Pediatric Rhabdomyosarcoma of the Head and Neck

Is There a Place for Surgical Management?

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Objective: To review and evaluate the place of surgical treatment in the management of rhabdomyosarcoma of the head and neck in children.


Setting: Tertiary pediatric referral center.

Patients: Twenty-nine consecutive children with non-orbital head and neck rhabdomyosarcoma.

Interventions: Surgery, chemotherapy, and radiotherapy.

Main Outcome Measures: Disease-free survival and long-term morbidity from treatment.

Results: Twenty patients had parameningeal and 9 had nonparameningeal head and neck tumors. All were treated with chemotherapy. For 18 patients, diagnostic biopsies were performed and they received radiotherapy. Eleven patients underwent surgery as definitive therapy. Using the Intergroup Rhabdomyosarcoma Study (IRS) staging system, 5 of these 11 patients had complete resection of tumor (IRS group I) and avoided radiotherapy. The other 6 patients required radiation because of compromised, regional, or incomplete resection of tumor. One had undergone regional resection with nodal involvement, and 2 had compromised resections with microscopic residual disease (IRS group II). Three had incomplete resections with gross residual tumor (IRS group III). Only 1 patient who underwent surgery ultimately died from recurrence at 2.7 years after an incomplete resection. The other 10 patients were relapse free at a median follow-up of 3.7 years (range 0.8-21.0 years). Long-term surgical morbidity was seen in 36% (4/11) of the patients and included facial nerve paralysis, trismus, and cosmetic deformity.

Conclusions: Children with localized disease of the head and neck are able to undergo complete surgical resection, with low long-term morbidity. By undergoing complete surgical resection, these children are able to avoid radiotherapy and its long-term complications, with no compromise in survival.


Rhabdomyosarcoma is the most common soft tissue tumor in children.¹ The Intergroup Rhabdomyosarcoma Studies (IRSs) have established that the ideal management of this disease is to use multimodality treatment, using a combination of surgery, chemotherapy, and radiotherapy.²⁻³ Despite the increased success of combining chemotherapy and radiotherapy with surgery for management of rhabdomyosarcoma, the survival of patients is still mostly dependent on their IRS surgical and pathological groupings (Table 1). Survival is highest in group I and lowest in group IV, with embryonal disease doing better than alveolar rhabdomyosarcoma.²⁻³ The IRS clinical grouping system depends on the completeness of surgical resection, which in turn depends on the anatomic subsite of the tumor and evaluation of the pathological specimen. In the head and neck region, 3 broad anatomic regions can be identified: orbital, parameningeal, and nonparameningeal.¹ Parameningeal sites include the nasopharynx and nasal cavity, paranasal sinuses, infratemporal and pterygopalatine fossae, and middle ear. Tumors at these sites are not normally amenable to complete surgical resection and, therefore, usually are classified as group III. Orbital tumors have an excellent prognosis after chemotherapy and radiotherapy, and surgery is limited to diagnostic biopsy.² The management of nonparameningeal tumors is more difficult. Complete surgical resection offers the best prognosis and allows avoidance of radiotherapy and the considerable comor-
PATIENTS AND METHODS

Patients treated for head and neck rhabdomyosarcoma at The Hospital for Sick Children from January 1, 1972, to December 31, 1998, were identified from the pathology and health record databases. The medical charts of 29 patients with nonorbital head and neck rhabdomyosarcoma were reviewed. Their sex, age, histological classification, treatment, morbidity, and survival data were collected. The tumor stages were reclassified retrospectively according to the IRS grouping system (Table 1).

All patients received chemotherapy according to their stages as in the IRS protocols. The drugs used included vincristine sulfate, doxorubicin hydrochloride, dactinomycin, cyclophosphamide, ifosfamide, and etoposide. Patients who were staged as groups I, II, III, and IV received external beam radiation as in the IRS protocols. Survival data were analyzed by the Kaplan-Meier method.2 However, surgery itself may carry significant morbidity, which depends on the site and extent of disease. The otolaryngologist and oncologist often are faced with the challenge of deciding which combination of therapeutic modalities offers the patient the best prognosis with the least morbidity. In this review of our experience at The Hospital for Sick Children, Toronto, Ontario, we examine the role of surgery in the management of pediatric head and neck rhabdomyosarcoma, with particular reference to long-term morbidity and disease-free survival.

RESULTS

Of a total of 48 patients with histologically confirmed head and neck rhabdomyosarcoma, 29 had nonorbital tumors. Twenty patients had parameningeal tumors and 9, nonparameningeal tumors. The tumor locations are summarized in Table 2. The age at diagnosis ranged from 3 months to 12.5 years (median, 4.9 years). The male-to-female ratio was 1.1:1. The predominant histological type was embryonal rhabdomyosarcoma (19 patients). Alveolar rhabdomyosarcoma was found in 6 patients. Two patients had embryonal tumors with an alveolar component, and 2 had undifferentiated sarcoma.

MANAGEMENT

Eleven patients underwent surgery as definitive therapy. Their stages and histological types are summarized in Table 3. The most common location was the cheek or parotid region (5 patients). The other 6 patients had rhabdomyosarcoma involving other sites, including the nasal cavity, the nasal ala, and the temporal, occipital, or submandibular regions.

In the 5 patients with rhabdomyosarcoma of the cheek or parotid region, resection was achieved via a parotidectomy approach, which was extended to include a neck dissection in 2 patients. In 1 patient with infratemporal fossa tumor extension, a hemimandibulectomy was performed to facilitate surgical access. Preservation of the facial nerve was possible in all but 1 patient.

Complete surgical resection with no evidence of microscopic disease (IRS group I) was achieved in 5 (45%) of 11 patients. These 5 patients were able to avoid radiotherapy but received chemotherapy according to their stages as in the IRS protocols. To achieve complete excision, frozen sections of the surgical margins were performed in the patients. Despite negative frozen sections, the final histological findings showed tumor encroachment of resection margins in 2 patients who then had further resections to remove any residual tumor. In both cases, subsequent histological examination detected no tumor present in the secondary resection specimen.
One patient experienced temporary skin breakdown as a result of radiotherapy. Permanent radiation-induced complications were common and often required remedial therapy. These included cataracts (n = 2), retinopathy (n = 1), keratopathy (n = 1), dental abnormalities (n = 2), growth hormone deficiency (n = 5), and hypothyroidism (n = 2). Secondary malignancies did not develop in any of the patients.

SURVIVAL

Follow-up ranged from 3 months to 21 years (median, 3.5 years). Four patients experienced relapse and all subsequently died. One of these patients developed local recurrence after incomplete resection and radiotherapy of a nasal cavity tumor 2 years 8 months after surgery. The other 10 patients who underwent surgery as definitive treatment or surgery plus postoperative radiotherapy were relapse free at a median follow-up of 3.7 years (range 0.8-21.0 years). There were no deaths or relapses in patients with group I and II tumors. Actuarial survival data calculated by the Kaplan-Meier method showed that the probability for relapse-free survival was 83% and for overall survival was 83% for the entire group of 29 patients.

Table 3. Summary of 11 Patients Who Underwent Surgery as Definitive Therapy

<table>
<thead>
<tr>
<th>Site</th>
<th>IRS Group</th>
<th>IRS Classification</th>
<th>Histological Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occiput</td>
<td>IA</td>
<td>Parameningeal</td>
<td>Embryonal</td>
</tr>
<tr>
<td>Wing of nose</td>
<td>IA</td>
<td>Nonparameningeal</td>
<td>Alveolar</td>
</tr>
<tr>
<td>Cheek and parotid</td>
<td>IB</td>
<td>Nonparameningeal</td>
<td>Alveolar</td>
</tr>
<tr>
<td>Cheek and infratemporal fossa</td>
<td>IB</td>
<td>Parameningeal</td>
<td>Alveolar</td>
</tr>
<tr>
<td>Cheek and parotid</td>
<td>IB</td>
<td>Nonparameningeal</td>
<td>Embryonal</td>
</tr>
<tr>
<td>Cheek and parotid</td>
<td>IIA</td>
<td>Nonparameningeal</td>
<td>Mixed embryonal and alveolar</td>
</tr>
<tr>
<td>Cheek and parotid</td>
<td>IIB</td>
<td>Nonparameningeal</td>
<td>Mixed embryonal and alveolar</td>
</tr>
<tr>
<td>Submandibular and cervical nodes</td>
<td>IIB</td>
<td>Nonparameningeal</td>
<td>Alveolar</td>
</tr>
<tr>
<td>Nasal cavity</td>
<td>III</td>
<td>Parameningeal</td>
<td>Embryonal</td>
</tr>
<tr>
<td>Temporal</td>
<td>III</td>
<td>Nonparameningeal</td>
<td>Alveolar</td>
</tr>
<tr>
<td>Nasal cavity and paranasal sinuses</td>
<td>III</td>
<td>Parameningeal</td>
<td>Undifferentiated</td>
</tr>
</tbody>
</table>

*IRS indicates Intergroup Rhabdomyosarcoma Study.

The remaining 6 patients (55%) had compromised, regional, or incomplete resection. One patient had complete resection of the primary tumor in the submandibular region but had disease involving 1 cervical node (IRS group II) in the neck dissection specimen. Two patients had compromised resections with residual microscopic disease (IRS group II). Three patients underwent incomplete resections (IRS group III). One had disease affecting the temporal region. Two patients had disease in the nasal cavity and initial biopsy specimens were inconclusive; more definitive surgery in the form of a lateral rhinotomy was performed. In all 3 cases there was gross residual disease.

The 6 patients in whom excision was incomplete received radiotherapy in addition to chemotherapy. The 18 patients in whom definitive surgery was not possible because of the tumor location or extent received radiotherapy in addition to chemotherapy after diagnostic biopsies were performed.

MORBIDITY

Surgical complications occurred in 4 patients and included transient (n = 4) or permanent (n = 1) facial nerve palsy, trismus (n = 2), and cosmetic deformity (n = 1). Four patients with tumors of the parotid or cheek regions developed transient facial nerve paralysis after surgery. One patient, in whom the facial nerve had to be sacrificed, subsequently required a number of facial reanimation procedures, including a free gracilis muscle transfer. In addition, this patient required surgery for trismus that developed after excision of the coronoid process. Two other patients developed trismus after resection of the coronoid process or pterygoid plates and underwent successful surgical division of the fibrous contracture. The patient with rhabdomyosarcoma of the nasal ala had considerable facial disfigurement and abnormality of facial growth that required several reconstructive procedures.

Since the introduction of the IRS protocols, the role of surgery in the management of rhabdomyosarcoma of the head and neck has been established. These studies demonstrated that combined-modality treatment using surgery, chemotherapy, and radiotherapy offers the best chance for survival in patients with rhabdomyosarcoma. Before these studies, surgery was the principal modality of treatment, with poor survival (8%-20%) and considerable morbidity. The IRS demonstrated that, with the use of combined chemotherapy, radiotherapy, and surgery, overall survival improved dramatically (25%-83%).

All modalities of treatment carry morbidity. Chemotherapy is the essential modality to prevent metastatic disease, regardless of whether surgery is performed or radiation given. Fortunately, the morbidity associated with chemotherapy is usually short term and readily treatable, although life-threatening sepsis may occur occasionally. Other long-term toxic effects from chemotherapy may occur but are rare, except for sterility in some patients after cyclophosphamide chemotherapy. The Third IRS study found that the prognosis was unchanged if cyclophosphamide was omitted from the chemotherapy regimen for nonparameningeal head and neck tumors with favorable histological characteristics. This change in regimen will reduce the risk of sterility and secondary leukemia. Morbidity from radiotherapy may be considerable and depends on the field and dose of radiation. Complications such as cataract formation, retinopathy, growth disturbance, and endocrine deficiency are particularly debilitating and permanent. Dental abnormalities have occurred in half of the long-term survivors of head and neck rhabdomyosarcoma and include root stunting, microdontia, and hypodontia.
of these complications and the risk for the development of a secondary malignancy, there is a strong rationale to avoid radiation when it is feasible to resect the tumor completely.

Surgery is a valuable treatment modality in this disease. The IRS showed that survival clearly is dependent on the amount of residual disease after surgery. In addition, if complete resection is achieved, patients are able to avoid radiotherapy and its potential complications without compromising survival. Recent data have shown, however, that patients with alveolar or undifferentiated rhabdomyosarcoma will have improved outcome if radiotherapy is added to the treatment regimen. Nevertheless, the role of surgery is limited by potential postoperative morbidity that depends on the site and extent of disease. Radiological investigations, including computed tomography and magnetic resonance images, are helpful in determining if there is bone erosion or intracranial extension that would preclude surgery. Tumors limited to soft tissue may not be well delineated and are difficult to distinguish from surrounding inflammatory reaction. An accurate assessment of the extent of tumor and its resectability is often possible only at the time of surgery. The management of orbital rhabdomyosarcoma is unique, because surgery does not confer any advantage over chemotherapy and radiotherapy in terms of survival. This combined modality is the treatment of choice for orbital rhabdomyosarcoma and avoids the significant morbidity from the loss of an eye. Similar considerations are applicable for other vital structures such as the larynx and pharynx, and most would consider laryngectomy too radical despite the theoretical added improvement in survival and the avoidance of radiotherapy. Some, however, argue that radiotherapy to the larynx carries a greater morbidity than laryngectomy.

Rhabdomyosarcoma affecting the parameningeal areas, including the nasopharynx, paranasal sinuses, and temporal bone, generally is not amenable to surgical resection. In these areas, radical surgery risks damage to major cranial nerves and disfigurement of the facial skeleton, and is unlikely to achieve complete resection. Treatment of tumors in these sites by chemotherapy and radiotherapy, with surgery limited to diagnostic biopsy, offers the least morbidity, with 5-year survival rates of up to 65% that are improving with newer intensive chemotherapy regimens. Recent reports have advocated radical surgical treatment for primary tumors and salvage treatment for the tumors at these sites, with promising results. However, further studies are needed to compare the survival and long-term morbidity outcomes of these procedures with the standard chemotherapy and radiotherapy protocols for management of tumors at these sites. Although it may be argued that reducing the bulk of disease may improve survival, this must be balanced against the morbidity after such surgery. In this series of head and neck rhabdomyosarcoma, parameningeal tumors were the most common. Successful resection was possible in only 2 patients, one with tumor in the ocipital region that extended to the vertebral body of C1, and the other with tumor originating from the cheek and extending into the infratemporal fossa. By definition, both tumors were classified as parameningeal tumors, although the occiput is an unusual site. The 2 patients with nasal cavity lesions who had surgery had incomplete resections.

In this series, we found that the most common site amenable to surgery was the cheek and parotid region. Structures at risk in this area include the facial nerve and the muscles and joints involved in mastication. Risk for facial disfigurement exists if considerable bone or skin resection is necessary. Postoperative morbidity was minimal in most patients, except when the facial nerve was deliberately sacrificed or when the coronoid process or muscles of the pterygoid plates were resected.

Localized disease at other sites was also amenable to surgery, with substantial morbidity in only 1 patient with tumor of the nasal ala, who required several reconstructive procedures.

Despite macroscopic excision and frozen-section control of the margins, complete resection may not be achieved. When the final histological examination shows tumor extending to the resection margin, we support the notion of reexcision if the initial operative findings suggest it is feasible. This revision surgery is again performed with frozen-section control of the margins. In this series, 2 patients required such revision, but in both, the surgical specimens from revision surgery showed absence of tumor. Nevertheless, we believe that this confirmation is necessary if radiotherapy is to be avoided.

Surgery is also useful as a “second-look” procedure in patients in whom partial responses are suspected radiologically or clinically. These patients actually may be reclassified as complete responders on results of biopsy during a second-look procedure. For those with confirmed partial responses, further alternative chemotherapy may produce a complete response. Debulking surgery to improve the appearance or to eliminate the offensive odor from necrotic tumor may be a useful palliative procedure in patients with uncontrolled disease extending through the skin. This was performed in one of the patients in this series, who lived for 6 months despite uncontrolled disease.

Despite the success of combined modalities for group III rhabdomyosarcoma, we believe that surgery plays a pivotal role in the management of such nonorbital head and neck tumors. We have shown that, for patients with localized disease and disease limited to the cheek region, complete resection is possible. These patients are able to avoid radiotherapy and its significant long-term morbidity without compromising survival. We have also found that long-term surgical morbidity is low in children with resectable nonorbital head and neck rhabdomyosarcoma. However, the surgeons and oncologists who treat children with this disease must weigh carefully the benefits of improved survival and avoidance of radiotherapy against the risks of surgery. For localized disease and disease affecting the cheek region, complete resection is often possible. However, an accurate assessment can only be determined at the time of surgery. In cases where unacceptable postoperative morbidity is expected, surgery must be abandoned and the patient treated with radiation.
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