.

HOW COMMON IS SADNESS?

Sadness is a normal response to distressing and discouraging life events (eg, illness). Studies of hospitalized patients often assess sadness. A PubMed search of the literature using *sadness and hospitalized patients* revealed 33 publications from 1980 to 2014 that employed variable methodologies and endpoints.[5–37] Sadness was often identified as part of depression scales (such as the Beck Depression Index, the Empiric Sampling Method questionnaire, the Mokken Questionnaire-10, or the Hamilton Depression Rating Scale), while the endpoints included the prevalence of sadness in a subpopulation of hospitalized patients (eg, patients on contact precautions[10]) or sadness as either a predictor of a negative outcome (eg, in patients with acute coronary syndromes, sadness was associated with more major cardiac events[16]) or in the context of the clinician's ability to respond to sadness (eg, reactions/responses to emotional distress in palliative care patients[6]).

WHAT IS THE DIFFERENTIAL DIAGNOSIS OF SADNESS?

Sources of sadness are complex and multifactorial (eg, biological, psychosocial, environmental). Moreover, sadness and expressions of sadness have been linked with neuroanatomical and neurophysiologic function and have been associated with increased activity in the left amygdala and right temporal pole[38]; hence, any disease that increases neuronal activity in these brain areas could contribute to sadness. There is no prevalence or incidence data on the medical and psychiatric conditions linked with sadness. Table 1 lists potential conditions linked with sadness based on our clinical experience within the psychiatric consultation service. The conditions linked with sadness are further discussed below.

Major Depressive Disorder

Although many practitioners mistakenly believe that depressed mood and sadness are one and the same, not every patient who looks sad feels depressed or meets the criteria for major depressive disorder. Sadness can be transient as the causes for it dissipate and as people distance themselves from the precipitating event. Some depressive states arise even in the absence of an identifiable external cause.[39] Depression, with one of its core features, sadness, is common. The lifetime incidence of depression in the United States is more than 12% in men and 20% in women.[40] Moreover, depression is more common in hospitalized patients than in the general population.

According to the *DSM-5*, major depressive disorder requires that an individual have a depressed mood or loss of interest or pleasure (anhedonia) characterized by sadness and accompanied by at least 5 neurovegetative changes including significant weight loss or gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive guilt, diminished concentration, and recurrent thoughts of death or suicide. These changes must last a minimum of 2 weeks and must interfere with the patient's level of functioning. Depressed mood in a setting of a general medical condition or substance use/abuse (such as alcohol and other illicit drugs) is not considered to be major depressive disorder but is a secondary depressive illness. Although depression can result in extreme sadness, clinical depression is not equivalent to sadness.

Adjustment Disorder

Stress (eg, from a serious or unusual event)[41] develops when a person perceives that he or she does not have the resources to deal with a situation in the past, present, or future.[42] Being hospitalized is stressful for some patients and their loved ones (because of discomfort, the novelty or associations of sounds produced from various monitoring devices, the hustle and bustle of clinical personnel, and clinical care [eg, involving phlebotomy, medication administration, procedures, poor prognoses, doctor-patient communications], lack of control, lack of privacy, pain and the suffering of others, and impaired function).

Adjustment reactions occur when a person is unable to adjust adequately to a particular stress or life event. According to the *DSM-5*, adjustment disorders are a heterogeneous group of stress response syndromes that occur after exposure to distressing (traumatic or nontraumatic) events that exceed what would be expected from the stressor and resulting in significant functional impairment. Adjustment

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disorders occur within 3 months of the identifiable stressor (excluding the death of a significant person in the presence of another Axis disorder, such as major depressive disorder). Emotional symptoms of an adjustment disorder include sadness, hopelessness, anxiety, worry, suicidal ideation, and neurovegetative symptoms, while behavior signs and symptoms include irritability, reckless behavior, ignoring important tasks, isolation, and aggressive behavior.[41] The more severe or persistent the stressor, the more likely it is for the disorder to develop, occurring more in inpatients (11%–21%) than in outpatients (2%–5%).[41]

Difficulty Coping

Coping describes a normal adaptation to manage stress.[38] When the ability to cope with medical illness is inadequate, sadness can set in. The nature and type of personality styles and their associated defense mechanisms affect coping ability. Active coping strategies alter how one perceives stress and include planning (eg, thinking about how to confront the stressor), acceptance (eg, accepting that the stressful event has occurred), and positive framing (eg, making the best of one's situation and trying to grow from it).[43] Avoidance entails denial (or an attempt to reject the reality) of the stressful event, behavioral disengagement (ie, giving up or withdrawing from the attempt) to attain the goal with which the stressor is interfering, venting (involving an increased awareness of one's emotional distress and discharging those feelings to others), and using humor (eg, making jokes about the stressor).[43] Avoidance may also involve distractions that keep a person from directly addressing the stressful event. Defensive styles also guide coping strategies. For example, those with an obsessive-compulsive personality tend to intellectualize, while those with a paranoid personality project their feelings onto others.[44] Ethnic, cultural, and socioeconomic factors can also influence coping strategies.[45]

Mood Disorder Secondary to Medical Illness

Sadness can be a component of depression secondary to a medical condition (ie, not related to another mental disorder such as major depressive disorder or adjustment disorder).[46] Medical illnesses (eg, infectious diseases [like influenza, mononucleosis, viral hepatitis], cancer [especially pancreatic cancer] sleep apnea [with hypoxia], endocrine disorders [eg, of the thyroid and adrenals], collagen vascular diseases [such as lupus], central nervous system diseases [such as multiple sclerosis, seizures, cerebrovascular accidents/strokes, brain tumors]) can present with depressed mood and sadness. Medications (including interferon, cimetidine, indomethacin, disulfuram, steroids) can also induce depressed mood and sadness.[47,48]

Demoralization

Although no standard definition for demoralization exists,[49] it has been referred to as insidious psychological distress among those with a medical illness.[50] A demoralized patient is one who feels disempowered, hopeless, rejected, despairing, and helpless and who has low esteem.[50–52] Although demoralization may coexist with major depressive disorder and adjustment disorders, not every demoralized patient meets *DSM-5* criteria for either of these psychiatric illnesses. Demoralization is prevalent in hospitalized patients (eg, roughly one-third of medical inpatients suffer from demoralization).[50] Given the host of psychosocial and physical limitations that are comorbid with many medical illnesses, some degree of reactive demoralization is normal and expected.[53] Demoralization differs from major depressive disorder because mood responsivity is preserved and reversal of the adverse situation rapidly restores the capacity to feel enjoyment and hope.[54]

Hypoactive Delirium

Delirium is a serious, transient, fluctuating, and reversible acute neuropsychiatric syndrome characterized by global cognitive dysfunction and impaired attention.[41] The prevalence of delirium in general hospital settings ranges from 15%–60%,[55] and it is even greater in intensive care unit patients. Delirium's signs and symptoms also include psychosis (eg, auditory and visual hallucinations, paranoid delusions) and psychomotor agitation or retardation that can be misconstrued as depression. To make a diagnosis of delirium, a patient must have a disturbance of consciousness with a diminished ability to focus or to maintain or shift attention, a change in cognition or the development of a perceptual disturbance not attributed to dementia, fluctuations over the course of the day, and evidence that the disturbance is caused by a general medical condition. Life-threatening causes of delirium include drug withdrawal (eg, from alcohol, benzodiazepines, barbiturates), Wernicke's encephalopathy, hypoxia, hypoglycemia, hypertension, hyper/hypothermia, hypoperfusion, intracerebral hemorrhage, meningitis/encephalitis, poisoning, and status epilepticus.

Grief

Grief is a normal and universal human response to loss[56] (its symptoms include sadness, tearfulness, and insomnia), and it typically lasts for 2 to 6 months and requires no treatment. However, grief does not result in low self-esteem or worthlessness, as may develop in depression. Grief is characterized by several stages.[57] The initial phase entails shocking disbelief that lasts for hours to days. In the next stage, sadness, anger, and hopelessness interspersed with normal functioning arise. This phase is followed by gradual acceptance and realization of the loss, which can last for months.[41] When extended periods of depression or thoughts of suicide appear, complicated grief, major depressive disorder, or an adjustment disorder need to be considered.

Cerebrovascular Accident/Stroke

Sadness and neurovegetative symptoms of depression have been observed in patients with acute stroke and in those with poststroke states. Depression is common after acute stroke (6%–52%).[58] Caeiro and colleagues[58] used the Montgomery-

Asberg Depression Rating Scale to assess depression in 178 acute stroke patients and found that 46% of the patients presented with depression. To date, how lesion location is correlated with depressive symptoms remains controversial. Some have shown that depression is more closely correlated with the left anterior (cortical or subcortical) areas of the brain, while others believe that right hemispheric lesions are more apt to induce depression.[60,61] Others have noted that depression was related to left hemispheric strokes.[62,63] About 20% of patients with stroke meet criteria for major depressive disorder in the poststroke period, which can lead to less participation in rehabilitative efforts.[59] Some of the psychosocial risk factors that increase a person's likelihood to develop poststroke depression include a history of major depressive disorder and a family history of major depressive disorder.

WHY IS IT IMPORTANT TO RECOGNIZE SADNESS?

Sadness is characteristic of common medical and psychiatric problems and is a potential harbinger to serious illness. These medical and psychiatric problems, in turn, also have physical, psychological, and behavioral effects on patients that may not resolve without treatment. Failure to evaluate and treat a patient's sadness could adversely impact a patient's hospital course, increase a patient's length of stay, and raise the cost of care. Carefully exploring why a patient is sad could save a patient's life, especially when thoughts of suicide arise.

HOW CAN SADNESS BE EVALUATED?

In addition to taking a comprehensive history, and asking directly about whether a patient is sad, several diagnostic tools can be used to assess sadness. Potentially serious medical illnesses should be ruled out (with a history, physical examination, laboratory testing, and imaging studies). Obtaining collateral information from the patient's family about the progression of symptoms associated with sadness may be meaningful (as in grief). Specific rating scales to inform the differential diagnosis include the 9-item Patient Health Questionnaire (for major depressive disorder) and Montreal Cognitive Assessment Test (for patients with delirium).

WHO SHOULD EVALUATE SADNESS?

Any physician who recognizes or suspects that a patient is sad (based on the physician's own feelings of sadness during patient interactions) should assess sadness with a thorough history. As clinicians interact and connect with patients, patients can evoke emotions and feelings in clinicians (ie, experience countertransference), which usually arises in therapeutic relationships. Hence, when one leaves a patient's room feeling sadder than when entering it, the patient is most likely sad, even if it was not explicitly discussed. After the initial evaluation, a psychiatric consultation can be arranged to provide a more detailed psychiatric evaluation if one suspects a comorbid psychiatric condition or if there are thoughts of suicide, self-harm, or death.

SHOULD SADNESS BE TREATED?

Unfortunately, there is no evidence-based treatment for sadness; instead, it is usually placed in the context of a treatable syndrome or disorder as outlined above. Treatment of sadness should depend on the underlying etiology (which can be complex and multifactorial) and its severity. Underlying medical causes should be treated first. Being supportive and empathic is a major component of managing sadness. Active symptom management, exploration of attitudes toward hope and the meaning of life, a search for a renewed purpose and role in life, cognitive restructuring of negative beliefs, spiritual/religious support, promotion of relatedness with others, and enhanced family functioning can reduce demoralization.[64] Brief psychotherapy (including brief psychodynamic, cognitive-behavioral, interpersonal therapies) can also mitigate sadness. Psychopharmacologic agents (including antidepressants, mood stabilizers, stimulants, and atypical antipsychotics) typically used for treating affective illness can also mitigate affective intensity, as can electroconvulsive therapy (especially in the severely ill when there is concern for drug-drug interactions).

REFERRAL AND FOLLOW-UP OF SAD PATIENTS

Referral of patients with sadness (eg, to psychologists, psychiatrists, social workers) should be based on the underlying etiology and the intensity of the experience and concerns about safety.

CONCLUSION

Sadness is a normal and universal emotional expression of grief, loss, hopelessness, stress, discouragement, or loneliness. However, sadness can also be a harbinger of a wide variety of common and serious medical and psychiatric illnesses and requires a thoughtful evaluation (by obtaining a history, observing interactions, and considering medical and psychiatric aspects). An awareness of countertransference reactions can also provide insights into a patient's sadness. Physicians of all disciplines can conduct the initial evaluation of sadness, while psychiatric consultation can be obtained when a more extensive psychiatric assessment is needed. Depending on the etiology of sadness, active medical symptom management, active listening, supportive care, use of pharmacologic agents, or other somatic treatments can treat the underlying causes of sadness. Referral for treatment should flow from the etiology and severity of symptoms.

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