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Clinicopathologic and radiologic features of extraskeletal myxoid chondrosarcoma: a retrospective study of 40 Chinese cases with literature review

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ABSTRACT

The aim of this study is to describe the clinicopathologic and radiologic features of 40 cases of extraskeletal myxoid chondrosarcoma (EMC) from China. There were 25 males and 15 females (sex ratio, 1.7:1). Apart from an adolescent, all patients were adults with a median age of 49 years. Twenty-four tumors (60%) occurred in the lower limb and limb girdles, especially the thigh, followed by the upper limb and limb girdles (20%) and trunk (10%). Other less commonly involved locations included the head and neck, sacrococcygeal region, and perineum. Tumors ranged in size from 1.5 to 19 cm (mean, 7 cm). By radiology, they appeared as hypoattenuated or isoattenuated masses on computed tomography with hyperintense signal on T2-weighted magnetic resonance imaging. Intralesional hypointense septa were present in most cases. Of the 40 tumors, 30 belonged to the classic subtype, whereas 9 cases were cellular, and 1 case had a rhabdoid phenotype. Tumor cells showed variable expression of synaptophysin (36%), S-100 protein (29%), epithelial membrane antigen (11%), and neuron-specific enolase (7%). Ki-67 index was remarkably higher in the cellular variant (mean, 30%). EWSR1-related rearrangement was detected in 12 of 14 cases tested by fluorescence in situ hybridization using break-apart probes. The overall 5- and 7-year survival was 71% and 60%, respectively. Awareness of the imaging features may help pathologists in the diagnosis of EMC. Fluorescence in situ hybridization also serves as a useful diagnostic tool for EMC, especially in the distinction from its mimics.

1. Introduction

Extraskeletal myxoid chondrosarcoma (EMC) is a distinctive soft tissue sarcoma characterized by multinodular or lobulated growth of uniform eosinophilic spindled to ovoid cells arranged in interconnecting cords or strands forming reticular or fine net-like pattern in a stroma abundant with myxoid to chondromyxoid matrix. Extraskeletal myxoid chondrosarcoma was first described by Stout and Verner in 1953 [1] and formally defined as a distinctive entity by Enzinger and Shiraki in 1972 [2]. Despite the term, there is no convincing evidence of cartilaginous differentiation. As the cell line of differentiation remains uncertain, it is currently categorized under the tumors of uncertain differentiation in the revised World Health Organization classification [3]. This tumor type is very rare, comprising less than 3% of all soft tissue sarcomas [4]. Although EMC has been well described in Western countries [5–15], case series from China have not been documented in the English literature. We present here our experience with 40 cases of EMC, with an emphasis on the histopathologic and radiologic correlation and recent genetic findings. We also undertake a review of the literature and discuss the prognostic factors.

2. Materials and methods

Forty cases of EMC were retrieved from the consultation files and surgical pathology profiles of 3 affiliated hospitals from 2006 to 2014. The clinical data and pathologic findings were obtained from the medical record, pathology report, or discharge summary. The follow-up information was taken from the clinicians or referring pathologists or by direct telephone contact with the patients and/or patients' relatives when available. Four-micrometer-thick hematoxylin and eosin–stained sections were reexamined.

Immunohistochemical study was performed on 4-μm-thick unstained sections generated from formalin-fixed, paraffin-embedded tissue. The

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primary antibodies used in the study include vimentin (V9, dilution 1:50), S-100 protein (polyclonal, dilution 1:200), synaptophysin (SY38, dilution 1:100), neuron-specific enolase (NSE) (dilution 1:100), epithelial membrane antigen (E29, dilution 1:100), pancytokeratin (AE1/AE3, dilution 1:50), smooth muscle actin (1A4, dilution 1:200), desmin (D33, dilution 1:100), CD34 (QBEnd 10, dilution 1:100), and Ki-67 (MIB1, dilution). All antibodies were bought from Dako company (Dako A/S, Glostrup, Denmark). Pretreatment was carried out according to manufacturer's recommendation. Omission of primary antibody and substitution by nonspecific immunoglobins were used as negative controls. Appropriate positive controls were run concurrently for all antibodies tested.

Interphase fluorescence in situ hybridization (FISH) studies for the EWSR1 rearrangement were carried out in 14 cases. Five-micrometer-thick sections generated from formalin-fixed, paraffin embedded tissues were incubated in a humidified chamber (HYBriteTM system; Vysis, Abbott, Des Plaines, IL) using the LSI EWSR1 dual-color, break-apart probe (Abbott Molecular/Vysis) according to the manufacturer's protocol. The fluorescence signals were analyzed using an Olympus BX51 fluorescence microscope (Olympus, Tokyo, Japan).

For statistical analysis, the Kaplan-Meier method, the Cox proportional hazards regression model, and log-rank test were used.

3. Results

3.1. Clinical findings

The clinical features of 40 patients with EMC are summarized in the Table. There were 25 males and 15 females with a sex ratio of 1.7:1. Age at presentation ranged from 16 to 72 years (median, 49 years). Twenty-four tumors (60%) occurred in the lower limb and limb girdles. Of them, 16 (40%) were in the thigh, 3 cases each in the groin and buttock, and 1 case each in the knee and foot. Eight tumors arose in the upper limb and limb girdles (20%), 4 in the trunk (10%), 2 in the head and neck (5%), and 1 case each in the sacrococcygeal region and perineum (2.5%). The most common complaint was a painless mass which was accompanied by local pain and tenderness in approximately 1/3 cases. Duration of the process before clinical presentation ranged from 1 month to 3 years (median, 6 months).

All patients were treated with surgery, and 2 patients had an amputation of the involved limb. Six patients received adjuvant radiotherapy. One patient received 3 circles of chemotherapy (ifosfamide alternative with vincristine, dactinomycin and cyclophosphamide agents). Twenty-one patients were followed up with median follow-up duration being 37 months (range, 5-85 months). Tumor recurrence was identified in 13 patients (61.9%) at a median interval of 13 months (range, 1-

Table
Clinical features of 40 EMCs

Case	Age/Sex	Site	Size (cm)	Histology	EWSR1	Treatment	Outcome	Follow-up
1	49/M	Forearm	5	Cellular	ND	WLE	Rec 3 times	UA
2	43/M	Left thigh	9	Classic	Positive	WLE	Rec (85 mo)	AWD (85 mo)
3	40/F	Left thigh	10	Classic	Positive	WLE	Rec (3 mo)	DOD (47 mo)
4	45/M	Left groin	5	Classic	ND	WLE + RT	Rec (24, 36, 84 mo)	AWD (63 mo)
5	62/M	Right thigh	3	Classic	ND	WLE + RT	Rec (12, 24 mo), Met (lung, 62 mo)	AWD (76 mo)
6	52/M	Left shoulder	15	Cellular	Positive	WLE	UA	UA
7	52/M	Perineum	7.5	Classic	Positive	WLE + RT	ANED (43 mo)	ANED (43 mo)
8	67/F	Right shoulder	14.2	Cellular	Positive	WLE	ANED (37 mo)	ANED (37 mo)
9	50/F	Left forearm	10	Cellular	Positive	WLE + RT	Rec (1 mo)	DOD (6 mo)
10	21/M	Left groin	6	Classic	Positive	WLE + CT	Rec (3 mo)	DOD (21 mo)
11	55/M	Left upper arm	7	Classic	Negative	WLE + RT	ANED (5 mo)	ANED (5 mo)
12	69/M	Left thigh	UA	Classic	ND	WLE	Met (pelvis, 24 mo)	AWD (24 mo)
13	20/M	Right chest	UA	Cellular	ND	Surgery	UA	UA
14	16/F	Sacrococcygeal	UA	Cellular	ND	Surgery	UA	UA
15	61/M	Right thigh	UA	Classic	ND	Surgery	Rec (13 mo)	AWD (74 mo)
16	30/M	Right thigh	UA	Classic	ND	Surgery	UA	UA
17	69/M	Right upper arm	8	Rhabdoid	ND	WLE	Met (lung, 52 mo)	DOD (63 mo)
18	56/F	Right knee	UA	Classic	ND	Surgery	UA	UA
19	55/F	Right thigh	UA	Classic	ND	Surgery	UA	UA
20	28/M	Right thigh	UA	Classic	ND	Surgery	UA	UA
21	62/M	Left chest	5.5	Classic	ND	Surgery	UA	UA
22	45/M	Left thigh	UA	Classic	ND	Surgery	ANED (61 mo)	ANED (61 mo)
23	43/M	Right thigh	UA	Classic	ND	Surgery	Rec (60 mo)	AWD (60 mo)
24	53/F	Right thigh	UA	Classic	ND	Surgery	UA	UA
25	21/F	Left erector spinae	7	Classic	Positive	Surgery	UA	UA
26	49/F	Right foot	UA	Classic	ND	Surgery	UA	UA
27	72/M	Right buttock	8	Cellular	ND	Surgery	DOD (6 mo)	DOD (6 mo)
28	57/M	Right thigh	9	Classic	Negative	Surgery	Rec (13 mo)	DOD (25 mo)
29	46/F	Left thigh	UA	Classic	ND	Surgery	UA	UA
30	39/M	Right thigh	1.5	Classic	Positive	Surgery	ANED (30 mo)	ANED (30 mo)
31	50/F	Left forearm	10	Classic	ND	Surgery	UA	UA
32	25/F	Abdomen	2.5	Cellular	Positive	Surgery	ANED (26 mo)	ANED (26 mo)
33	37/M	Right thigh	19	Classic	ND	Surgery	UA	UA
34	37/F	Right neck	5	Classic	ND	Surgery + RT	Rec (24 mo)	AWD (24 mo)
35	28/F	Right elbow	UA	Classic	Positive	Surgery	UA	UA
36	72/M	Right groin	5	Cellular	ND	Surgery	UA	UA
37	47/M	Right buttock	6	Cellular	Positive	Surgery	ANED (22 mo)	ANED (22 mo)
38	54/M	Left parotid gland	4	Classic	ND	Surgery	UA	UA
39	51/F	Right buttock	UA	Classic	ND	Surgery	UA	UA
40	42/M	Right thigh	5	Classic	ND	WLE	Rec (48, 72 mo)	AWD (72 mo)

Abbreviations: AWD, alive with disease; ANED, alive with no evidence of disease; DOD, died of disease; Rec, recurrence; WLE, wide local excision; RT, radiotherapy; CT, chemotherapy; ND, not done; UA, unavailable.