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Original Contribution

Anesthetic management of patients undergoing resection of carcinoid metastasis to the brain☆

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Abstract

Background: Carcinoid tumors are derived from enterochromaffin cells and may release physiologically active compounds into the systemic circulation, leading to the development of carcinoid syndrome. Occasionally, these tumors metastasize to the brain, warranting biopsy or resection. In these surgical patients, the perioperative implications for anesthetic management are not heretofore defined in the indexed literature.

Methods: Patients who had craniotomy for biopsy or resection of intracranial carcinoid tumors were retrospectively identified at a single medical center. Patient demographics, perioperative anesthetic management, adverse events, and outcome were summarized in this case series.

Results: Eleven patients were identified; median age was 60 years (range = 42-78 years), and 45% were male. Immediately before surgery, 4 patients (36%) were receiving a somatostatin analog drug, and no patient had unchecked carcinoid syndrome. All patients received general anesthesia that included inhaled isoflurane and nitrous oxide, and all had invasive arterial blood pressure monitoring. One patient developed sustained hypotension after induction of anesthesia, likely related to hypovolemia and anesthetic drugs, but the possibility of carcinoid mediator release cannot be excluded. There were no other signs or symptoms of carcinoid syndrome in this or any other patient. Of all 11 patients, 10 (91%) experienced either significant disease progression (n = 2; 18%) or death (n = 8; 73%) from carcinoid disease, its sequelae, or an undetermined cause within 3 years after surgery. Of note, 3 of the deaths occurred shortly after surgery, on postoperative days 3, 7, and 8.

Conclusions: In our experience, carcinoid tumor metastasis to the brain—whether because of tumor makeup or prior treatment—is unlikely to produce symptoms of new-onset carcinoid syndrome intraoperatively; however, the risk cannot be completely excluded. Postsurgical prognosis was poor, both within the hospital and after hospital discharge.

1. Introduction

Carcinoid tumors originate from enterochromaffin cells and can be found in any tissue derived from the endoderm, with most arising in the gastrointestinal tract or lung. They

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account for fewer than 5% of all malignancies [1–3]. Although some carcinoid tumors are solitary, they often metastasize to lymph nodes, liver, lung, peritoneum, and pancreas [1]. The incidence of central nervous system metastases is rare and ranges from 1.5% to 5% of all metastatic carcinoid tumors [2,4]. Because of the rarity of central nervous system metastases, there are no firm guidelines on treatment. Surgical removal may be used in an attempt to lessen mass-associated neurologic symptoms and mortality [2,4,5].

In approximately 10% of patients who have carcinoid tumors, the neuroendocrine cells synthesize a variety of bioactive compounds that, when released into the systemic circulation, can lead to a constellation of physiologic effects known as *carcinoid syndrome* [6]. Histamine and serotonin are significant causative agents in carcinoid syndrome; however, there are additional compounds that mediate carcinoid syndrome including bradykinin, catecholamines, prostaglandins, kallikrein, and neuropeptides [6]. Manifestations of mediator release include hypertension or hypotension, cutaneous flushing, bronchospasm, gastrointestinal hypermobility, and carcinoid heart disease. Severe cases can be life threatening or fatal [7].

Physiologic stress, exercise, ingestion of foods high in serotonin content, physical manipulation of the tumor, and induction of anesthesia can all trigger carcinoid syndrome; however, carcinoid syndrome may also occur spontaneously [6]. The use of medications that evoke histamine release can precipitate carcinoid syndrome. Sympathomimetic medications, such as ephedrine, can also cause the release of vasoactive mediators from carcinoid tumors and trigger carcinoid syndrome [8].

The primary considerations when caring for patients with carcinoid tumors in the perioperative period include (1) managing systemic physiologic manifestations of *chronic* mediator release by the tumor; (2) minimizing new-onset, *acute* release of mediators; and (3) monitoring for and treating systemic manifestations of new-onset, *perioperative* mediator release [3,6]. In the specific instance of patients having craniotomy to biopsy or remove an intracranial carcinoid tumor, there is additionally a fourth goal—that is, the management of intracranial volume, intracranial pressure, and cerebral perfusion pressure—which may be complicated by the release of the aforementioned substances by the tumor.

There are several reports and reviews that document the treatment options and complications of carcinoid syndrome and the relation to anesthesia. One study completed at our institution aimed to define the medical, surgical, and radiological treatment-related outcomes in patients with intracranial carcinoid [5], yet there are no reports in the indexed literature that document the anesthetic implications of surgical resection of intracranial carcinoid metastases. Our objective was to describe the perioperative anesthetic management of patients undergoing biopsy or surgical resection of intracranial carcinoid tumors, characterize any adverse perioperative events attributed to the carcinoid tumors (including events related to anesthetic, vasopressor, and other drugs), and describe the overall outcome in these patients.

2. Materials and methods

2.1. Selection criteria

After receiving approval from the Mayo Clinic Institutional Review Board, we identified the records of patients 18 years or older who underwent resection of carcinoid brain tumors at Mayo Clinic Rochester between January 1, 2000, and February 1, 2015, and who consented to allow their medical records to be used for research. Our search was conducted by using *International Statistical Classification of Diseases–9* and Current Procedural Terminology codes for carcinoid tumors and intracranial procedures, respectively, in addition to free-text searches for "brain carcinoid" or "intracranial carcinoid" in the electronic medical record. The medical record of each patient was reviewed to confirm the diagnosis of intracranial carcinoid disease and that surgical resection of the intracranial tumor was conducted. Histologic diagnosis was confirmed as carcinoid tumor for each subject included in the study.

For each subject included in the series, data pertaining to demographics, comorbid illnesses, carcinoid tumor sites, prior medical and surgical treatment of carcinoid tumors, and evidence for carcinoid syndrome were abstracted from the medical record. Each anesthetic record was reviewed for anesthetic technique, use of vasoactive drugs, physiologic monitoring used, hemodynamic data, and evidence of *carcinoid syndrome* (defined as unexplained hypotension or hypertension, cutaneous flushing or rash, increased ventilatory pressures or bronchospasm, decreased peripheral oxygen saturations, gastrointestinal hypermobility, or carcinoid heart disease as manifested by new murmur or evidence on echocardiogram). Perioperative complications were also noted. Subject records were reviewed and followed until February 1, 2015. Complications and/or deaths from a direct result of carcinoid disease and carcinoid-independent causes were documented.

3. Results

3.1. Demographics

Eleven patients underwent craniotomy for resection of carcinoid metastases to the brain during the study period. Demographics, disease characteristics, perioperative data, and clinical outcomes are summarized in Tables 1 to 4, respectively.

The time interval between the initial diagnosis of extracranial carcinoid tumor and the diagnosis of brain metastasis is documented in Table 2. Median time between