Anesthesiology
72:991–995, 1990

General Anesthesia Prior to Treatment of Anterior Mediastinal Masses in Pediatric Cancer Patients

Lynne R. Ferrari, M.D.,* Robert F. Bedford, M.D.†

Many children with malignant diseases who present with an anterior mediastinal mass must undergo general anesthesia for tissue diagnosis or tumor resection. One hundred sixty-three pediatric patients over a period of 6 yr were admitted to Memorial Sloan-Kettering Cancer Center with a diagnosis of anterior mediastinal mass. Forty four of these patients required surgery and their records were reviewed. In recent years perioperative radiation therapy has been advocated for this patient group prior to their receiving general anesthesia. If a tissue diagnosis has not been made, preoperative radiation therapy may distort histologic findings and prevent accurate diagnosis. All patients with an anterior mediastinal mass who must receive general anesthesia in our institution do so prior to treatment with radiation or chemotherapy even in the presence of cardiovascular or respiratory symptoms. No patient died or sustained permanent injury as a result of their anesthetic or operative experience. Two patients who experienced difficulty on induction of anesthesia required tracheal intubation with a rigid bronchoscope. Two patients developed airway obstruction during anesthetic maintenance that was corrected with changes in patient position. Four patients were unable to have their tracheas extubated at the conclusion of surgery and one patient required tracheal reintubation in the immediate postoperative period. These patients were treated with radiation therapy and chemotherapy after tissue for diagnosis had been obtained. The authors conclude that in the absence of life-threatening preoperative airway obstruction and severe clinical symptoms general anesthesia may be safely induced prior to radiation therapy. (Key words: Anesthesia: pediatric. Surgery, thoracic: mediastinal mass.)

IN THE PEDIATRIC POPULATION the mediastinum is the primary site of involvement in 16–36% of non-Hodgkin's lymphomas and 54–81% of Hodgkin's lymphoma.[1] Rapidly evolving symptoms of respiratory compromise or superior vena cava syndrome represent true emergencies that mandate prompt treatment.

The risks associated with general anesthesia in this group of patients are widely recognized. Tracheal or bronchial obstruction can arise unexpectedly at any time during anesthesia and surgery including induction, intubation, positioning, or extubation.[2–7,8] In addition, profound hypoxemia may occur when compression of the great vessels occurs despite patency of the airway.[5–7,9]

In recent years, preoperative radiation therapy has been advocated for this patient group prior to their receiving general anesthesia in an attempt to decrease these risks.[1–6,10] If an exact tissue diagnosis has not been made, however, then preoperative radiation therapy is not universally beneficial to the patient. On one hand, many childhood tumors, particularly lymphomas, are extremely radiosensitive and shrink markedly following a single treatment; thus, there is a reduced likelihood of perioperative complications.[11–13] On the other hand, an accurate diagnosis of tumor cell type is essential in order to initiate an optimal treatment regimen including cell type specific chemotherapeutic agents. It is the strong conviction of the pathologists at Sloan-Kettering Cancer Center that prebiopsy irradiation of tumor tissue distorts cellular morphology and impairs accurate histologic diagnosis. Even when preoperative radiation is limited to the central mantle of a mediastinal mass there may be sufficient scatter of the radiation beam to compromise the accuracy of tissue diagnosis. The risk of this approach then is that the patient may receive a suboptimal chemotherapy/radiation treatment regimen.

For these reasons, all patients with anterior mediastinal masses who require general anesthesia for diagnostic procedures at our institution do so without preanesthetic radiation therapy, even when respiratory or cardiovascular symptoms are present. The following report summarizes our recent experience with these patients and highlights several important principles related to their anesthetic management.

Methods

PATIENT POPULATION

We reviewed the records of 163 consecutive patients, ages 18 yr or younger, who were admitted over a 6-yr period to our hospital, and who had an anterior mediastinal mass as a component of their disease. The presence of an anterior mediastinal mass was confirmed on chest x-ray by an attending radiologist. Masses that were 3–4 cm in diameter at the widest point were classified as "moderate." Masses greater than 4 cm were classified as "large." Forty-four of these patients underwent a surgical procedure requiring general anesthesia prior to treatment; the anesthetic records from these procedures were examined in detail.

Patients that required general anesthesia and surgery underwent either of two procedures: Excision of an intact lymph node was performed to obtain tissue for analysis

* Assistant Professor of Anesthesiology.
† Professor of Anesthesiology.
Received from the Department of Anesthesiology and Critical Care Medicine, Memorial Sloan-Kettering Cancer Center; and the Department of Anesthesiology, Cornell University Medical College, New York, New York. Accepted for publication February 2, 1990.
Address reprint requests to Dr. Ferrari: 780 Boylston Street, Boston, Massachusetts 02199.

if prior blood and bone marrow examination failed to provide a specific histologic diagnosis. Debulking of the mass was performed if symptoms were not relieved by the initial treatment regimen of radiation and/or chemotherapy. The 119 patients who had an anterior mediastinal mass as a component of their disease but did not require anesthesia and surgery were admitted to the hospital for reasons unrelated to mass. These patients had an accurate histologic diagnosis and were undergoing successful treatment of their disease but required hospitalization for iv hydration, treatment of sepsis, blood transfusion, or in-hospital administration of chemotherapy.

Nine of the 44 patients who required general anesthesia (20%) were symptomatic preoperatively. These findings are summarized in table 1. Cough in the supine position was the most common symptom, present in all nine of these patients' histories. Other symptoms were as follows: superior vena cava syndrome, five patients; supine dyspnea, four patients; decreased breath sounds, three patients; wheezing, three patients; stridor and retractions, one patient each. Two patients had recent onset of murmur referable to the pulmonary artery. Neither dysphagia nor pulsus paradoxicus was present in any patient.

Operative Management

All patients received an anticholinergic prior to arrival in the operating room. Standard monitoring applied prior to induction of anesthesia included: EKG, automatic blood pressure cuff and pulse oximeter. In patients without symptoms suggestive of respiratory compromise anesthesia was induced with an iv opioid and sodium thiopental. After documenting the ability to ventilate the lungs, tracheal intubation was facilitated with succinylcholine 1–2 mg/kg intravenously. Muscle relaxant was omitted if ventilation was not easily accomplished, and a slow inhalation induction was performed.

In patients with evidence of airway compromise or with symptoms suggestive of potential respiratory embarrassment (*i.e.*, cough or supine dyspnea), preanesthetic medication and monitoring were provided in the same fashion as in the symptom-free group, except that venous access was secured *via* a lower extremity to obviate problems related to complete superior vena cava obstruction. A rigid bronchoscope was available in the operating room for use by the surgeon to secure an airway in the event of total tracheal compression. Anesthesia was induced with the patient in either the semi-Fowler or full sitting position. Patients less than 6 yr of age were given ketamine 1–2 mg/kg intravenously to facilitate both separation from parents and acceptance of a face mask. In older children anesthesia was induced with halothane in oxygen by mask maintaining spontaneous ventilation. If it was possible to assist or control ventilation with positive pressure, then patients were paralyzed and the trachea was intubated. If positive pressure ventilation was ineffective or controlled ventilation resulted in airway obstruction, patients were allowed to spontaneously breath increasing concentrations of halothane in oxygen *via* mask until anesthetic depth was sufficient to obtund pharyngeal reflexes. Tracheal intubation was then performed without the aid of muscle relaxation. Spontaneous ventilation was continued throughout the surgical procedure.

TABLE 1. Correlation of Symptoms with Radiographic Findings

Symptoms	Points	Diameter of Mediastinal Mass on X-Ray
Symptomatic	9	—
Cough	9	>4 cm
Superior vena cava syndrome	5	>10 cm
Decreased breath sounds	4	>4 cm
Wheezing	3	>4 cm
Stridor	1	>4 cm
Retractions	1	>4 cm
New onset murmur	2	>4 cm
Asymptomatic	35	3–10 cm

Results

No patient died or sustained permanent injury as a result of their operative experience. As might have been expected, however, there were several episodes of cardiorespiratory compromise encountered in this high-risk population.

Two of the nine patients with preoperative respiratory symptoms developed airway difficulties during either anesthetic induction and/or tracheal intubation. One was a 14-yr-old patient with a small-cell mediastinal tumor and new onset of a cardiac murmur referable to the pulmonary artery. The other was a 14-yr-old with non-Hodgkin's lymphoma and cough preoperatively. The lungs of both were easy to ventilate with positive pressure by mask prior to paralysis yet both developed total airway obstruction after administration of muscle relaxant. In both cases, ventilation was re-established only after deliberate mainstem intubation was performed using a rigid bronchoscope to determine the level of tracheal obstruction and then passing an endotracheal tube beyond it. No adverse hemodynamic events occurred in either patient.

Two patients developed airway obstruction during maintenance of anesthesia. One was an 18-month-old male with Hodgkin's lymphoma, the youngest patient in our series. He presented with a large anterior mediastinal mass, severe stridor, superior vena cava syndrome, and cyanosis on crying. Anesthesia was induced with ketamine 1 mg/kg intravenously followed by spontaneous mask

ventilation with halothane in 100% oxygen. Intubation was performed easily and without complications. However, every attempt to control ventilation was unsuccessful. Positive pressure breathing failed to cause chest wall expansion, although spontaneous breathing resulted in effective ventilation as determined by capnometry. With the child in the sitting position, every attempt to expose the surgical field by turning the patient's head was again met with ineffective ventilation presumably due to extrinsic compression of the distal end of the endotracheal tube by tumor. Despite the surgeon's complaints regarding positioning, biopsy of a cervical lymph node was accomplished uneventfully with the head in neutral position. The second patient presented with only nocturnal cough and a moderate size anterior mediastinal mass on x-ray. He had an uncomplicated induction *via* mask while in the sitting position and successful intubation without muscle relaxant but experienced wheezing and inability to ventilate the lungs when placed in the supine position. Despite adequate ventilation and oxygenation while spontaneously breathing halothane in 100% oxygen, the position change resulted in a decrease of the hemoglobin oxygen saturation from 100 to 68%. Effective ventilation was resumed only when the patient was returned to the sitting position. It was then possible to complete the operation uneventfully.

We could not extubate the tracheas of three patients at the conclusion of surgery. The 18-month-old male with Hodgkin's lymphoma exhibited persistent intercostal retractions and hemoglobin desaturation while breathing 100% oxygen although he was fully awake and responsive at the conclusion of surgery. Faced with these findings it was decided that his trachea should remain intubated and he should be allowed to breathe spontaneously in the intensive care unit while chemotherapy was administered. Over the next 48 h there was diminution of tumor size on sequential chest radiographs and the intercostal and suprasternal retractions disappeared. His trachea was then extubated uneventfully. The trachea of a 13-yr-old female with nodular sclerosing Hodgkin's disease and mild cough preoperatively could not be extubated secondary to stridor and wheezing that developed only on emergence from anesthesia. She was brought to the recovery room while the trachea was still intubated and she was treated with methylprednisolone 20 mg. Four hours after the conclusion of surgery, signs of airway obstruction cleared and her trachea was extubated uneventfully. A 14-yr-old male with non-Hodgkin's lymphoma and no clinical abnormalities preoperatively, experienced airway obstruction during induction of anesthesia. His trachea was intentionally left intubated at the conclusion of surgery and was treated with a 3-day cycle of chemotherapy (cytoxan, vincristine, daunorubicin, methotrexate, and methylprednisolone) that did not reduce the tumor mass. Single-dose radiation therapy, consisting of 4 Gy to the mediastinum, resulted in dramatic reduction in tumor size on chest radiograph. His trachea was easily extubated on the fourth postoperative day.

TABLE 2. Perioperative Complications

Points	Event	Treatment
2	Inability to ventilate after succinylcholine	Mainstem intubation with rigid bronchoscope
2	Inability to ventilate intraoperatively	Change in patient position
4	Inability to extubate trachea	Radiation therapy Steroids Chemotherapy
1	Inability to ventilate postoperatively	Intubation Radiation therapy

One 16-yr-old patient with histiocytic lymphoma and preoperative superior vena cava syndrome developed total airway obstruction in the recovery room 30 min after extubation following an otherwise uncomplicated anesthetic. She was noted to have inspiratory stridor, intercostal retractions and clinically apparent cyanosis. Her trachea was reintubated without the aid of muscle relaxant and an unobstructed airway was re-established. She was transferred to the intensive care unit where she received treatment with lasix, dexamethasone, vincristine, and cytoxan. Re-evaluation 24 h later revealed little change on chest radiograph. She was treated with 4 Gy of radiation to the mediastinum resulting in marked diminution in tumor size. Her trachea was extubated without incident 72 h postoperatively.

The results of these findings are summarized in table 2. In addition, three patients who presented with superior vena cava syndrome experienced no perioperative problems. A fourth patient who presented with the clinical finding of cough preoperatively had an uneventful anesthetic course.

Discussion

Many authors have described anesthetic complications in patients with anterior mediastinal masses and the literature is replete with suggested anesthetic plans to be implemented when this situation is encountered.[1–7,10] It is not our intention to reiterate the anesthetic management of this patient population and the reader is directed to the appropriate references. What is our intention, however, is to examine the advisability of general anesthesia and the preoperative treatment of the patient including the omission of preoperative radiation therapy.

When the diagnosis of malignancy is considered in such a patient an initial step is bone marrow aspiration and examination. This may provide the diagnosis but often it is inconclusive and tissue sample from a mass or adjacent

lymph nodes must be examined. Although local anesthesia may be attempted for superficial tissue sampling in the older patient, our experience has been that general anesthesia is a more effective alternative in the younger child. The depth of sedation required to render the small child amenable to tissue biopsy under infiltration of local anesthesia is sufficiently deep that spontaneous ventilation and oxygenation may be impaired. Positioning the patient to expose cervical lymph node tissue carries the risk of mechanical obstruction of the unprotected airway as well. In general our experience supports recommendations to administer general anesthesia with the following caveats: preserve spontaneous ventilation whenever possible, proceed with induction with the patient in the sitting position, secure iv access in a lower extremity, and be prepared to change the patient's position whenever cardiorespiratory compromise becomes apparent. A functioning rigid bronchoscope and a skilled bronchoscopist must be readily available and the possibility of emergency cardiopulmonary bypass must be considered.[2]

It is suggested that preoperative CT scan of the chest and flow volume loops are predictive of patients who might be at risk for adverse events under general anesthesia.[2] These studies are very helpful if they are available but many of the younger patients are uncooperative and require heavy sedation to obtain CT scans. Because sedation of these patients in an area other than the operating room was felt to be unsafe and the diagnostic imperative was to obtain tissue before treatment could be started, anesthesia was induced without the benefit of these additional studies.

To our knowledge, ours is one of very few reports of a large series of cancer patients with this condition undergoing general anesthesia. The first report, published in 1976 by Piro's group of radiation oncologists, was concerned with anesthetic difficulties encountered during staging laparotomy for Hodgkin's disease.[3] They concluded that preoperative radiation therapy directed at mediastinal masses could eliminate many anesthesia-related complications. This recommendation has been cited multiple times in the anesthesiology literature with what we believe to be little critical analysis.[1,2,4–6,10] For instance, of the 74 records that Piro *et al.* reviewed, 62 patients had a prior tissue diagnosis. It is entirely reasonable to recommend preoperative radiation when a positive tissue diagnosis has been obtained.[14] In fact, their group of patients who had zero complications following irradiation only included patients undergoing staging laparotomy after a tissue diagnosis had been confirmed. Their experience and recommendation is therefore not applicable to the patient in whom the diagnosis is not known.

Despite increased awareness of the anesthetic implications of anterior mediastinal masses, and what we believe to be a better understanding of their anesthetic management, many of the complications reported by Piro *et al.* were similar to those we observed. Among their 74 anesthetics, five were associated with "life threatening complications:" one of these was postoperative atelectasis and clearly was not an intraoperative anesthetic complication. One patient encountered difficulty during anesthetic induction and mainstem intubation was necessary to bypass a compromised segment of airway. In three other patients respiratory compromise requiring emergent tracheal reintubation at the end of operation occurred. The trachea of one patient was successfully extubated after appropriate head positioning, another recovered a few hours postoperatively without any apparent intervention, while one required emergent treatment before tracheal extubation could be accomplished.

As was the case in several of our patients, the transition from anesthesia and tracheal intubation to the awake state without an artificial airway can be as problematic as the induction/intubation period. Pain, anxiety, and coughing during emergence from anesthesia may increase intrathoracic pressure and worsen pre-existing obstruction distal to the end of the endotracheal tube. Tachypnea may increase turbulence in previously narrowed upper airways, thus limiting effective air exchange.[2,10] If airway compromise is encountered at this time however, and tissue has been obtained for diagnosis, it is now appropriate to institute antitumor therapy to diminish the size of the mass before tracheal extubation is attempted.

On the other hand, in the absence of a tissue diagnosis,[2,10] it is difficult to justify empiric treatment with radiation therapy in the pediatric population. Although most anterior mediastinal masses are lymphomatous in origin, benign conditions such as cystic hygroma, teratoma, thymoma dermoid tumor, and hemangioma may present in a similar fashion.[2,12,15–18] Radiation therapy for these diagnoses is not only unwarranted but may delay proper diagnosis and treatment. In a review by Halpern *et al.*, several cases of failure to accurately make a tissue diagnosis after radiation therapy were cited. In children who received preoperative radiation, tissue samples submitted for examination could only be read as "atypical" inflammatory reaction. It was only when the patients went untreated and presented with more severe and widespread disease that the correct diagnosis of Hodgkin's disease could be made.

The pathologists at our institution strongly advise against preoperative radiation therapy for similar reasons. On frequent occasions biopsy specimens from either directly or indirectly radiated tissue have been read as nonspecific inflammation or fibrosis.‡ This occurrence has led to delays in diagnosis and inability to properly treat

‡ Personal communication.

the underlying disease. Other centers have noted similar difficulty in making an accurate histologic diagnosis after high-dose steroid therapy has been instituted.[16]

In contrast to the experience of Piro *et al.*, the tissue diagnosis was unknown in all but one of our patients. In a pediatric population, it is difficult at best to obtain tissue under local anesthesia; thus there is an almost universal need for general anesthesia. On the other hand, the higher incidence of problems in our series probably reflects the greater risk of anesthetizing pediatric patients with anterior mediastinal masses. We believe, however, that anticipation of the problems that occur in children under general anesthesia and the ability to rapidly alter both the patients' position and the anesthetic technique are the most important factors in preventing anesthetic complications whenever this high-risk situation is encountered. We conclude from our data that the benefits of obtaining an accurate tissue diagnosis and initiating an appropriate therapeutic regimen outweigh the possible risks inherent in anesthetizing children with anterior mediastinal masses.

References

1. Halpern S, Chatten J, Meadows T, Byrd R, Lange B: Anterior mediastinal masses: Anesthetic hazards and other problems. J Pediatr 102:407–410, 1983
2. Neuman G, Weingarten A, Abramowitz R, Kushins L, Abramson A, Ladner W: The anesthetic management of patients with an anterior mediastinal mass. ANESTHESIOLOGY 60:144–147, 1984
3. Piro A, Weiss D, Hellman S: Mediastinal Hodgkin's disease: A possible danger for intubation anesthesia. Int J Radiat Oncol Bio Phys 1:415–419, 1976
4. Bittar D: Respiratory obstruction associated with induction of general anesthesia in a patient with mediastinal Hodgkin's disease. Anesth Analg 54:399–403, 1975
5. Mackie A, Watson C: Anaesthesia and mediastinal masses. Anaesthesia 39:899–903, 1984
6. Northrip D, Bohman B, Tuesada K: Total airway occlusion and superior vena cava syndrome in a child with anterior mediastinal tumor. Anesth Analg 65:1079–1082, 1986
7. Levin H, Bursztein S, Heifetz M: Cardiac arrest in a child with an anterior mediastinal mass. Anesth Analg 64:1129–1130, 1985
8. Azizkhan RG, Dudgeon DL, Buck JR, Colombani PM, Yaster M, Nichols D, Civin C, Kramer SS, Haller JA: Life-threatening airway obstruction as a complication to the management of mediastinal masses in children. J Ped Surg 20:816–822, 1985
9. Marshall M, Trump D: Acquired extrinsic pulmonic stenosis caused by mediastinal tumors. Cancer 49:1496–1499, 1982
10. Sibert K, Biondi J, Hirsch N: Spontaneous respiration during thoracotomy in a patient with a mediastinal mass. Anesth Analg 66:904–907, 1987
11. Janin Y, Becker J, Wise L, Schneider K, Schwartz D, So H: Superior vena cava syndrome in childhood and adolescence: A review of the literature and report of three cases. J Ped Surg 17:290–295, 1982
12. Silverman N, Sabiston D: Mediastinal masses. Surg Clin North Am 60:757–777, 1980
13. Wychulis A, Payne W, Clagett O: Surgical treatment of mediastinal tumors. J Thorac Cardiovas Surg 62:379–391, 1971
14. Link M: Non Hodgkin's lymphoma in children. Pediatr Clin North Am 32:699–717, 1985
15. Mullen B, Richardson J: Primary anterior mediastinal tumors in children and adults. Ann Thorac Surg 42:338–345, 1986
16. King M, Telander R, Smithson W, Banks P, Han M: Primary mediastinal tumors in children. J Pediatr Surg 17:512–520, 1982
17. Mark J, Stolar C, Altman R: Surgery of tumors of the mediastinum, Thoracic Oncology. Edited by Roth J, Ruckdeschel J, Weisenberger T. Philadelphia, W. B. Saunders, 1989, pp 419–429
18. Lonberg M, Bains M, McCormank P, Martini N, Bosl G: The management of mediastinal germ cell tumors: The Memorial Sloan-Kettering experience, Thoracic Surgery: Frontiers and Uncommon Neoplasms. Edited by Martini N, Vogt-Moykopf I. St. Louis, C. V. Mosby, 1989, pp 233–236