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Treatment Results of Rhabdomyosarcomas of Head and Neck

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두경부의 횡문근육종에서 다방면요법의 효과

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최근 횡문근육종을 치료함에 있어서 수술적 요법, 방사선 치료, 항암 약물요법을 적절히 병행함으로써 치료에 따르는 후유증을 극소화하면서 괄목할만한 생존율 향상을 가져오게 되었다.

특히 두경부의 횡문근육종은 소아에서 다발하고 병소의 위치에 따라서 각각 다른 임상적 특성을 가지며 수술적 절제를 했을 때 기능 및 외견상 결손이 크므로 별도의 연구 대상이 되어 왔으며 수술적 방법보다는 방사선 치료 및 항암 약물요법이 강조되고 있다.

저자들은 1976년부터 1987년까지 두경부 횡문근육종으로 진단받고 연세 암센터에서 항암 약물요법 및 방사선 치료를 받은 22명의 환자를 대상으로 하여 발생 부위, 조직 병리, 병기별 분포 및 생존율, 치료 방법에 따른 생존율을 후향성으로 분석하였다. 22명의 환자중 10세 미만이 12예로 가장 많았고, 13명이 배아세포형이었으며, 임상병기는 병기 III이 가장 많아서 14예였다.

병소의 위치는 안와가 6명으로 가장 많았고, 뇌수막주변부가 7명(상악동 3명, 중이도 2명, 비강 1명, 비인강 1명), 기타 9명(경부 5명, 이하선 2명, cheek 2명)이었다.

5년 무병 생존율은 안와 종양에서 가장 높아서 50%였고, 안와외 두경부가 37.5%, 뇌수막주변부가 16.7%로 가장 낮았으며, 낮은 병기(병기 III), 배아세포형, 항암 약물 요법 병용군에서 상대적으로 높은 생존율이 관찰되었다.

KEY WORDS : Rhabdomyosarcoma · Radiotherapy.

Introduction

Rhabdomyosarcoma(RMS) is a highly malignant soft tissue sarcoma that can arise in any site of the body containing striated muscle or its mesenchymal anlage. Because RMS is protean in its presentation, site, stage and extent of disease, and pathologic characteristics of the tumor contribute to prognostic factors that influence therapeutic decisions. These factors are interrelated and best discussed as a function of specific site. The most frequently involved site is the head and neck area(43%)[1].

RMS of the head and neck is primarily a disease of childhood, as opposed to peripheral skeletal RMSs, which are more common in the 40~60 age group, and may be considered separately from other RMSs, as they create specific problems and have a distinct prognosis[2].

Radiation therapy can contribute significantly to the local control of the primary site. Surgical excisions of RMS of the head and neck area are usually not reasonable if one wishes to avoid mutilation or loss of function[3][4].

In recent years reports have called attention to the improved results in the management of RMS with coordinated, multidisciplinary treatment, and combined extended chemotherapy[4][5][6][7][8].

We have made pathological and clinical observations on 22 cases of RMS arising in structures of the head and neck. The following retrospective study was undertaken to evaluate site, stage and extent of disease, and pathologic characteristics of the tumor contribute to prognostic factors that influence therapeutic decisions.

Materials and Methods

Fifty-two patients with a diagnosis of RMS presented at the department of Radiation Oncology, Yonsei University Hospital from 1976 through 1987. Among them, 22(42.3%) had RMS originating in the head and neck(Fig. 1).

The site of the primary tumor are listed in Table 1. Six of 22 tumors originated in the orbit. The seven tumors occurred in the maxillary antrum, middle ear canal, nasal cavity, and nasopharynx (termed parameningeal sites). In nine patients, the primary site was in the cheek or adjacent area, i.e., parotid, neck or cheek.

The ages on admission ranged from eight months to fifty-eight years. The distribution of the patients by age is shown in Fig. 2. The presence of more female than male patients is not accord with the reports by most authors that male patients outnumber female patients slightly.

All patients were staged according to the Intergroup Rhabdomyosarcoma Study(IRS) grouping system, fourteen patients(63.6%) had stage III and 5(22.7%) had stage IV disease. There were only three patients(13.6%) who had stage I or II disease and received complete resection grossly(Table 2).

The histological distribution was analyzed in all patients except six, the embryonal form was most common, accounting for 81.2%(13 cases), and remainder were alveolar form and there was no pleomorphic form(Table 3).

Although radiation therapy and combination

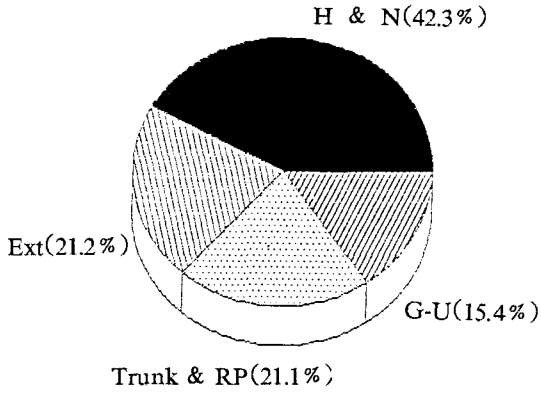

Fig. 1. Distribution of primary tumors.

Table 1. Distribution by site

Primary Site	No. of Pts.(%)
Orbit	6(27.3)
Parameningeal sites	7(31.8)
Maxillary antrum	3(13.6)
Middle ear canal	2(9.1)
Nasal cavity	1(4.5)
Nasopharynx	1(4.5)
Other Head & Neck	9(40.9)
Neck	5(22.7)
Parotid	2(9.1)
Cheek	2(9.1)
Total	22(100)

chemotherapy after the conservative surgery was recommended, five patients received postoperative radiation therapy only because of financial problem(Table 4).

All patients were treated with CO-60 teletherapy unit or 4MV Linac X-ray. The tumor volume was adequately delineated by physical examination, surgical findings, and radiographic procedures. The dose to the primary site was less than 5,000 cGy in seven cases, and more than 5,000 cGy in fifteen cases, delivered in daily fractions of 180 to 200 cGy, treating 5 days per week(Table 5).

Chemotherapy with VAC(Vincristine, Actinomycin-D, Cyclophosphamide) regimens was used for 3 months in 7 cases, 6 months in 4 cases, and more than 6 months in 6 cases (Table 6).

All patients continued to be examined by phy-

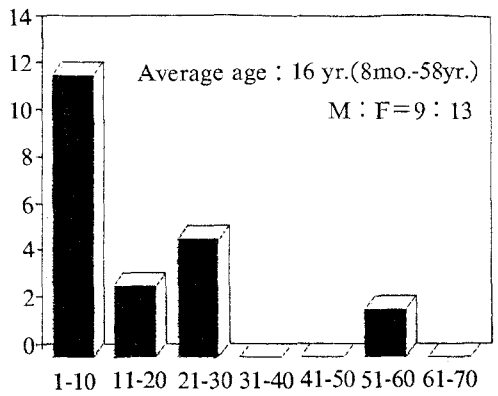

Fig. 2. Distribution by sge.

Table 2. Relationship of primary sites to clinical groups

Primary Site	Clinical Groups			
	I	II	III	IV
Orbit	0	1	3	2
Parameningeal	0	0	4	3
Other H & N	1	1	7	0
Total	1	2	14	5

Table 3. Relationship of primary sites to pathological subtypes for 16 patients*

Primary Site	Pathological Subtypes		
	Embry.	Alveo.	Pleom.
Orbit	5	0	0
Parameningeal	2	2	0
Other H & N	6	1	0
Total	13	3	0

*Exclusion of 6 Pts with undetermined pathological subtypes

Table 4. Treatment modalities

Primary Site	Treatment modalities	
	Op.+RT+CT	Op.+RT
Orbit	4	2
Parameningeal	5	2
Other H & N	8	1
Total	17(77.3%)	5(22.3%)

Table 5. Radiotherapy dose

Dose (cGy)*	No. of patients(%)
−2999	2(9.1)
3000−3999	2(9.1)
4000−4999	3(13.6)
5000−5999	9(40.9)
6000−	6(27.3)

*1.8−2 Gy/day, 5 days/wk

Table 6. Chemotherapy

−17/22(77.3%)

−Regimen : VAC(Vincristine, Actinomycin-D, Cyclophosphamide)

−Duration : −3 mo : 7 pts

3−6 mo : 4 pts

6 mo − : 6 pts

sical and radiological examination every 3 months during the first two years and at six-month interval thereafter. Survival was calculated from the start of radiation therapy to the date of death or the most recent follow-up date if the patient was alive. The survival curves were plotted using the life table method.

Results

The initial complete response rate for stage III patients was 50% as compared to stage IV patients with 0% (Table 7).

Local control was achieved in 85% (11/13) when patients were irradiated more than 5,000 cGy, as compared to 50% (3/6) with less than 5,000 cGy (Table 8).

The overall five-year disease free survival rates by primary site were 50% for orbital origin and 16.7% for parameningeal sites (Fig. 3).

The five-year survival rates for stage III and IV were 32.1% and 0%, respectively (Fig. 4).

The five-year survival rate for the embryonal subtype was 32.5% as compared to 0% for the alveolar form (Fig. 5).

The five-year survival rate was 33.3% when the combination chemotherapy was used, as compared to 0% when chemotherapy was not combined (Fig. 6).

Discussion

Although RMS may arise in virtually any site of the body containing striated muscle or its mesenchymal anlage, the most frequently involved site is the head and neck area (43%), in which 9% of tumors are confined to the orbit. Other common sites in the head and neck include the paranasal sinuses, oropharynx and nasopharynx, and the temporoparotid area[1].

RMS most commonly occurs in the childhood/adolescent years. There are two peak age frequences, one at age 2 to 6, primarily with tumor

Table 7. Response rate in patients of clinical group III & IV

Response	Clinical Groups		Total
	III (%)	IV (%)	
CR	7(50.0)	0	7(36.8)
PR	5(35.8)	2(40.0)	7(36.8)
NR	1(7.1)	2(40.0)	3(15.8)
PD	1(7.1)	1(20.0)	2(10.6)
Total	14(100)	5(100)	19(100)

Table 8. Response by RT dose

RT Dose	Response				Total
	CR	PR	NR	PD	
−2999	0	0	1	1	2
3000−3999	0	1	1	0	2
4000−4999	1	1	0	0	2
5000−5999	3	3	1	1	8
6000−	3	2	0	0	5
Total	7	7	3	2	19

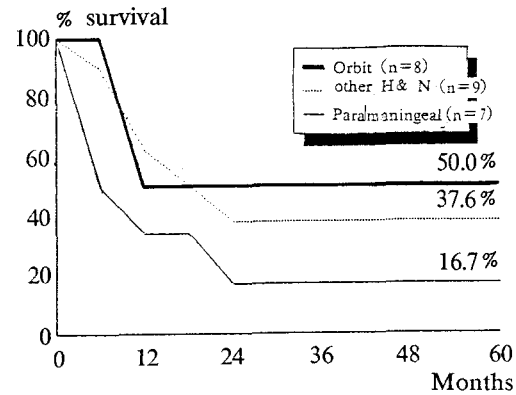

Fig. 3. Disease free survival rates by primary site.

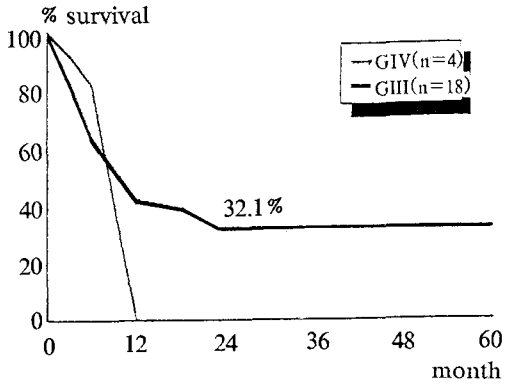

Fig. 4. Disease free survival rates by clinical group.

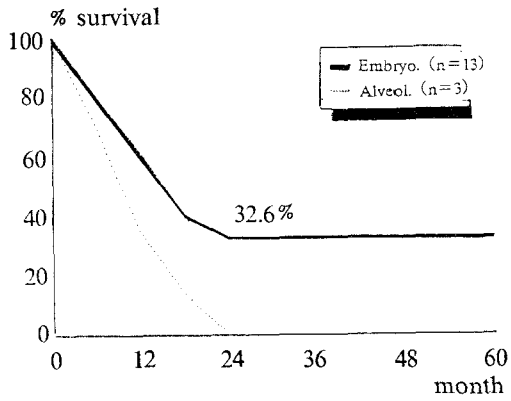

Fig. 5. Disease free survival rates by pathological subtype.

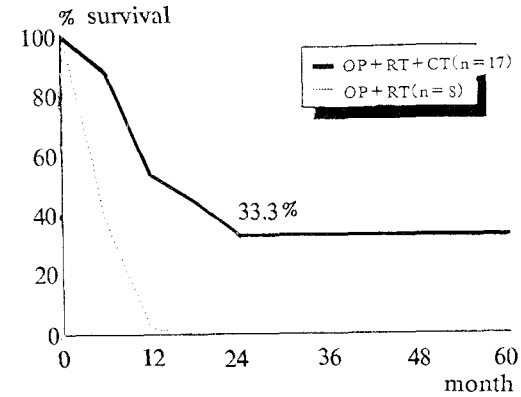

Fig. 6. Disease free survival rates by treatment modality.

of the head and neck, prostate, vagina, and urinary bladder : and one in adolescence, with tumors of the extremity, testis, or paratesticular tissues[2].

RMSs are classified into 3 histological types : embryonal, alveolar, pleomorphic. The embryonal is the most frequent type(70%) followed by the alveolar(20%), pleomorphic is the "adult" variety and is rarely described today. Embryonal RMS occurs most commonly in the head and neck region and is primarily a tumor of young children up to the age of 5. Alveolar RMS is more frequently seen in the extremities and are mainly tumors of adolescents and young adults from 10 to 25 years of age[5].

In general, progression of RMS seems to involve local structures early, and eventually spreads to distant sites by both hematogenous and lymphogenous flow[9]. The biological behavior of RMS, however, seemed to be greatly influenced by the anatomic location of the primary tumor and the histologic subtype[10]. The orbit is a frequent primary site and associated with a good prognosis[11][12]. Probably this is related to the paucity of lymphatics in the orbit and its bony confines, which makes wide invasion of tumor less likely and earlier diagnosis more probable. In contrast to the good prognosis of orbital lesions, tumors located in the nasal cavity, nasopharynx and maxillary antrum(termed parameningeal sites), irrespective of their histologic subtypes, have a poor prognosis presumably because of abundant lymphatics, ease of extension to neighboring structures, and lack of anatomical confines to the tumor.

It is known that lymph node metastases may appear in approximately 15% of extraorbital head and neck sites, most commonly when the nasopharynx is the primary site. Hematogenous metastases are detected at the time of presentation in approximately 20% of patients, the most common sites are the lung, bone marrow, bone, liver, distant muscle, and breast[13].

A multidisciplinary approach using surgery, irradiation, and chemotherapy is important in the management of RMS : however, the optimal sequence and specific application of each modality are still being investigated.

RMSs are invasive tumors that characteristically are poorly circumscribed and are surrounded by a pseudocapsule, which makes complete resection from normal surrounding tissue technically challenging and difficult to judge accurately.

The concept of "reasonable surgery" evolved, in which less destructive and disfiguring operative procedures were used[14]. Reasonable surgery implies removal of bulk tumor with maximal conser-

vation of anatomical structures, enhanced preservation of vision, voice, deglutition, and appearance in patients with primary tumors of head and neck.

Initial intensive chemotherapy is now being used as a means of providing pharmacologic debulking, potentially allowing for a more conservative surgical approach, or more localized radiation therapy. However, chemotherapy alone is not adequate to eradicate gross disease[15]. Among patients with head and neck primary tumors, 29% developed local recurrences with intracranial extension and died from locoregional uncontrolled disease. The most extensive experience in combination chemotherapy is with VAC or VAC plus Adriamycin(VACA).

Adequacy of irradiation implies careful attention to volume as well as dose. Because RMS tends to infiltrate tissue planes widely, tumors often extend beyond a fascial compartment, and when near the central nervous system, tend to extend to the meninges beyond the obvious visible margins. Treatment portals should be designed to encompass the involved region at the time of presentation before chemotherapy, with wide margins encompassing surgical sites and biopsy tracks.

High-dose irradiation is necessary to ensure local control even when multiagent chemotherapy is given. Local control of gross disease requires radiation doses of 50 Gy to 55 Gy, whereas microscopic disease can often be controlled with doses less than 50 Gy[16].

Conclusion

From the analysis of our own experience and literature review, we concluded as follows :

1) H& N RMS is far more common in children, and embryonal subtype is most frequent.

2) Better prognosis is suspected in orbital origin, embryonal subtype, and lower clinical group.

3) Combined modality therapy is recommended to improve cure rate and quality of life.

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