

# Carcinoid Syndrome

Carcinoid Tumors are GI endocrine tumors that synthesize, store, and release a variety of polypeptides, biogenic amines, and prostaglandins. Although rare (1-2 per 100,000), carcinoid is the most common GI endocrine tumour. Approximate 2-5% of these patients will exhibit carcinoid syndrome, the hallmark of which is flushing with diarrhea, hemodynamic instability +/- bronchospasm. Carcinoid heart disease is present in 20-40% patients with carcinoid tumours.

## ANESTHETIC CONSIDERATIONS:

- Concerns of malignancy:
  - 4 Ms: mass, medications, metastatic conditions, metabolic.
- Determine presence of carcinoid syndrome:
  - **Airway:**
    - Obstruction secondary to airway or bronchial tumours
  - **Respiratory:**
    - risk of bronchospasm (rare in patients with normal pulmonary function, higher risk in asthmatics)
  - **CVS:**
    - carcinoid heart disease (20-40%)
    - tricuspid regurgitation - avoid increased PVR
    - pulmonic stenosis
    - typically R sided heart lesions because the lung inactivates humoral substances prior to reaching the L heart
    - hemodynamic instability (secondary to release of vasoactive substances – histamine, prostaglandins, etc.)
  - **GI**
    - Diarrhea (associated hypovolemia and electrolyte abnormalities)
- **Other:**
  - Hypoproteinemia, possibly altered drug pharmacology
  - Pellagra (niacin deficiency)
  - Prevent/manage perioperative carcinoid crisis
  - Avoid sympathetic stimulation (pain, exogenous catecholamines, stress response) due to increased hormone release from tumor.
  - Avoid 5HT, histamine and catecholamine-releasing drugs
  - Premedicate with anxiolytics and octreotide
  - Evaluate presence of coexisting diseases (10% also have MEN-1)

## ANESTHETIC GOALS:

- Avoid perioperative carcinoid crisis by preventing sympathetic surges
  - Avoid:
    - sympathomimetics
    - 5HT releasing agents
    - pain
    - hypercarbia
    - acidosis
    - hypovolemia
- Perioperative administration of octreotide to prevent vasoactive mediator release

## HISTORY

- **\*\* Determine the local effects of the tumor, the extent of multisystem disease and to decide if this is an “active” tumor with carcinoid symptoms\*\***
- Carcinoid symptoms =
  - Episodic cutaneous flushing often with predictable triggers such as stress, eating, BM, alcohol consumption = most common presentation
  - Hypertensive headache
  - Syncope with flushing
  - Palpitations
  - Lacrimation
  - Nausea / vomiting, episodic watery diarrhea, chronic abdominal pain
  - Episodic asthma poorly responsive to medications
- Local tumor effects =
  - Endobronchial tumor with obstructive symptoms +/- focal wheeze
  - GI obstructive symptoms, abdominal pain, GI bleeding
- Carcinoid heart disease =
  - Palpitations, pedal edema, ascites
  - Investigations
- Treatment
  - Medications – octreotide available as IM once-monthly slow-release preparation
  - Previous de-bulking surgery ? Complications ?
  - Heart failure management – medications (often loop diuretics + digoxin), fluid + salt restriction

## PHYSICAL

- **VITALS** - may see histamine-induced hypotension and vasodilatation or serotonin-induced hypertension
- **HEENT** - airway or endobronchial tumor with obstruction
- **RESP** - bronchospasm, wheeze, focal wheeze if airway obstructing lesion
- **CVS**
  - Assess adequacy of fluid balance – can be hypovolemic due to chronic vasoconstriction and diarrhea
  - Assess right-sided valvular status
    - Tricuspid regurgitation: elevated JVP with prominent V wave, RV heave and S3 gallop, pansystolic murmur along lower left sternal border (louder with inspiration), Afib, ascites, edema, hepatomegaly



- Consider octreotide 50 mcg/h IV infusion to prevent mediator release
- **Emergence**
  - Good pain control essential
  - Ondansetron – as antiemetic and 5-HT blocker
  - May experience delayed emergence from elevated serotonin levels
  - Octreotide management depends on presence / absence of residual tumor – consult endocrinology for octreotide management (usually some tumor is left and if patient was on octreotide preoperatively, it is maintained postoperatively)
    - If discontinuing perioperative octreotide infusion, do so gradually

#### DISPOSITION & MONITORING

- Observation in ICU/obs unit postoperatively

#### COMPLICATIONS

- **Carcinoid crisis** – may occur at any point perioperatively
  - Typically, occurs with surgical tumor manipulation, sympathetic stimulation or secondary to drugs that cause histamine or catecholamine release
  - Symptoms:
    - Hypotension
    - Wheezing/bronchospasm
    - Diarrhea
    - Flushing
  - Immediately inform surgeon to stop
  - Administer 100% oxygen
  - Discontinue anesthetic if hypotension present
  - Restore intravascular volume, administer phenylephrine
  - Administer drugs that decrease mediator release or effect:
    - First line = Octreotide 25-100 mcg IV (up to 1000 mcg boluses, repeat PRN) – controls flushing, hypotension, wheeze, diarrhea in 75% cases
    - Other drugs used =
      - Histamine blockers (H<sub>1</sub> and H<sub>2</sub>)
      - Aprotinin (kallikrein inhibitor)
      - Ondansetron (may limit serotonin symptoms and is the antiemetic of choice in these patients)
  - Bronchospasm
    - Usually responds to octreotide
    - β<sub>2</sub>-agonists, theophylline, epinephrine may exacerbate it
    - Corticosteroids, inhaled ipratropium bromide and antihistamines may be safely used

#### PATHOPHYSIOLOGY

- Incidence of clinically diagnosed cases = 1-2/100,000 (higher at autopsy)
- Usually presents in 5-7<sup>th</sup> decade of life
- Carcinoid tumors are neuroendocrine tumors which secrete proteins and monoamines
  - Serotonin is the most common mediator released
  - Others are histamine, bradykinin, kalikrein, substance P, prostaglandins, gastrin, corticotropin, neurokinin
- 70-90% of tumors are found in the GI tract, the rest are in bronchi, breast, ovaries
- Metastatic lesions almost always go to the liver
- Carcinoid syndrome is seen in 2-5% patients with carcinoid tumor
- Higher incidence of carcinoid syndrome is seen with extra-GI tumors or liver mets (GI tumours release vasoactive mediators into the portal venous circulation and they are metabolized by the liver before they reach systemic circulation)
- Carcinoid heart disease = high levels of circulating serotonin causes myocardial fibrosis which affects the right side of the heart (TR, PS, plaques in vena cava, coronary sinus and PA) and may result in right heart failure
  - Vasoactive mediators are inactivated by metabolism in the lungs so left-sided involvement is rare
- Tryptophan (essential amino acid) stores are depleted in the production of serotonin, so proteins and niacin synthesis is impaired = hypoproteinemia (hypoalbuminemia) and pellagra (dermatitis, diarrhea, dementia from niacin deficiency)
- Tumors are treated with surgery (limited response to chemo, resistant to radiation)
- 10-20% patients with carcinoid have another coexisting malignancy
- 10% of carcinoid tumors are associated with MEN-1 (parathyroid, pancreatic, pituitary)
- Common scenarios = OR for tumor de-bulking, relief of intestinal obstruction, “appendicitis”, liver resection or transplant, heart valve replacement, thoracic surgery for lung or bronchial carcinoid resection
  - Occasionally, patients are undergoing surgery unrelated to their disease and carcinoid tumor is diagnosed based on intraoperative carcinoid crisis in previously undiagnosed patient
- Hepatic tumours may be treated with hepatic artery embolization in the radiology suite – same anesthetic considerations and management as if they were an open resection plus: abdominal pain, fever, N / V +/- liver dysfunction post-procedure
- Patients at highest risk of perioperative complications are those with carcinoid heart disease and high urine levels of 5-hydroxyindoleacetic acid (5-HIAA – metabolite of serotonin)
  - These complications are greatly reduced if octreotide used
  - Octreotide acetate = long-acting somatostatin analogue
    - It inhibits serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin and pancreatic polypeptide release
    - Acute administration has no significant side effects
    - It can be given IV, SC or IM

#### REFERENCES

- Faust. Anesthesiology Review.  
Fox D et al. Carcinoid heart disease: presentation, diagnosis and management. Heart 2004; 90: 1224-8.  
Graham et al. Perioperative management of selected endocrine disorders. Int Anesth Clinics 2000; (38): 31-63.  
Kinney M et al. Perioperative risks and outcomes of abdominal surgery for metastatic carcinoid tumours. BJA 2001; 87(3): 447-52.  
Miller 7<sup>th</sup> Edition Chapter 35; UpToDate: Clinical Features of the Carcinoid Syndrome