Mood Change in a Patient with a Carcinoid Tumor

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Consultation-liaison psychiatry specializes at the interface between medicine, surgery, and psychiatry. Patients are seen and evaluated based on comorbid medical and psychiatric problems. We report the case of a man with a carcinoid tumor and complicated postoperative course who developed a significant change in attitude

CASE

The patient is a 27-year-old man in the US military with no pertinent past medical history. He first sought medical care due to sharp periumbilical pain, profound loss of appetite, and nausea. His laboratory tests were unremarkable and he was initially treated for gastroenteritis. Repeated similar episodes while still under medical care prompted a computed tomography scan that demonstrated ileocecal intussusception with scattered enlarged intra-abdominal lymph nodes. A subsequent surgery and biopsy confirmed a stage 3 carcinoid tumor of the appendix. Despite initial efforts, there was persistent ileocolic intussusception with associated small bowel obstruction. The patient's recovery was complicated by an abdominal abscess, ultimately leading to sepsis and warranting a right hemicolectomy.

The patient spent the next 4 months recovering from these procedures; however, the cancer diagnosis, repeated hospitalizations, multiple surgeries, and complicated recovery significantly affected his psychological well-being. He subsequently presented to psychiatry for evaluation.

Upon presentation, his evaluation revealed noteworthy changes in his personality since his cancer diagnosis. His medical condition had transformed him from an adventurous person into someone who avoided sports and challenging activities. His alteration in demeanor and physical limitations resulted in him feeling ineffectual at work and ambivalent about both his military career and future in general.

The patient admitted to struggles with adjusting and adapting to changes in his lifestyle since the carcinoid tumor diagnosis and

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ensuing surgeries. He endorsed increased stress and persistent worries concerning disease and death. He described two episodes of prolonged, self-resolving anxiety that had occurred since his last surgery. Other associated symptoms included difficulty with concentration, muscle aches, insomnia, diarrhea, and abdominal pain. A basic medical test for depression and anxiety to include complete blood count with differential, a comprehensive metabolic panel, and thyroid-stimulating hormone was unremarkable.

DIAGNOSIS

Adjustment Disorder with Depressed Mood and Anxiety

He was diagnosed with an adjustment disorder with depressed mood and anxiety. After discussion of this diagnosis, he was eager and open to psychotherapy and psychopharmacologic treatment. Psychotherapy was begun first with supportive and then with cognitive-behavioral therapy. Due to continued depressed mood, medication treatment was considered. Before initiation of antidepressants, the patient's 24-hour urine specimen was assessed for 5-hydroxyindoleacetic acid (HIAA) excretion and the result was 4.4 mg. Because the patient's 24-hour urine 5-HIAA excretion was low, treatment with a selective serotonin reuptake inhibitor (SSRI) was deemed an appropriate option. Citalopram at a dose of 20 mg daily was initiated.

The patient returned for a follow-up evaluation 1 week later to assess any changes in his symptoms. He described worsening of anxiety, but not with enough associated symptoms to qualify as panic disorder or generalized anxiety disorder. As a result, he was prescribed clonazepam to target his worsening symptoms of anxiety. He experienced few side effects from citalopram; however, a decrease in sexual functioning had left him frustrated with the antidepressant. After evaluation of side effects, the patient underwent several medication changes until he was stable with minimal side effects and no reports of sexual dysfunction on a regimen of 10 mg/day of escitalopram and 1 mg of clonazepam twice daily. Over the subsequent months, the patient's disposition gradually improved, his mood brightened, and he noted that "I feel like myself again."

DISCUSSION

Carcinoid tumor is a rare neuroendocrine neoplasm occurring most commonly in the appendix, lungs, and along the gastrointestinal (GI) tract.[1] The worldwide incidence is approximately 2 per 100,000 people, with the average age of diagnosis being 61.4 years.[2] The presentation will vary based on the location of the tumor. The majority of carcinoid neoplasms are located in the GI tract, subsequently producing symptoms of abdominal pain, diarrhea, and occasional flushing.[3]

Carcinoid syndrome, which manifests in approximately 20% of patients with carcinoid tumors, occurs secondary to the release of metabolically vasoactive amines into the systemic circulation (**Figure 1**). This syndrome rarely occurs in the absence of hepatic metastases because vasoactive amines are efficiently metabolized by the liver.[3] Infrequently, carcinoid syndrome has been associated with tumors located in the lungs because serotonin bypasses first-pass metabolism in the liver, leading to increased levels.[4]

Common symptoms of carcinoid syndrome include skin flushing, diarrhea, tachycardia, shortness of breath, wheezing, telangelectasia, and pellagra. The most common symptom is flushing, which occurs in over 90% of people.[5] The least common symptom is pellagra, occurring in approximately 5% of patients with carcinoid tumors. Pellagra manifests as a direct result of depleted niacin levels secondary to increased serotonin production. The presentation will often include a beefy tongue and red skin lesions localized to the face and neck.[6]

In addition to the physical symptoms caused by carcinoid tumors and carcinoid syndrome, patients may also suffer from psychiatric complications. Results from two previous studies demonstrated the presence of depressive symptoms in half of patients with carcinoid tumors who had elevated urinary 5-HIAA levels.[7,8] In patients with a serotonin-secreting carcinoid tumor, as opposed to healthy people, up to 60 times more (60% vs 1%) dietary tryptophan is shunted to 5-hydroxylation, resulting in excessive quantities of serotonin (5-HT), 5-hydroxytryptophan, and 5-HIAA in the body. This excessive shunting decreases the amount of tryptophan

available to cross the blood-brain barrier, which is essential to produce 5-HT in the central nervous system. This results in a relative deficiency of 5-HT in the brain, which in turn increases the risk for depressive symptoms.[9]

The diagnosis of carcinoid tumors is complicated by the variability in the presenting symptoms and location of the tumor. Often, carcinoid tumors are incidentally found during surgeries, laparotomies, and endoscopies.[10] As a result, the diagnosis is usually delayed approximately 2 years from onset of symptoms, with a range up to 20 years.[11]

The most appropriate way to assess for the presence of a serotonin-secreting tumor is to measure the patient's 24-hour urinary 5-HIAA level. The normal range of urinary 5-HIAA excretion is 2 to 8 mg per 24 hours. Values greater than 25 mg per 24 hours are suggestive of carcinoid syndrome.[12] False-positive elevations in 5-HIAA can be caused by serotonin-rich foods like bananas, walnuts, avocados, and pineapples, so the patient's diet should be taken into consideration.[13]

When there is a suspicion for carcinoid syndrome in a patient with depressive symptoms, it is imperative to avoid SSRI medications in favor of a nonserotonergic form of pharmacotherapy. Giving an SSRI medication has the potential to worsen carcinoid tumor symptoms due to an exacerbation of the already elevated serotonin levels in the body.[7] In these cases, appropriate alternatives would include psychotherapy for mild-to-moderate depression with consideration for a concomitant nonserotonergic antidepressant such as bupropion.

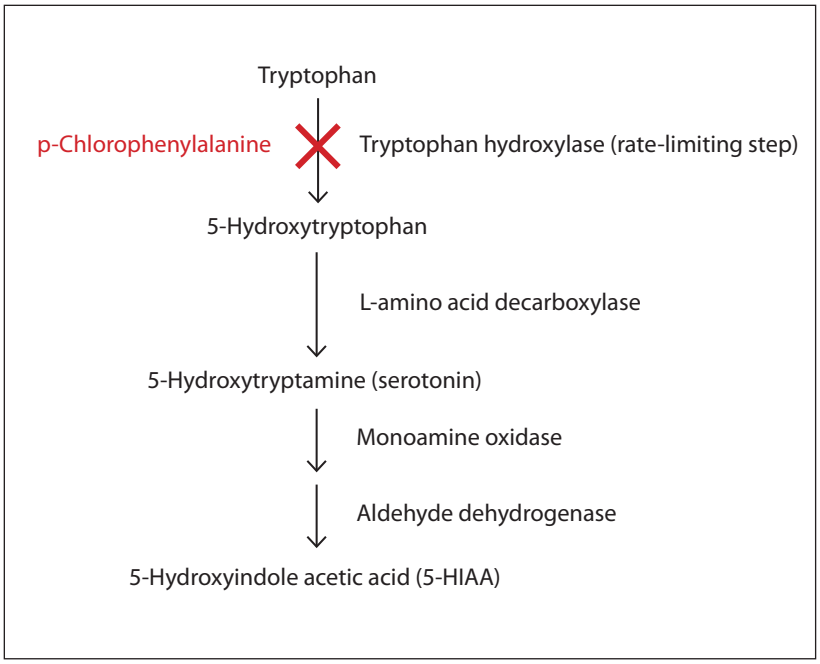

Figure 1. Diagram of serotonin synthesis and metabolism.

An acceptable time to administer an SSRI in the presence of a carcinoid tumor is when laboratory data do not support the presence of excess serotonin secretion and the patient does not have active symptoms of carcinoid syndrome. Ultimately, not all carcinoid tumors secrete serotonin and not all serotonin-secreting tumors become symptomatic. Although it is possible for SSRI medications to unmask a case of carcinoid tumor or aggravate ongoing symptoms, it has been shown that once the SSRI is discontinued, the patient's previous psychiatric symptoms will return.[14]

It is our recommendation that a multidisciplinary approach be implemented to evaluate the use of SSRIs and other serotonin-elevating psychotropic medications in patients with concern for carcinoid syndrome. The psychiatry, surgery, and endocrinology services should collaborate to determine if the benefits of SSRI and other serotonergic agents outweigh the possible adverse effects. In patients with carcinoid syndrome displaying active GI and systemic symptoms, SSRIs should be avoided; however, as shown in the case presented here, patients without active carcinoid syndrome symptoms or patients recovering from carcinoid tumor removal may tolerate the use of SSRIs without provocation of symptoms. Our patient had physically recovered from the removal of the carcinoid tumor and had not experienced GI symptoms for over 7 months. In this case, the use of SSRIs to treat anxiety secondary to extensive medical encounters as

well as to address drastic changes in his quality of life was appropriate.

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