Neuroendocrine Cancer

The Rare Cancer that Killed Steve Jobs

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Neuroendocrine cancer is a rare cancer affecting only 125,000 patients in the United States, about five in 100,000 cases are diagnosed in a year. Neuroendocrine cancer is frequently misdiagnosed, and has the unfortunate legacy of originally being known as a benign “cancer-like” disease. Patients can go months, or even years, before receiving a proper diagnosis, resulting in disease spread. Pancreatic neuroendocrine cancer is the same cancer that Apple executive, Steve Jobs, was first diagnosed with in 2003 and eventually succumbed to in 2011.

Neuroendocrine cancer was first named “karzinoide" ("carcinoma-like") in 1907 by Siegfried Oberndorfer, a German doctor who was the first to identify the distinct clinical entities of these tumors, and emphasized their benign nature. In 1929, Oberndorfer amended his original classification to describe that these tumors that formed in the small bowel could be malignant and metastasize.

Etiology

What makes neuroendocrine cancers unlike other forms of cancer is in their very nature. They form in the neuroendocrine system’s glandular endocrine-hormone producing cells that are extensively dispersed throughout the body. The most frequent site of origin for neuroendocrine cancers is in the small intestine, right colon or appendix and are classified as mid-gut. Less frequently they will be found in the foregut, which includes the lung, pancreas, stomach or duodenum. Hindgut involvement is found in the transverse colon, sigmoid colon, or rectum. Very rarely primaries arise from the ovaries, testes, liver, kidneys, bile ducts and other areas throughout the endocrine system. Sometimes the disease can be genetic, but there is no known cause for this cancer.

Since these cancers form in endocrine cells, they can secrete various substances, which are frequently used as markers to measure the disease progression. Almost all neuroendocrine tumors secrete serotonin, bradykinin, and chromogranin-A at varying levels. Other substances these tumors secrete are substance-P, pancreastatin, neurotensin, pancreatic polypeptide, neurokinin-A, motilin as well as other peptide hormones.

Symptoms

Functional neuroendocrine tumors are those which secrete a substance that causes a symptom. Serotonin, the

most common peptide to be secreted by these tumors, causes symptoms such as flushing, diarrhea, and wheezing, which are often diagnosed as Irritable Bowel Syndrome, Crohn's, asthma or even the effects of menopause. These symptoms are known as Carcinoid Syndrome. The diarrhea can be chronic, resulting in weight loss, and the excess serotonin can cause a very specific form of heart valve damage. A severe form of carcinoid syndrome is known as Carcinoid Crisis that can be life threatening. Carcinoid Syndrome (or Crisis) can be triggered by what is known as the five "E's" including 1) epinephrine – from over the counter medications and anesthesia, 2) eating – large meals and certain foods, 3) emotions – stressful situations, 4) exercise – heavy activities, trauma or surgery and 5) ethanol – alcoholic beverages.

Other functional neuroendocrine tumors can secrete insulin, glucagon, vasoactive polypeptide, gastrin, histamines, and somatostatin. From dysregulation of blood sugars, excessive stomach acid, skin rashes, explosive diarrhea, foul smelling, greasy stools, and wheezing, the symptoms can be debilitating, if not life threatening. In the case of pancreatic tumors, they can change and secrete different or various hormones over time.

There are also non-functional neuroendocrine tumors that do not secrete excessive substances, therefore, do not have symptoms. Pancreatic polypeptide and ghrelin are two substances that can be secreted in excess, but neither have a known clinical syndrome, so they are classified as non-functioning.

Treatment

As with most cancers, the first line of defense, if possible, is surgery. If surgery is not possible or is unsuccessful, there are other treatments available to patients. Somatostatin analogues such as octreotide can alleviate some of the side effects of the substances secreted by behaving as a universal "off-switch" for the excess secretions. Data suggests that somatostatin analogue medications may make the tumors less active. There are several forms of chemotherapies, either intravenous or oral medications that can be used, depending on the site of origin or aggressiveness. Finally, there are targeted radiotherapy treatments available in Europe that are currently in trials in the United States that are able to bind to the tumors, but can cause collateral damage to kidneys. The disease is, in many cases, incurable but manageable, but ultimately still deadly for many patients.

Conclusion

Neuroendocrine cancer can be a manageable disease depending on its severity. If a patient is properly diagnosed early in their disease, they can live for many years with intervening treatments. The largest obstacle to diagnosis is awareness, both in the medical community and in the general population. As it is a rare disease, many doctors will never even see a patient and there is little funding for research. Patients may bounce from doctor to doctor trying to obtain a diagnosis. There are dedicated specialists throughout the world and patients frequently have to travel for treatment. Despite the lack of research funds, new treatments are being studied, thanks to the specialists and several pharmaceutical companies. The patient community tends to be highly educated in their illness and there are a number of foundations worldwide dedicated to educating and supporting the patient community.

Since my diagnosis of pancreatic neuroendocrine cancer in 2007, I have learned a lot about this disease. My symptoms began roughly fifteen years prior to my diagnosis, but, was diagnosed with all the common misdiagnoses – IBS, asthma, eczema, and pre-diabetes. I have undergone two major surgeries, done an unsuccessful round with a targeted chemotherapy called Afinitor, and get a shot of a long-acting somatostatin analogue called Sandostatin every four weeks. My disease and well-managed, my scans currently show “no evidence of disease.” I have no symptoms and a good quality of life. My aspiration is that through my experience, I am able to help spread awareness within the medical community, and other patients, who are looking for hope and possibly a diagnosis.

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