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Carcinoid Syndrome (Carcinoid Tumor)

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What is a carcinoid tumor?

A carcinoid tumor is a tumor that develops from enterochromaffin cells. Enterochromaffin cells are hormone-producing cells that normally are found in the small intestine, appendix, colon, rectum, bronchi, pancreas, ovaries, testes, bile ducts, liver, as well as other organs. Enterochromaffin cells produce many types of hormones for example, histamine, serotonin, dopamine, tachykinins, and other substances that have profound effects on the circulatory system (heart and blood vessels), the gastrointestinal tract, and the lungs. For example, serotonin can cause diarrhea, histamine wheezing, and tachykinins flushing due to dilation of blood vessels.

Since carcinoid tumors develop from enterochromaffin cells, they frequently retain the capability of producing the same hormones, often in large quantities. When these hormones circulate in the blood, they can cause symptoms of carcinoid syndrome, which is discussed later.

The important characteristic of carcinoid tumors that sets them apart from other gastrointestinal tract tumors is their potential to cause the carcinoid syndrome. Most other gastrointestinal tract tumors (such as colon cancers or small bowel lymphomas) cause symptoms primarily due to their local effects on the intestines such as abdominal pain, intestinal bleeding, and intestinal obstruction. Although carcinoid tumors may also cause these local symptoms, they may also produce and release hormones that cause the carcinoid syndrome. Often, symptoms of the carcinoid syndrome can be more devastating than the local symptoms.

What is the carcinoid syndrome?

The carcinoid syndrome is a combination of symptoms caused by the hormones released by the tumors into the blood stream. The symptoms of the carcinoid syndrome vary depending on which hormones are released by the tumors. The common hormones released are serotonin, bradykinin (a molecule produced by enzymes at the site of an injury and then binds to receptors to cause pain), histamine, and chromogranin A (a general marker for neuroendocrine tumors). Typical carcinoid symptoms include:

- flushing
- diarrhea
- abdominal pain
- and wheezing due to bronchospasm (airway narrowing)
- valvular heart disease
- surgery can provoke a complication known as carcinoid crisis.

Flushing

Flushing is the most common symptom of carcinoid syndrome. An estimated 90% of the patients have flushing some time during their illness. Flushing is characterized by redness or purple discoloration of face and neck (or upper body) accompanied by a warm sensation. Episodes of flushing typically occur suddenly, either spontaneously or brought on by emotional stress, physical stress, or drinking alcohol. Episodes of flushing can last minutes to hours. Flushing can be accompanied by palpitations, low blood pressure, or fainting if blood pressure becomes too low to supply blood to the brain. Rarely, flushing can be accompanied by high blood pressure. Hormones responsible for flushing have not been clearly identified; possible candidates include serotonin, bradykinin, and substance P.

Diarrhea

Diarrhea is the second most common symptom of carcinoid syndrome. An estimated 75% of patients with carcinoid syndrome have diarrhea. Diarrhea often occurs with flushing but also can occur alone. Diarrhea in the carcinoid syndrome is most likely caused by the hormone serotonin. Medications that block the action of serotonin such as ondansetron (Zofran) often alleviates the diarrhea. Sometimes diarrhea in the carcinoid syndrome can be due to a local effect of the tumor obstructing the small intestine.

Heart disease

Heart disease occurs in an estimated 50% of patients with the carcinoid syndrome. Carcinoid syndrome typically causes scarring and stiffness of the tricuspid and pulmonic valves of the right side of the heart. Stiffness of these two valves decreases the ability of the heart to pump blood from the right ventricle to the lungs and to the rest of the body and leads to heart failure. Typical symptoms of heart failure include an enlarged liver (due to the backup of blood returning to the failing heart which is unable to pump all of the blood returning to it), swelling of the feet and ankles (edema), and swelling of the abdomen due to fluid accumulation (ascites). The damage to the tricuspid and pulmonic valves of the heart in the carcinoid syndrome is most likely caused by prolonged exposure to high levels of serotonin in the blood.

Carcinoid crisis

Carcinoid crisis is a dangerous condition that can occur at the time of surgery. It is characterized by a sudden and profound drop in blood pressure causing shock, sometimes accompanied by an abnormally fast heart rate, high blood glucose, and severe bronchospasm. Carcinoid crisis can be fatal. The best way to prevent carcinoid crisis is to treat patients undergoing surgery with somatostatin (see below) before surgery begins.

Wheezing

Wheezing occurs in approximately 10% of the patients with carcinoid syndrome. It is a result of bronchospasm (constriction of the bronchial airways) caused by hormones released by the carcinoid tumors.

Abdominal pain

Abdominal pain is common in patients with carcinoid syndrome. The pain may be due to tumor metastases in the liver, tumor invading neighboring tissues and organs, or tumor causing bowel obstruction (please see small bowel carcinoid tumors below).

How common are carcinoid tumors and carcinoid syndrome?

The prevalence of carcinoid tumors is difficult to determine since many carcinoid tumors are not detected because they produce no symptoms. In one autopsy series, carcinoid tumors were estimated to have a prevalence of 8/100,000 people annually, but 90% of the carcinoids found at autopsy were not the cause of death.

The carcinoid syndrome is very rare. This is because many carcinoid tumors do not produce hormones. Another reason that the syndrome is rare is that hormones released by carcinoid tumors, particularly from tumors within the abdomen, often are destroyed by the liver before they reach the general circulation to cause symptoms. For example, hormones produced by small intestinal carcinoid tumors are released into the portal vein. The portal vein blood passes through the liver before reaching the heart and the general circulation. As the portal vein blood passes through the liver, the hormones are destroyed by the liver.

Only those carcinoid tumors that can release hormones directly into the general circulation (and not into the portal veins which pass through the liver) can produce the carcinoid syndrome. Thus, the most common cause of carcinoid syndrome is small intestinal carcinoid tumors that have metastasized to the liver. The metastases in the liver can release hormones directly into the circulation. Another rare example is carcinoid tumors of the bronchial airways. Carcinoid tumors in the bronchial airways can release hormones directly into the general circulation via the pulmonary veins without passing through the liver.

What is the prognosis and natural history of carcinoid tumors?

Carcinoid tumors can be benign (non-cancerous) or malignant (cancerous). Benign carcinoid tumors are typically small (less than 1 cm). They usually can be removed completely and, in most cases, they do not come back. Cells from benign carcinoid tumors do not spread to other parts of the body. Benign carcinoid tumors typically produce no symptoms and are commonly found by chance during flexible sigmoidoscopy or upper gastrointestinal endoscopy.

Cancerous carcinoid tumors are typically large (larger than 2 cm) at the time of diagnosis. Cells from these malignant tumors can invade and damage tissues and organs near the tumor. Moreover, malignant cells can break away and enter the bloodstream or lymphatic system and spread to form new tumors in other parts of the body. (The distant tumors are called metastases.) Common sites for carcinoid metastases include the lymph nodes, liver, lung, bone, and skin.

Carcinoid tumors between 1.0 and 2.0 cm in size have approximately a 10% chance of being cancerous at the time of diagnosis.

Carcinoid tumors are typically slow growing. They grow much more slowly than other cancers such as colon, pancreas, liver, and lung cancer. Many small carcinoid tumors produce no symptoms and are not fatal; they are found incidentally at autopsy. Even patients with larger, malignant carcinoid tumors (with or without metastasis) can survive years or decades with a good quality of life. This is especially true with modern treatments to control the carcinoid syndrome and to control the growth of the carcinoid tumors. However, there is a rare form of carcinoid tumor called adenocarcinoids that are more aggressive than the typical malignant carcinoid tumor, and they have a poor prognosis. An experienced pathologist can identify adenocarcinoid tumors by examining the tissue from the tumor under a microscope.

Where do carcinoid tumors occur?

Carcinoid tumors can be found wherever there are enterochromaffin cells, essentially, throughout the body. The majority (65%) of carcinoid tumors are found in the gastrointestinal tract. The origin of gastrointestinal carcinoid tumors is most commonly the small intestine, appendix, and rectum. Less common origins are the stomach and colon; and the least common origins are the pancreas, gallbladder, and liver (though carcinoid tumors in the liver usually are metastasis from elsewhere).

Approximately 25% of carcinoid tumors are found in the bronchial airways and the lung. The remaining 10% can be found almost anywhere. In some cases, doctors cannot locate the site of origin of the carcinoid tumors, though they know by the symptoms of the carcinoid syndrome that they are present.

Small intestinal carcinoid tumors

In general, small intestinal tumors (whether benign or cancerous) are rare, much more rare than colon or stomach cancers. Nevertheless, carcinoid tumors comprise one third of all small intestinal tumors, and are most commonly found in the ileum (the lower part of the small intestine close to the colon). Small intestinal carcinoid tumors typically produce no symptoms or produce only vague abdominal pain. Therefore, it is difficult to detect carcinoid tumors of the small intestine early, while they still can be completely removed and the patient cured. The few small carcinoid tumors that are found early usually are found incidentally when x-rays or procedures are performed for other purposes. Typically, small intestinal carcinoid tumors are diagnosed late, often years after the onset of symptoms and usually after local and distant metastases already are present.

Approximately 10% of small intestinal carcinoids cause the carcinoid syndrome. Presence of the carcinoid syndrome usually means that the tumor is malignant and has spread to the liver.

Small intestinal carcinoid tumors often obstruct the small intestine when they reach a large size. Symptoms of small bowel obstruction include crampy abdominal pain, nausea and vomiting, and sometimes diarrhea. Obstruction can be caused by two different mechanisms. The first mechanism is by enlargement and growth of the tumor into the lumen (channel) within the small intestine. The second mechanism is by kinking of the small intestine due to fibrosing mesenteritis, a condition caused by the tumor in which extensive scarring occurs in the tissue surrounding the small intestine. Fibrosing mesenteritis sometimes obstructs the arteries supplying blood to the intestines, resulting in death of a portion of the intestine (gangrene). The gangrenous intestine can rupture and be life-threatening.

Appendiceal carcinoid tumors

While tumors of the appendix are rare, carcinoid tumors are the most common tumor of the appendix, comprising approximately half of all appendiceal tumors. In fact, carcinoid tumors are found in 0.3% of resected (removed) appendices, but most of them are smaller than 1 cm and do not cause symptoms. They are found mostly in appendices removed for unrelated reasons. Most authorities believe that appendectomy is adequate treatment for these small appendiceal carcinoid tumors. The chances that a tumor would recur after appendectomy are very low. Appendiceal carcinoid tumors larger than 2 cm at the time of diagnosis have approximately a 30% chance of being malignant and having local metastases. Thus, larger appendiceal carcinoid tumors need more extensive surgery such as removal of the right colon rather than simple appendectomy. Fortunately, large appendiceal carcinoid tumors are rare. Carcinoid tumors limited to the appendix, even metastatic to local tissues, usually do no cause the carcinoid syndrome.

Rectal carcinoid tumors

Rectal carcinoid tumors are often discovered incidentally at the time of flexible sigmoidoscopy or colonoscopy. Carcinoid syndrome is rare with rectal carcinoid tumors. The probability of having metastases (malignant carcinoid) correlates with the size of the tumor; those larger than 2 cm have a 60-80% chance of having metastases, and those smaller than 1 cm have less than a 2 % chance of having metastases. Therefore, small rectal carcinoid tumors usually can be successfully removed by simple excision, but the larger tumors (larger than 2 cm) need more extensive surgery that may involve removal of part of the rectum.

Gastric (stomach) carcinoid tumors

There are three types of gastric (stomach) carcinoid tumors; types I, II, and III.

Type I gastric carcinoid tumors, which account for 75% of gastric carcinoids, are typically smaller than 1 cm and usually are benign. There can be multiple tumors scattered throughout the body of the stomach. They typically develop in patients with pernicious anemia or chronic atrophic gastritis, conditions in which the stomach stops producing acid. The lack of acid causes the cells in the stomach that produce the hormone gastrin to secrete large amounts of gastrin into the blood. (Gastrin is a hormone normally produced by the body to stimulate stomach acid. Acid in the stomach shuts off the production of gastrin. In pernicious anemia or chronic atrophic gastritis, the lack of acid results in the production of increasing amounts of gastrin.) Gastrin, in addition to stimulating acid, also stimulates the growth of enterochromaffin cells in the stomach into benign carcinoid tumors. Treatment of type I carcinoid tumors include medications such as the somatostatin-type drugs which shut off production of gastrin or surgical removal of the gastrin producing part of the stomach.

Type II gastric carcinoid tumors are extremely rare and are very slow growing with a low probability of becoming malignant. They occur in patients with a rare genetic disorder called MEN (multiple endocrine neoplasia) type I. These patients have tumors in other endocrine glands such as the pituitary gland, parathyroid gland, and the pancreas.

Type III gastric carcinoid tumors tend to be larger than 3 cm and tend to be sporadic (occurring one or two at a time) in otherwise normal stomach (without the presence of pernicious anemia or chronic atrophic gastritis). Type III tumors usually are malignant and tend to invade deep into the stomach wall and metastasize. Type III tumors can cause local symptoms of abdominal pain and bleeding, as well as symptoms due to carcinoid syndrome. Type III gastric carcinoids usually require surgical removal of the stomach as well as the surrounding lymph nodes.

Colonic carcinoid tumors

Colonic carcinoid tumors typically occur in the right colon (ascending colon and right half of the transverse colon). Like small bowel carcinoid tumors, colonic carcinoid tumors are often discovered late. Thus, the average size of the tumors at the time of diagnosis is 5 cm, and metastases are present in two thirds of patients. Carcinoid syndrome is rare with colonic carcinoid tumors.

How are carcinoid tumors and carcinoid syndrome diagnosed?

There are several aspects to the diagnosis of carcinoid tumors:

- Diagnosing the primary carcinoid tumor (the original tumor)
- Diagnosing the carcinoid syndrome
- Diagnosing local tumor metastasis (such as in the lymph nodes adjacent to the primary tumor) and distant metastasis (such as in the liver, bone, and skin)

Diagnosis of carcinoid tumors

In clinical practice, the diagnosis of carcinoid tumor is most commonly made incidentally when tests and procedures are performed for other purposes. For example, carcinoid tumors in the rectum and colon are incidentally found during colonoscopy performed for colon cancer screening, for iron deficiency anemia, or for chronic diarrhea. Carcinoid tumors of the appendix are found when appendectomies are performed for symptoms of appendicitis. Gastric carcinoid tumors are incidentally discovered when upper gastrointestinal endoscopies are performed for symptoms of ulcer, dyspepsia, abdominal pain, or anemia. If these incidentally-found carcinoid tumors are less than 1 cm in size, the prognosis is good because most of them have not metastasized, and can be cured by complete excision.

Barium small intestinal study. Finding primary small bowel carcinoid tumors early before they become malignant and metastasize is difficult. Small bowel tumors (carcinoid tumors included) are difficult to diagnose because the traditional barium small intestinal x-rays are usually not accurate in detecting small intestinal tumors that are not yet obstructing the intestine. Furthermore, most of the small intestine cannot be reached by either the upper endoscope or the colonoscope. Therefore, small intestinal carcinoid tumors are often diagnosed late, often after liver metastases or carcinoid syndrome has occurred.

The diagnosis of small intestinal tumors becomes easier when tumors cause small bowel obstruction either by its large size, or by causing scarring around the intestine (fibrosing mesenteritis) which leads to kinking of the small intestine (as discussed previously). Simple x-rays of the abdomen and barium small intestinal studies both can demonstrate small intestinal obstruction, and computerized axial tomography CT scan of the abdomen can demonstrate the extensive scarring of fibrosing mesenteritis. Sometimes, the carcinoid tumor is found at the time of surgery performed to relieve the small intestinal obstruction.

Capsule enteroscopy. In the past several years, capsule enteroscopy has become available. Capsule enteroscopy is a novel technology in which a small capsule is swallowed that contains a camera and a source of light. Thousands of images are obtained by the capsule as it tumbles through the small intestinal, and these images are transmitted to a receiver worn around a patient’s waist. Many small intestinal diseases (ulcers, cancers, lymphomas, bleeding blood vessels, as well as carcinoid tumors) have been discovered by capsule enteroscopy. It is this author’s belief that more and more small intestinal carcinoid tumors will be discovered early as capsule enteroscopy becomes more widely used.

Sometimes primary carcinoid tumors of the small intestine or colon can be diagnosed by nuclear medicine octreotide scanning or by CAT scan of the abdomen, but more commonly, these scans are more useful in detecting metastases from carcinoid tumors. (See below.)

Diagnosis of carcinoid syndrome

One way to diagnose carcinoid tumors is by diagnosing the carcinoid syndrome first, and then by searching for the primary carcinoid tumor and its metastases. In patients with episodic attacks of flushing, diarrhea, and sometimes wheezing, the diagnosis of carcinoid syndrome can be confirmed by measuring the excretion of 5-hydroxyindolacetic acid (5-HIAA) in urine collected over a 24 hour period.

Urine for 5-HIAA. In normal, healthy individuals, a majority of the amino acid tryptophan from the diet is converted in the body to nicotinic acid. Carcinoid tumors that cause the carcinoid syndrome, convert most of the tryptophan to serotonin and 5-HIAA. Normal individuals typically excrete less than 8 mg of 5-HIAA in 24 hours. Patients with the carcinoid syndrome can excrete between 100-2000 mg of 5-HIAA in 24 hours. When the

urine samples are properly collected and tests properly performed, abnormally elevated urinary 5-HIAA provide an accurate diagnosis of carcinoid syndrome and should initiate efforts to search for the carcinoid tumors and its metastases.

Certain foods and medications can interfere with the accuracy of measurements of 5-HIAA in the urine by either falsely increasing or decreasing the 5-HIAA values. These medications and foods should be avoided for 2 days before and the day of urine collection.

Foods that falsely elevate 5-HIAA values include avocados, pineapples, bananas, kiwi, plums, egg plant, walnuts, hickory nuts, and pecans. Medications that falsely elevate 5-HIAA values include (acetaminophen) Tylenol, Robitussin, Phenobarbital, Ephedrine, Nicotine, fluorouracil (Carac, Efudex, Fluoroplex) , and mesalamine (Asacol, Pentasa, and Colazal).

Medications that can falsely lower 5-HIAA values include aspirin, heparin, alcohol, methyldopa, imipramine, isoniazid, levodopa, phenothiazines, and MAO inhibitors.

Chromogranin A. Chromogranin A is a protein produced by carcinoid tumors. It is not as widely used as urinary 5-HIAA for diagnosing the carcinoid syndrome, but it is used by doctors for predicting prognosis. Thus, the blood levels of chromogranin A correlates with the amount of tumor in the body (also known as the tumor burden). Patients with very high chromogranin A levels have worse survival than those with lower levels.

Diagnosing carcinoid tumor metastasis

CT and MRI scans. CT and MRI (magnetic resonance imaging) scans are commonly used in the evaluation of abdominal pain, weight loss, abnormal liver tests, and other symptoms. When liver tumors or abnormal lymph nodes are found on these scans, needles can be inserted into the tumors or nodes to obtain tissue for diagnosis. If adequate amounts of tissue are obtained, an experienced pathologist can diagnose carcinoid tumors by examining the tissue under a microscope. Unfortunately, tumors found by CT and MRI scans most often represent metastases, with liver metastases being the most common. CT and MRI scans are not useful for detecting primary carcinoid tumors in the small intestine or the colon when they are still small and resectable.

Indium 111 octreotide scans. Carcinoid tumor cells, like all other cells, have membranes that surround their contents. The cells of approximately 90% of carcinoid tumors have membranes covered with receptors for a hormone called somatostatin. Somatostatin binds to these receptors. Octreotide is a chemical made to resemble somatostatin, and therefore also binds to the receptors. When radioactive indium 111-labeled octreotide is injected into a patient's vein, the radioactive octreotide will bind to the membrane of carcinoid tumors. When the patient then is placed under a nuclear camera, the carcinoid tumors will appear as bright spots on the scan. This octreotide scan is very accurate (more accurate than CT and MRI scans) in detecting liver and other metastases of carcinoid tumors and is also more accurate than CT scans and MRI scans for detecting primary carcinoid tumors. Patients who have carcinoid tumors that appear on octreotide scans also are more likely to respond to treatment with octreotide. (See below.) Sometimes, additional carcinoid tumors are found in the liver and lymph nodes with the octreotide scan that are not seen by CT scan.

Indium111-octreotide scans have limitations. The rate of detection of primary carcinoid tumors by the octreotide scan is still only 60%. Scans usually cannot detect primary carcinoid tumors smaller than 1 cm. Scans also cannot detect carcinoid tumors that do not have somatostatin receptors or have receptors that do not bind octreotide. There are two other nuclear scans (PET scans and radioactive MIBG scan) that can be used in conjunction with the octreotide scan that may improve accuracy, but experience with these two scans are limited.

In practice, CT, MRI, and octreotide scans often are used in combination to detect carcinoid tumors, often with accuracy rates approaching 90%. Accurately identifying all of the sites of the carcinoid tumor has important implications for treatment. For example, if only liver metastases are found, the patient potentially can be treated by surgical resection of both the primary tumor and the liver metastasis. If carcinoid tumor metastases are found in the liver as well as other organs, then the patient will not be a good surgical candidate.

Bone scan. In approximately 10% of patients with carcinoid tumors the tumor metastasizes to the bones and can cause bone pain. Bone scans using radioactive phosphate are accurate for detecting these bony metastases.

How are carcinoid tumors and carcinoid syndrome treated?

There are many options for the treatment of carcinoid tumors:

- observation
- surgery
- cryotherapy, radiofrequency ablation, hepatic artery embolization
- interferon and chemotherapy
- radiation therapy
- medications for the control of the carcinoid syndrome

Since carcinoid tumors vary widely in their size, malignant potential, prognosis, extent of metastasis, and symptoms, treatment should be customized for each individual. Because the carcinoid syndrome and metastatic carcinoid tumors are rare and their treatments are complex, many patients should be treated by a team of doctors--gastroenterologists, oncologists, radiologists, cardiologists, and surgeons--in medical centers experienced and equipped to treat carcinoid tumors.

Observation

Some patients with unresectable carcinoid tumors may have neither local symptoms nor the carcinoid syndrome. These patients can be observed without surgery or medications because carcinoid tumors are slow growing, and the patients may not develop symptoms for a prolonged period of time.

Surgery

Surgery is used for 1) curative resection, 2) relief of symptoms such as small intestinal obstruction or intestinal bleeding, and 3) reducing the size of tumors that are not completely resectable, a process called tumor debulking, to decrease the tumor burden and decrease the amount of hormone produced by the tumors.

Small rectal carcinoid tumors usually are benign and often can be completely excised for cure. Type 1 gastric carcinoid tumors also usually are benign and often can be removed for cure. Small appendiceal carcinoid tumors usually are removed and cured at the time of appendectomy.

Carcinoid tumors of the small intestine and the colon often are large and have already metastasized at the time of diagnosis. Most patients with metastases are not candidates for surgical cure because surgery cannot completely remove the entire tumor. Occasionally, a patient may have a solitary metastasis confined to a portion of the liver. Such patients can be treated with surgical resection of the primary tumor and resection of that part of the liver containing the tumor (partial hepatectomy). There are a limited number of patients with multiple metastases that are confined to the liver. Partial hepatectomy cannot be performed in these patients because of the multiple locations of the tumors. A small number of these patients have been treated successfully with liver

transplantation.

Cryotherapy, radiofrequency ablation, hepatic artery embolization

Cryotherapy, radiofrequency ablation , and hepatic artery embolization all are techniques for debulking unresectable tumors (mainly liver metastasis) in order to decrease tumor burden and to treat the carcinoid syndrome. Effective debulking can improve the carcinoid syndrome and also prolong survival. Probes that freeze (cryotherapy) or deliver radiofrequency waves (RF ablation) can be inserted into the liver to debulk the liver of metastases from carcinoid tumors. Hepatic artery embolization involves blocking the arterial blood supply to carcinoid tumors (using oil-gelatin sponge particles) in the liver followed by chemotherapy to debulk the remaining the liver tumors. Alternatively, radioactive microspheres can be injected into hepatic arteries to kill the liver tumors.

Interferon and chemotherapy

Interferon is a substance that inhibits the replication of some viruses and the growth of some tumors. Interferon has been used to treat patients with chronic hepatitis B and C. Interferon also has been found to arrest the growth of carcinoid tumors in some patients. Interferon has significant side effects, however.

Chemotherapy has been used alone or in combinations with other therapies to treat carcinoid tumors with metastases. The agents used include 5-fluorouracil (5-FU), cyclophosphamide, streptozotocin, and doxorubicin. The tumors do not frequently respond to treatment (a response is seen in under 30% of tumors), and the duration of response usually is only a few months. The side effects and toxicity of chemotherapy can be high.

Radiation therapy

External radiation has been used to alleviate pain due to the presence of metastases from carcinoid tumors in the spine. It also may reduce the size of the tumor in the spine. External radiation usually is not effective in treating tumors within the liver.

Medications for the control of the carcinoid syndrome

The most important treatment modality for the carcinoid syndrome is octreotide, a synthetic hormone similar in structure to the naturally-occurring hormone, somatostatin. Somatostatin is widely distributed in the body where it can inhibit the secretion of many other hormones including growth hormone, insulin, and gastrin. It exerts its action by binding to specific receptors on the membranes of cells that produce and release hormones and chemical substances. Octreotide, like somatostatin, binds to receptors on the cells of carcinoid tumors and inhibits the manufacture and release of tumor hormones. Octreotide is very effective in controlling the symptoms of flushing and diarrhea that are part of the carcinoid syndrome. Octreotide has been found to reduce the excretion of 5-HIAA in some patients. Octreotide also has been found to slow the growth of carcinoid tumors, and, in a few patients, even reduce the size of the tumors and their metastases. Treatment with octreotide prior to surgery is important in order to prevent life-threatening carcinoid crisis in patients with carcinoid syndrome undergoing surgery. Some doctors are advocating using octreotide even in patients without carcinoid syndrome to control the growth of the carcinoid tumors.

Octreotide generally is well tolerated. Side effects include nausea, headache, dizziness, abdominal pain, diarrhea, elevated blood sugar levels, and gallstones. The major drawback of octreotide is the need to inject it under the skin three times daily. Other longer-acting synthetic hormones resembling somatostatin (for example, lanreotide) can be given intramuscularly every two weeks, but they are not yet available in the U. S.

Patients with carcinoid syndrome should take vitamin supplements, especially nicotinic acid, since carcinoid tumors can cause a deficiency of nicotinic acid. In some patients, diarrhea caused by the carcinoid syndrome may respond to Imodium, Lomotil, ondansetron (Zofran), or cyproheptadine (Periactin). Patients also should avoid alcohol, spicy foods, physical stress, and ephedrine-containing medications such as nasal decongestants in order to avoid the precipitation of carcinoid syndrome by the release of hormones and chemical substances from the tumor. Patients with chronic diarrhea should take minerals supplements as well as vitamins since any cause of chronic diarrhea can lead to deficiencies of minerals.

Carcinoid Syndrome and Carcinoid Tumors at a Glance

- Carcinoid tumors are rare tumors that develop from hormone-producing cells called enterochromaffin cells that occur throughout the body with approximately 65% originating in the gastrointestinal tract and 25% in the lungs.
- Carcinoid tumors can occur almost anywhere in the gastrointestinal tract but primarily in the stomach, small intestine, appendix, colon, and rectum.
- Carcinoid tumors can be benign or malignant.
- The carcinoid syndrome is a syndrome that is caused by the release of hormones from carcinoid tumors, but only 10% of carcinoid tumors cause the carcinoid syndrome.
- The carcinoid syndrome may include manifestations such as abdominal pain, wheezing, facial flushing, diarrhea, heart disease, and “carcinoid crisis.”
- arcinoid tumors can be diagnosed by endoscopy, barium small intestinal x-ray studies, and by capsule enteroscopy.
- Metastatic carcinoid tumors can be diagnosed by CT or MRI scans, indium 111 octreotide scans, and bone scans.
- Carcinoid tumors can be managed with observation, surgery, cryotherapy, radiofrequency ablation, hepatic artery embolization, interferon therapy, chemotherapy, and radiation therapy.
- he carcinoid syndrome can be controlled with medication.

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