Carcinoid Tumor

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A 46-year-old man, Mr. P, presented to the emergency department with chest pain for two days. Myocardial infarction was ruled out while in the emergency department, and a computed tomography scan of the chest demonstrated an anterior mediastinal mass measuring approximately 4 cm x 4.5 cm x 5 cm with multiple pulmonary nodules. Mr. P's past medical history included diabetes mellitus and gout, but no family history of any type of malignancy. His physical examination was unremarkable. A needle biopsy was performed but was nondiagnostic. Initial differential diagnoses included neuroendocrine tumor, lymphoma, lung cancer, thymic cyst, or germ cell tumor.

Mr. P had a repeat biopsy that was interpreted as a neuroendocrine tumor on two separate occasions. While waiting for further interpretation, tests including laboratory evaluation of chromogranin-A, serotonin, and urinary 5-hydroxyindoleacetic acid (5-HIAA) were performed. Levels of chromagranin A and 5-HIAA were within normal limits. Multiple scans then were ordered for tumor staging and to detect possible distant metastases. A positron-emission tomography (PET) scan with F-labeled fluorodeoxyglucose uptake was conducted, demonstrating PET positivity in the left lower lobe, mediastinum, and right apex, but activity in the liver and retroperitoneal nodes were difficult to interpret. A scintigraphy with octreotide was conducted on Mr. P with a result of diffuse positivity in the mediastinum that was interpreted as being consistent with a carcinoid tumor. A subsequent magnetic resonance image showed no evidence of metastasis to the brain or liver and no evidence of a pancreatic, adrenal, or pituitary neoplasm. This excluded pancreatic endocrine tumor, adrenal gland tumor, pheochromocytoma, and multiple endocrine neoplasia as a diagnosis.

A third pathology examination determined that Mr. P had a carcinoid tumor involving the thymus gland. Based on all pathology reports, the tumor was classified as having features consistent with all three grades of differentiation—well, moderately, and poorly differentiated—indicating that the tumor was heterogeneous with some areas having higher rates of proliferation than others. On pathology review, the Ki-67 protein, a protein marker that is coupled with rates of cell proliferation and has been found to be useful in grading neuroendocrine tumors, was found to be less than 15% in Mr. P, indicating an intermediate grade neuroendocrine tumor.

Carcinoid Tumors

Carcinoid tumors are a type of neuroendocrine tumor. They are indolent in nature and stem from neuroendocrine cells within various organs in the body, with a majority occurring within the gastrointestinal tract (Pinchot, Holen, Sippel, & Chen, 2008). Carcinoid tumors can develop in the small bowel, colon, appendix, rectum, stomach, thymus, bronchus, or the lung. The American Cancer Society (2010) reported that about 11,000–12,000 carcinoid tumors are diagnosed in the United States every year. Incidence rates are double among men older than age 50 and in women younger than age 50 compared to all other age groups, with a higher overall incidence rate among African Americans compared to Caucasians (Zuetenhorst & Taal, 2005). Data have shown that the incidence rates for carcinoid tumors continue to increase. The reason for this increase remains unclear, but it may possibly stem from an aging population and the improvement of available diagnostic tools.

Symptom Presentation and Diagnosis

Neuroendocrine tumors have a slow proliferative rate, but often patients will present with metastatic disease (Zuetenhorst & Taal, 2005). Thymic carcinoid primarily affects men aged 40–60 years. Many patients present with no symptoms, but, when present, they may include chest pain, cough, dyspnea, or superior vena cava syndrome. These symptoms occur because of tumor compression or invasion into neighboring structures that cause symptoms (Parra, Remacha, Costilla, & Caleron, 2002).

Carcinoid tumors can secrete neuropeptides that have been associated with carcinoid syndrome, a syndrome of hormonal excess (Benson, Myerson, & Hoffman, 2007). Clinical features include flushing of the skin, diarrhea with possible abdominal cramping, and cardiac anomalies secondary to elevated levels of serotonin (Kulke et al., 2008) (see Figure 1). Serum levels of serotonin and chromogranin A (a protein found in carcinoid tumors) and 24-hour urine for 5-HIAA are evaluated to diagnose carcinoid syndrome. Elevated levels of chromogranin A have been associated with tumor burden. Urinary 5-HIAA is a byproduct of serotonin breakdown, thus indicative for levels of serotonin. Chromogranin A has a lower specificity than 5-HIAA (86% and 100%, respectively), but has a higher sensitivity than 5-HIAA (68% and 35%, respectively) (Zuetenhorst & Taal, 2005). Carcinoid tumors have somatostatin receptors on their cell membranes; therefore, the use of nuclear scintigraphy with radiolabled octreotide can be used to aid in the diagnosis of carcinoid tumors. Scintigraphy sensitivity has been shown to be between 80%–90%. Not only does this provide a reliable diagnostic tool, it also gives details regarding response to octreotide as therapy (Zuetenhorst & Taal, 2005).

Unique features of Mr. P's case made the diagnosis challenging. Three pathologists interpreted the differentiation grade differently, and it took until the third interpretation before the tumor was correctly identified as thymic carcinoid. If the pathologist had known what the clinical presentation of the patient was, it may have supported interpretation of the tumor as a thymic carcinoid as opposed to a neuroendocrine tumor. Had the third opinion not been sought, the patient might not have been treated with chemotherapy because most carcinoid tumors do not respond to chemotherapy.