

## Long-term Survivors of Adult Rhabdomyosarcoma of Maxillary Sinus Following Multimodal Therapy: Case Reports and Literature Reviews

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Rhabdomyosarcoma of the maxillary sinus is uncommon in adults. The clinical course and appropriate treatment strategy for the disease remains to be elucidated. This article describes two adult patients with rhabdomyosarcoma of the maxillary sinus who achieved long-term survival after undergoing multimodal therapy. We also reviewed the literature regarding 23 patients who were 15 years of age or older and had rhabdomyosarcoma of the maxillary sinus and were treated between 1950 and 2000. Results of our analysis suggest that multimodal therapy may become the mainstay treatment for adult rhabdomyosarcoma of the maxillary sinus. We believe that adequate surgical procedures, planned radiotherapy, aggressive chemotherapeutic agents and the best supportive care for complications may improve the prognosis of patients with this disease. (*Chang Gung Med J* 2010;33:466-71)

**Key words:** maxillary sinus, rhabdomyosarcomas, adult

**R**habdomyosarcoma (RMS) originates from immature mesenchymal cells that are committed to skeletal muscle differentiation. It is considered to be the most common malignant tumor of soft tissue in children under 15 years of age, accounting for 5% to 10% of all childhood malignancies.<sup>(1)</sup>

There are quite different clinical courses and outcome between adult and child patients of rhabdomyosarcomas. Adult rhabdomyosarcomas do not show a male preponderance, as is noted in pediatric patients. Adult rhabdomyosarcomas occur with a predilection in the extremities, while pediatric rhabdomyosarcomas occur predominantly in the head and neck sites. More than 60% of adult patients have regional and distant metastases at diagnosis, mainly in the lung and bone. By contrast, only 15% of children with rhabdomyosarcomas present with metasta-

tic diseases, which carry a poor prognosis. Using a multimodal treatment strategy combining surgery, chemotherapy and radiotherapy, the five-year survival rate in children significantly improved from 25% in 1970 to 75% at present. Although experiences from childhood RMS are extrapolated widely to adults with this disease, therapeutic success has been limited and long-term survival rates remain poor with a range of 35-45%.

The head and neck is an extremely rare location of adult rhabdomyosarcomas, and the five-year survival rate is 8% or less in this situation. They should be considered as a distinct clinical entity with special considerations for their management from that of pediatric rhabdomyosarcomas. RMS of the paranasal sinus accounts for 10% to 15% of adult head and neck RMS.<sup>(1)</sup> These tumors are often advanced and

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locally invasive, and the ethmoid or maxillary sinus is the most common site affected.<sup>(1)</sup>

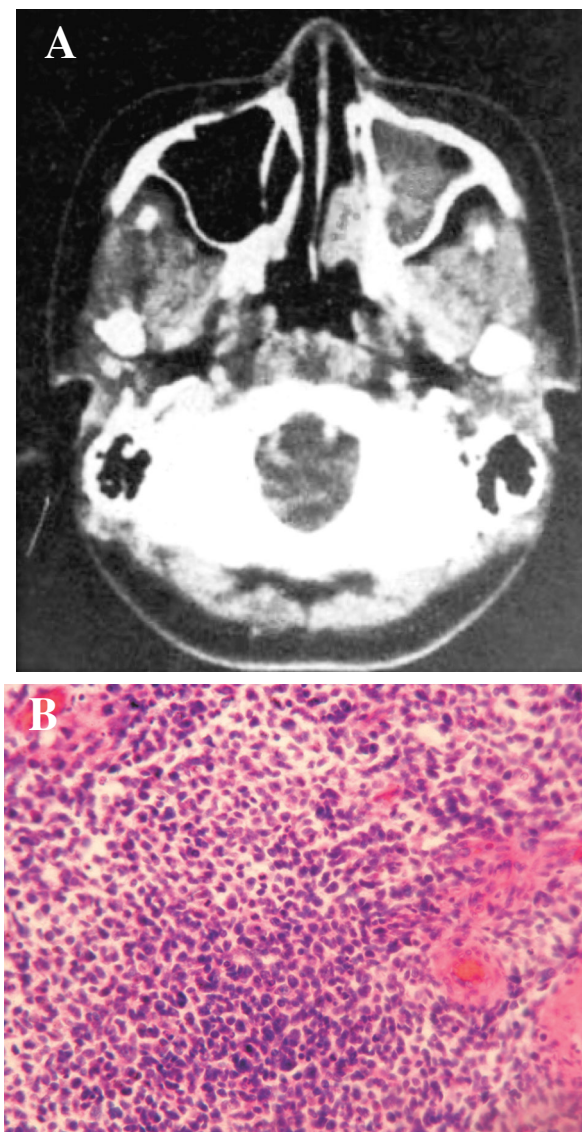
Although a clinical series of RMS in the maxillary sinus have been discussed,<sup>(2)</sup> some intriguing phenomena regarding tumor characteristics and treatment modality remain to be discussed. Moreover, a poor prognosis is associated with maxillary rhabdomyosarcoma rather than that in paranasal sinuses because extensive local disease is usually found at the time of diagnosis, making surgical excision difficult or impossible, and because these tumors have often metastasized already when treatment is initiated. Reports in the literature have presented encouraging results in the therapy of childhood rhabdomyosarcoma, using combinations of surgery, radiotherapy and chemotherapy. The effects of such a combined regimen may improve the results for adult rhabdomyosarcoma.<sup>(1-3)</sup>

Herein, we describe two cases of adult RMS of the maxillary sinus that reached complete response and long-term survival following multimodal therapy. These patients' treatment outcomes suggested that intensively planned therapy is feasible and tolerable in patients with advanced adult RMS of the maxillary sinus. A retrospective review was also conducted on patients older than 15 years of age who had RMS of the maxillary sinus between 1950 and 2000. Tumor characteristics and the treatment modality of this specific disease are discussed.

## CASE REPORTS

### Case 1

A 22-year-old woman was hospitalized in December 1989 with a 1-month history of epistaxis. Imaging evaluation and pathologic analysis confirmed embryonal rhabdomyosarcoma of the left maxillary sinus (Fig. 1), placing the patient in the Intergroup Rhabdomyosarcoma Study (IRS) group III. The patient received four courses of preoperative chemotherapy consisting of doxorubicin (50 mg/m<sup>2</sup>), dacarbazine (1000 mg/m<sup>2</sup>), vincristine (1.4 mg/m<sup>2</sup>), and cyclophosphamide (700 mg/m<sup>2</sup>) at 4-week intervals, and radiation therapy (total 2,800 cGy). After radical maxillectomy, the patient received adjuvant chemoradiotherapy with high-dose methotrexate (2 g/m<sup>2</sup>), followed by a tumor bed boost with radiation (600 cGy). The cancer reached complete remission and at the time of writing, she has remained well

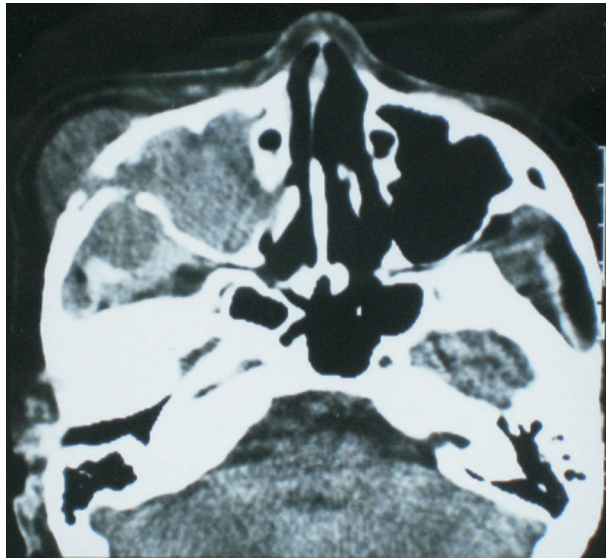


**Fig. 1** (A) The computed tomography of head and neck shows a tumor occupied left maxillary sinus which extends to nasal cavity. (B) Tumor cells with large round nuclei. Rhabdomyosarcoma of the embryonal type. H & E  $\times$  100.

during 19 years of regular follow-up at our clinic.

### Case 2

A 16-year-old girl presented to the outpatient clinic in August 1996 with a 1-month history of right hemifacial pain. The physical examination showed a tender mass, about 5  $\times$  3 cm, in her right cheek (Fig. 2). After imaging evaluation and total maxillectomy,



**Fig. 2** The computed tomography of head and neck reveals a soft-tissue density tumor extending from right maxillary sinus to face, combined with bony destruction.

the pathologic analysis revealed embryonal rhabdomyosarcoma of the right maxillary sinus, placing the patient in IRS group III. Postoperatively, she received four courses of chemotherapy consisting of vincristine ( $1.4 \text{ mg/m}^2$ ) and actinomycin D ( $1 \text{ mg/m}^2$ ), repeated at 3- to 4-week intervals, and radiation therapy (total 6,840 cGy). The patient responded well to this multiagent therapy and the cancer reached complete remission. She has been free from any local recurrence and has undergone regular follow-up at our clinic for more than 12 years.

## DISCUSSION

In reviewing the literature of patients older than 15 years with RMS of the maxillary sinus between 1950 and 2000, a total of 23 patients were obtained, including two from our own experience. The patients were analyzed with respect to the following: (1) age and gender; (2) symptoms at presentation; (3) histological classification; (4) tumor stage; and (5) modality of therapy. The cases were culled from larger head and neck neoplasm series or from articles attempting to illustrate tangential points.

Clinical stages of the patients were obtained from the descriptions in the published reports or the patients' medical records. The patients were classi-

fied into groups I through IV, based on the amount of tumor resected as defined by the IRS clinical grouping classification.

To offset the problems of the rarity of this disease, the small number of patients and the incomplete medical records in this series, a descriptive format was adopted to present the results.

### Age and gender

Patient ages ranged from 15 to 77 years and the median age was 29.2 years. More than two-thirds of patients were younger than 30 years of age at diagnosis, with a rapid drop-off in reported cases thereafter. Fourteen patients were female (60.9%) and nine patients were male (39.1%) in the current analysis. The sex distribution of this study showed a modest preponderance of females to males (1.5:1) overall.

### Symptoms, tumor stage and histological classification

The median delay from the onset of symptoms to the time of diagnosis was 75 days (range, 1 day to 7 months). The possible causes of delay in diagnosis included suspected infection, failure to establish correct diagnosis, history of trauma, prolonged observation of mass, and delay in seeking medical advice and so on. The common presenting symptoms included nasal congestion, nasal discharge and epistaxis, which comprised 42.9% of total cases. Pain of the cheek was the major facial symptom (22.8%). If RMS invaded the orbits, proptosis and visual disturbance were the main ocular symptoms (22.8%). Late diagnosis may affect the prognosis and treatment outcomes of patients with this specific disease. Therefore, a timely tissue biopsy is prudent if infection has not improved after drainage and antibiotic use, or if unexplained facial swellings persist for more than 1 month.

More than 95% of reported cases of adult RMS of the maxillary sinus were classified as IRS group III at diagnosis. Only two patients presented with bone and bone marrow metastases as IRS group IV (case 19 and 20).

The pathological feature revealed that the embryonal form was by far the most frequent lesion, accounting for 47.8% of the total cases. Alveolar and pleomorphic subtypes represented up to 42.4% and 9.8% of cases, respectively. No botryoid form was found in this analysis.



### Treatment modality

More than 65% of the patients received surgical treatment in our analysis. Surgical procedures included the Caldwell-Luc approach (two cases), extended Denker's operation (two cases), maxillectomy without orbital exenteration (one case), maxillectomy with orbital exenteration (three cases) and radical maxillectomy (seven cases).

Since most patients with adult rhabdomyosarcoma of the maxillary sinus were in the advanced stages at the time of diagnosis, radiotherapy and chemotherapy were used as an adjunctive therapy. The percentage of patients receiving radiation therapy was 82.3%. The range of the total radiation dose was from 3,500 cGy to 6,840 cGy. The median dose of radiation was 5400 cGy. 52.1% of the total cases received chemotherapy. More than three-fourths of these patients were treated with at least three agents. A wide variety of protocols were used with combined chemotherapy, most of which contained doxorubicin, vincristine and/or cyclophosphamide/ifosfamide. These regimens were applied in neoadjuvant, concurrent chemoradiotherapy and postoperative adjuvant settings.

Of the 23 patients in the current series,<sup>(2-20)</sup> 18 (78.2%) received two treatment modalities, including six who underwent surgery plus radiotherapy, one who underwent surgery plus chemotherapy and four who underwent radiotherapy plus chemotherapy. Six patients received surgery, chemotherapy and radiotherapy.

The tumors derived from the maxillary sinuses were advanced, and the patients were less tolerant of complications after surgery.<sup>(1)</sup> Additionally, the introduction of new chemotherapeutic agents and a new mode of radiotherapy translated into significant improvements in survival in patients with pediatric RMS during the past 25 years. Chemoradiotherapy appears to be the mainstay treatment and the role of surgery has been drastically reduced and has become an alternative for local radiotherapy, partial removal, biopsy of the tumor or a salvage protocol. However, surgery should be recommended as an option for management in light of the known complications of existing therapy.

In conclusion, we demonstrated that there were two long-term survivors with adult RMS of the maxillary sinus following surgery and chemoradiotherapy. We believe that employing adequate surgical pro-

cedures, planned radiotherapy, aggressive chemotherapeutic agents and the best supportive care for complications may offer the optimal treatment protocol for improving the prognosis of patients with this disease. Because most current literatures are case reports and lack information on the long-term outcome of treatment, we also hope that there will be a randomized trial to better define the role of combined modality therapy in the coming years.

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# 成人上顎竇橫紋肌肉瘤患者接受多型式治療後可達到長期存活 ——病例報告及文獻回顧

吳宗翰 黃仁聖 王宏銘<sup>1</sup> 王正旭 葉光揚

上顎竇橫紋肌肉瘤在成人屬罕見疾病，其臨床病程及適合的治療方法仍有待闡明。本文報告兩例成人上顎竇橫紋肌肉瘤患者，在接受多型式治療 (multimodality therapy) 後獲得長期存活。我們並回顧 1950 年到 2000 年的文獻中大於 15 歲的患者共 23 位。我們的分析指出多型式治療是極重要的治療方式；適當的手術、放射線治療、化學治療及支持治療能改善疾病預後。(長庚醫誌 2010;33:466-71)

**關鍵詞：**上顎竇，橫紋肌肉瘤，成人