

Case Report

Extensive alveolar-type paranasal sinus and orbit rhabdomyosarcoma with intracranial invasion treated successfully

Shih-Chou Chen^a, Youn-Shen Bee^{a,b,*}, Muh-Chiou Lin^a, Shwu-Jiuan Sheu^{a,c}

^aDepartment of Ophthalmology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, ROC

^bYuh-Ing Junior College of Health Care and Management, Kaohsiung, Taiwan, ROC

^cNational Yang-Ming University School of Medicine, Taipei, Taiwan, ROC

Received February 2, 2010; accepted August 21, 2010

Abstract

We report a case of extensive paranasal sinus and orbit rhabdomyosarcoma (RMS) with intra-cranial invasion treated successfully with chemotherapy and radiotherapy. A 13-years-old male patient complained of painless and progressive proptosis of his left eye for two weeks. Ocular examination showed elevated intraocular pressure, limited extraocular movement, proptosis, and conjunctival ciliary injection in the left eye. Brain CT and MRI demonstrated a large enhancing soft tissue mass lesion with bone destruction involving left ethmoid sinus, nasal cavity, maxillary sinus, and orbital cavity with crossing of the midline to the right ethmoid sinus, nasal cavity, and intra-cranial invasion across the frontal base. The pathology of tumor biopsy revealed rhabdomyosarcoma, alveolar type. Systemic survey showed no evidence of distant metastasis. Then, the patient received combined radiochemotherapy with Taiwan Pediatric Oncology Group Rhabdomyosarcoma 2007 High-risk Treatment Protocol. No light perception in his left eye with optic disc atrophy was noted at the beginning of radiotherapy. After 44 weeks of combined radiochemotherapy, the tumor regressed, and no recurrence has been noted until now. In young patients with sudden-onset proptosis, RMS should be considered, and early diagnosis is crucial due to more effective prognosis with current radiochemotherapy protocol. Copyright © 2011 Elsevier Taiwan LLC and the Chinese Medical Association. All rights reserved.

Keywords: Alveolar type; Orbit tumor; Paranasal sinus tumor; Radiochemotherapy; Rhabdomyosarcoma

1. Introduction

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in childhood. The annual incidence is approximately 4.5 cases per million in children under the age of 20.¹ RMS can arise from striated skeletal muscle and other locations where skeletal muscle is not typically found. All patients with alveolar RMS have a poor prognosis, with a median survival time of 17 mo. Intracranial extension and an age greater than 10 yrs were also associated with an unfavorable outcome.² Here, we report a case of paranasal sinus and orbit RMS with intra-cranial invasion presenting with initially rapid proptosis treated

successful with chemotherapy and radiotherapy for about one year. Current treatment in Taiwan is also discussed.

2. Case report

A 13-year-old male Chinese complained of painless and progressive proptosis of his left eye for two weeks. He denied any ocular history, trauma history, or systemic disease. In ocular examination, his best corrected visual acuity (BCVA) was 6/5 OD and 6/6 OS. The intraocular pressure (IOP) was 16 mmHg OD and 28 mmHg OS. Exophthalmometry revealed 16 mm OD and 22 mm OS, respectively, and limited extraocular movement (EOM) was noted. Timolol-XE 0.5% QD OS was prescribed, and brain computed tomography scan (CT) was arranged immediately.

Brain CT demonstrated a large enhancing soft tissue mass lesion with bone destruction involving the left ethmoid sinus,

* Corresponding author. Dr. Youn-Shen Bee, Department of Ophthalmology, Kaohsiung Veterans General Hospital, 386, Ta-Chung 1st Road, Kaohsiung 813, Taiwan, ROC.

E-mail address: ysbee@vghks.gov.tw (Y.-S. Bee).

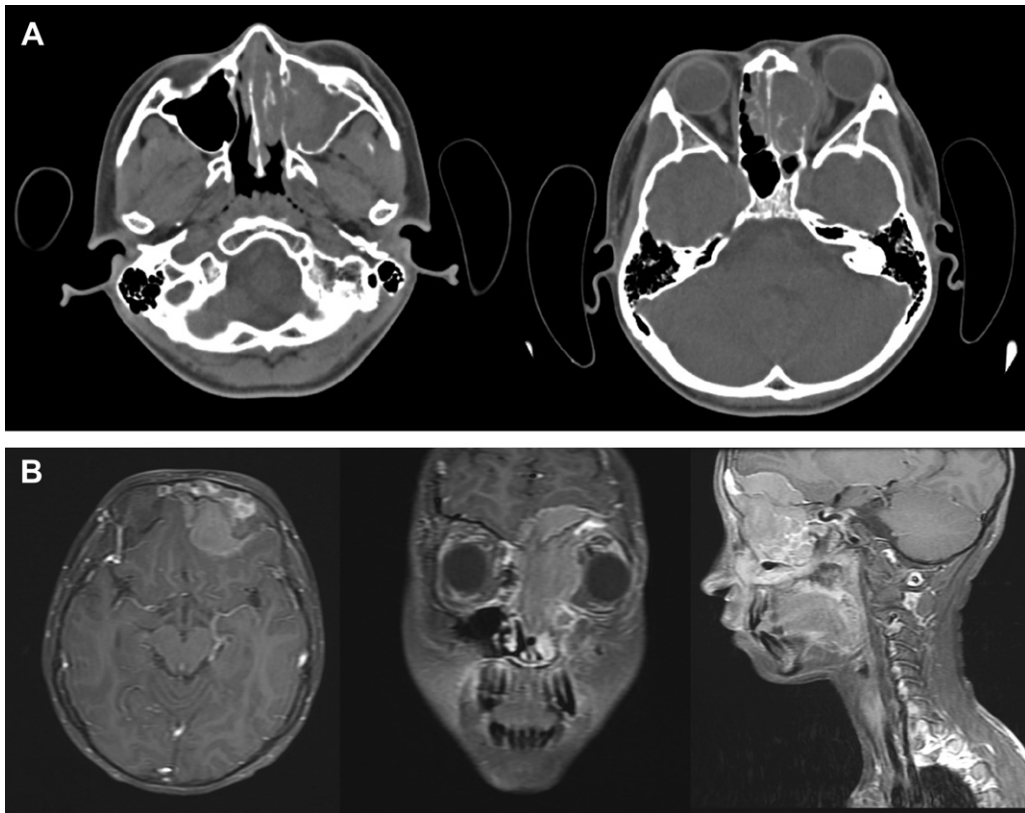


Fig. 1. (A) Brain computed tomography demonstrated a large soft tissue mass lesion involving the left paranasal sinus, nasal cavity, and orbital cavity with crossing of the midline to the right paranasal sinus and nasal cavity. (B) Brain magnetic resonance imaging axial view, coronal view, and sagittal view revealed obvious intracranial extension with cribriform plate destruction to bilateral frontal base regions.

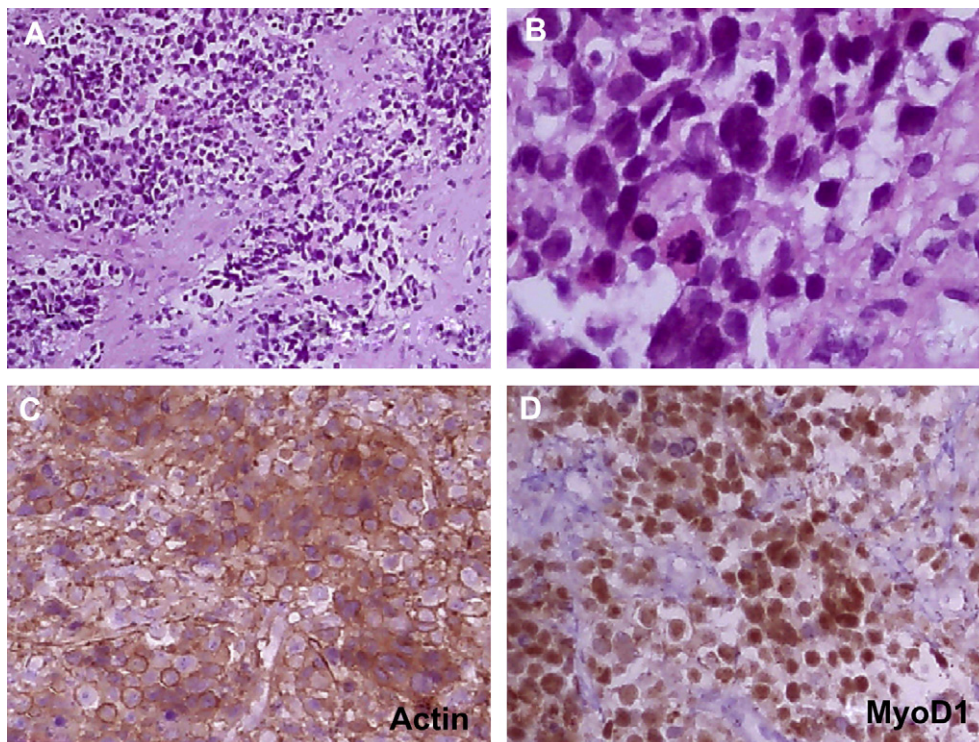


Fig. 2. (A) (B) In hematoxylin and eosin stain, there were many high nuclear/cytoplasmic ratio small blue round cells along connective tissue strands. (C) Muscle-specific Actin stain and (D) skeletal muscle specific MyoD1 stain were positive.

left frontal sinus, left nasal cavity, left maxillary sinus and left orbital cavity with crossing of the midline to involve the right ethmoid sinus, right frontal sinus and right nasal cavity. It also revealed intracranial extension with cribriform plate destruction to bilateral frontal base regions (Fig. 1A). Brain magnetic resonance imaging (MRI) showed a similar result (Fig. 1B).

Trans-nasal tumor biopsy was performed. In hematoxylin and eosin (H&E) stain, there were many high nuclear/cytoplasmic ratio small blue round cells along connective tissue strands. Muscle-specific Actin stain and skeletal muscle specific MyoD1 stain were positive (Fig. 2). Hence, the pathology result was rhabdomyosarcoma, alveolar type. Systemic survey including CT for neck, chest, and abdomen, T-spine MRI, bone scan, lumbar puncture, and abdominal ultrasound showed no evidence of lymph node metastasis or distant metastasis. The patient belonged to stage 3 by TNM staging system and clinical group III by Intergroup rhabdomyosarcoma study group (IRSG) clinical grouping system.^{3,4}

After complete work-up, the patient was enrolled in the Taiwan Pediatric Oncology Group Rhabdomyosarcoma 2007 High-risk Treatment Protocol (TPOG RMS 2007 high-risk protocol) for combined radiochemotherapy. He was enrolled in the high-risk protocol due to parameningeal tumors with evidence of base of skull erosion and intracranial extension. This protocol includes radiotherapy of totally 50.4 Gy in 28 fractions and chemotherapy with VAC (vincristine + actinomycin + cyclophosphamide) for a total of 44 weeks' treatment course (Table 1).

The patient's visual acuity in left eye decreased to no light perception, and left optic atrophy was noted at the beginning of treatment. His left eye proptosis subsided, and follow-up brain CT after 39 wks of treatment revealed regression of the mass lesion (Fig. 3). After the complete 44-wk treatment course, no grade 3 or grade 4 non-hematologic laboratory abnormalities developed, and no recurrence has been noted as of one year after treatment. The TPOG RMS 2007 high-

Table 1
TPOG RMS 2007 high-risk protocol with radiotherapy for totally 50.4 Gy in 28 fractions and chemotherapy with VAC (vincristine + actinomycin + cyclophosphamide) for a total of 44 weeks of treatment course

TPOG RMS 2007 High-risk treatment – VAC alone																						
1. Includes all patients with non-parameningeal primaries and patients with parameningeal primaries, stage 4 alveolar (any age) or embryonal ≥ 10 yr of age without evidence of intracranial extension, base of skull erosion, or cranial nerve palsy.																						
2. Includes all patients with parameningeal tumors with any of the following: (1) evidence of base of skull erosion, cranial nerve palsy, or intracranial extension or spinal cord compression, OR (2) any patient requiring EMERGENCY RT OR (3) physician's preference selection of VAC Alone Regimen.																						
3. Patients with evidence of intracranial extension (touch, displace, invade, distort, or signal abnormality of dura) OR any patient requiring EMERGENCY RT should have VAC chemotherapy and begin RT at week 0.																						
4. Patients with evidence of parameningeal tumors + any of the following: (1) skull base erosion, OR (2) cranial nerve palsy, OR (3) metastatic skull disease (displace or indent dura, compress brain parenchyma) OR (4) any patients with paraspinal tumors that touch or displace the cord, should have VAC chemotherapy and begin RT at week 15.																						
Week	0	1	2	3	4	5																
	V	V	V	V	V	V																
	A+	–	–	A+	–	–																
	C	–	–	C	–	–																
	←	RT (start day 0)													→							
Induction week	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	E**	
	V	V	V	V	V	V	V	V	E	V	V	V	V	V	–	–	–	V	V	V	V	
	A	–	–	A	–	–	A	–	V	–	–	–	–	–	–	–	–	A	–	–	V	
	C	–	–	C	–	–	C	–	A	–	C	–	–	C	–	–	–	C	–	–	A	
								L	←	XRT (week 15–22)						→						L
Continuation week	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44			
	V	V	–	V	–	–	V	V	V	V	–	–	V	V	–	V	–	–	–	E**		
	A	–	–	A	–	–	A	–	–	A	–	–	A	–	–	A	–	–	–	V		
	C	–	–	C	–	–	C	–	–	C	–	–	C	–	–	C	–	–	–	A		
																					L	

VAC (VCR max. 2 mg, AMD max. 2.5 mg, Cyc no max. limits).

V: vincristine 1.5 mg/m² iv.

A: actinomycin D 0.045 mg/kg iv 5 min one dose.

C: cyclophosphamide 2.2 g/m² IV 30 min.

Mesna: 60% of Cyc, either 20% at hr 0,4,8 or 60% CI 8 hr will do.

Age	VCR dose	AMD dose	Cyc dose
≥ 3 yr	1.5 mg/m ² iv push	0.045 mg/kg ² one dose iv	2.2 gm/m ² iv 30 min
≥ 1 yr and < 3 yr	0.5 mg/kg ² iv push	0.045 mg/kg ² one dose iv	73 gm/kg ² iv 30 min
< 1 yr	0.025 mg/m ² iv push	0.025 mg/kg ² one dose iv	36 gm/kg ² iv 30 min

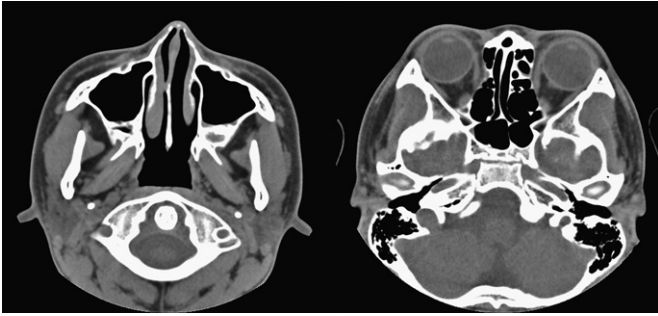


Fig. 3. Brain computed tomography after 39 weeks of treatment revealed the regression of the soft mass lesion.

risk protocol was approved by our institutional review board, and informed consent was obtained from patient and his parents.

3. Discussion

RMS is the most common soft tissue sarcoma and the most common primary orbital malignancy in childhood. The annual incidence is approximately 4.5 cases per million in children under the age of 20.¹ Among all areas in the body, the head and neck region is the most frequent site, accounting for 35–40% of cases.⁴ Among RMS of the head and neck in children, orbit accounts for 16%, and paranasal sinuses account for 10%.⁵ Due to their close proximity to the skull base and central nervous system, tumors in paranasal sinuses, infratemporal fossa, nasal cavity, middle ear, and nasopharynx are defined as parameningeal tumors.⁶ In nonmetastatic RMS, parameningeal tumor belongs to stage 2 or 3 and orbital tumor belongs to stage 1. The survival rate of RMS from parameningeal site is poorer than that from RMS from orbit.⁷

RMS from paranasal sinuses often presents with paranasal sinuses swelling, pain, proptosis, epistaxis, sinusitis, obstruction, and cranial nerve palsies.⁸ They are often advanced and locally invasive when the definite diagnosis is made,⁹ and the same situation was seen in our patient.

There are several major histology subtypes in RMS. Embryonal subtype accounts for nearly 70%, with better prognosis, and alveolar subtype accounts for more than 20% with a relatively poor prognosis.⁷ RMS involving the head or neck is the most common embryonal types, but recent studies revealed that sinonasal RMS is the predominant alveolar subtype.¹⁰ Hence, sinonasal RMS has poor prognosis probably due to the difficulty of surgical resection and alveolar histology.

In recent years, the survival rate of RMS has greatly improved with the multimodal therapy proposed by the Intergroup Rhabdomyosarcoma Study Group (IRSG). In non-metastatic RMS, the estimated 5-yr overall survival rate was 88% in embryonal type and 72% in alveolar type.⁷ Multimodal therapies include combined surgery, chemotherapy, and

radiotherapy. If a complete resection is possible, surgical removal of tumor with subsequent radiochemotherapy is suggested. Due to the impossibility of complete resection, our patient received combined radiochemotherapy.

Most RMS patients in Taiwan are enrolled in the ongoing TPOG RMS 2007 protocol. Patients are allocated to low-risk/intermediate-risk/high-risk group based on age, primary site, TNM stage, IRSG clinical grouping, lymph node status, and histology. Our patient belonged to the high-risk group due to parameningeal tumors with evidence of base of skull erosion and intracranial extension. His mass lesion regressed, and no recurrence was noted for one year.

Due to the multimodal therapy, RMS patients have a better prognosis than before. Hence, the early diagnosis of RMS is crucial due to the more effective current treatment protocol. Especially when a young patient presents with rapid unilateral proptosis, we should keep in mind the possibility of RMS.

We have presented a rare case of alveolar-type paranasal sinus and orbit RMS with intra-cranial invasion treated successfully with radiochemotherapy. Although his visual acuity in left eye was no light perception after initial radiotherapy, the tumor regressed without relapse for one year after the complete 44-wk treatment course. No grade 3 or grade 4 non-hematologic laboratory abnormalities developed during the treatment course. The long-term follow up and investigation is crucial.

References

- Li Jun, Thompson TD, Miller JW, Pollack LA, Stewart SL. Cancer incidence among children and adolescents in the United States, 2001–2003. *Pediatrics* 2008;**121**:e1470–7.
- Fyrmpas G, Wurm J, Athanassiadou F, Papageorgiou T, Beck JD, Iro H, et al. Management of pediatric sinonasal rhabdomyosarcoma. *J Laryngol Otol* 2009;**123**:990–6.
- Lawrence W, Anderson JR, Gehan EA, Maurer H. Pretreatment TNM staging of childhood rhabdomyosarcoma: a report of the intergroup rhabdomyosarcoma study group. *Cancer* 1997;**80**:1165.
- Crist WM, Anderson JR, Meza JL, Fryer C, Raney RB, Ruymann FB, et al. Intergroup rhabdomyosarcoma study-IV: Results for patients with nonmetastatic disease. *J Clin Oncol* 2001;**19**:3091–102.
- Hicks J, Flaitz C. Rhabdomyosarcoma of the head and neck in children. *Oral Oncol* 2002;**38**:450–9.
- MacArthur CJ, McGill TJ, Healy GB. Pediatric head and neck rhabdomyosarcoma. *Clin Pediatr* 1992;**31**:66–70.
- Meza JL, Anderson J, Pappo AS, Meyer WH. Analysis of prognostic factors in patients with nonmetastatic rhabdomyosarcoma treated on intergroup rhabdomyosarcoma studies III and IV: The children's oncology group. *J Clin Oncol* 2006;**24**:3844–51.
- Callender TA, Weber RS, Janjan N, Benjamin R, Zaher M, Wolf P, et al. Rhabdomyosarcoma of the nose and paranasal sinuses in adults and children. *Otolaryngol Head Neck Surg* 1995;**112**:252–7.
- Anderson GJ, Tom LW, Womer RB, Handler SD, Wetmore RE, Potsic WP. Rhabdomyosarcoma of the head and neck in children. *Arch Otolaryngol Head Neck Surg* 1990;**116**:428–31.
- Ahmed AA, Tsokos M. Sinonasal rhabdomyosarcoma in children and young adults. *Int J Surg Pathol* 2007;**15**:160–5.