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Anti-CD10 (56C6) expression in soft tissue sarcomas

Kemal Deniz*, Ganime Çoban, Turhan Okten

Department of Pathology, Erciyes University, Faculty of Medicine, 38039 Kayseri, Turkey

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ABSTRACT

CD10 is known to be expressed in certain types of leukemia, in lymphomas and also in various types of carcinoma. However, data regarding CD10 expression in soft tissue sarcomas is scarce. Two hundred and two retrospective soft tissue sarcoma specimens were evaluated for CD10 expression immunohistochemically. The clinical records of these patients were reviewed, and clinical data was obtained for all patients. Our results showed that 90 of the 202 cases were found to express CD10. 72% of malignant fibrous histiocytomas, 45% of fibrosarcomas, 34% of rhabdomyosarcomas, 50% of leiomyosarcomas, 22% of liposarcomas, 72% of malignant peripheral nerve sheath tumors, and 0% of the primitive neuroectodermal tumors were positive for CD10. Nearly half of the soft tissue sarcomas were found to express CD10. Stronger CD10 expression was found in high grade sarcomas.

Introduction

The common acute lymphoblastic leukemia antigen (CALLA) is a membrane-bound endopeptidase, and is expressed by lymphoid precursors, B lymphocytes. CD10 was initially described as a tumor-specific antigen for acute lymphoblastic leukemia [9]. Since its description, CD10 has also been found to be positive in other types of leukemia and lymphomas [11,15]. It has also been reported to be expressed in epithelial neoplasms, including renal cell carcinoma, hepatocellular carcinoma, gastric, and colonic adenocarcinoma [1,2,10]. However, little is known about CD10 expression in soft tissue sarcomas, and this topic has not been adequately addressed in the English literature. The lack of sufficient data in the literature encouraged us to conduct the present study.

Materials and methods

Study group

The records of the Pathology Department of Erciyes University Hospital were reviewed for soft tissue sarcomas collected between January 2000 and December 2010. A total of 202 cases, including surgical resection specimens and consultation cases, were selected for this study. The clinical data, including patient age, gender, clinical features and medical history, were obtained from the medical records. None of these patients received chemotherapy or radiation therapy prior to surgery.

Light microscopy and grading

The hematoxylin and eosin-stained sections were examined under a light microscope by two pathologists (KD, GC). All tumors were graded using the French grading system, which evaluates tumor differentiation, mitosis, and necrosis. Some of these parameters are used to define overall grade. The grading scheme is summarized in Table 1 [15].

Immunostaining

Formalin-fixed, paraffin-embedded tissue blocks and hematoxylin and eosin-stained slides were obtained from the archives of the Department of Pathology. One representative block was selected for immunohistochemical study. The 4-μm-thick sections were mounted on poly-L-lysine-coated slides and deparaffinized and hydrated through graded alcohol to water. Immunohistochemical staining was performed using antibody to CD10-clone 56C6 (Thermo Fisher Scientific, Fremont, CA) at 1:20 dilution with an incubation time of 30 min on a Ventana Benchmark autostainer. Cytoplasmic brown staining for CD10 was considered positive. The percentage of the CD10-positive tumor cells was scored as follows: focal <50% of the tumor cells and diffuse ≥50% of the tumor cells. The staining intensity of CD10 expression was graded as weak and strong.

Statistical analysis

All statistical analyses were performed with SPSS software package. The chi-square test was used to test the difference between the groups. $p < 0.05$ was regarded as statistically significant. Univariate analysis and multiple logistic regression analysis were used to test

* Corresponding author. Tel.: +90 532 492 22 38; fax: +90 352 651 61 77.
E-mail addresses: drkdeniz@yahoo.com, kdeniz@erciyes.edu.tr (K. Deniz).

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Table 1
Histopathological grading criteria for soft tissue sarcomas [7].

Tumor grade	Tumor differentiation	Mitosis count	Tumor necrosis
Grade 1 (2 and 3)	Sarcoma closely resembling normal adult mesenchymal tissue (1)	0–9/10 HPF (1)	None (0)
Grade 2 (4 and 5)	Sarcomas for which histological typing is certain (2)	10–19/10 HPF (2)	≤50% tumor necrosis (1)
Grade 3 (6–8)	Embryonal and undifferentiated sarcomas; sarcomas of uncertain type (3)	≥20/10 HPF (3)	>50% tumor necrosis (2)

the correlation between CD10 expression and grading parameters, tumor grade, and tumor cell pleomorphism.

Results

Clinical findings

A review of the clinical data revealed 90 female patients and 112 male patients. The median age was 53 years (range 1–101 years). Tumor size ranged from 1 to 40 cm in the greatest diameter (median 6 cm).

Light microscopy and grading

Among the 202 soft tissue sarcoma cases, there were 39 malignant fibrous histiocytomas, 40 fibrosarcomas, 34 leiomyosarcomas, 26 rhabdomyosarcomas, 23 liposarcomas, 14 primitive neuroectodermal tumors (PNET), 11 malignant peripheral nerve sheath tumors (MPNST), 6 synovia1 sarcomas, 3 alveolar soft part sarcomas, 4 epithelioid sarcomas, and 1 angiosarcoma and 1 clear cell sarcoma. When the grading scores were translated to an overall grade, 42 tumors were categorized as grade 1 (G1), 91 tumors as grade 2 (G2), and 69 tumors as grade 3 (G3). The scores of the grading parameters are summarized in Table 2. Pleomorphism, which is characterized by different nuclear sizes of tumor cells, was detected in 75 of the 202 tumors, determined at least three times.

Immunohistochemistry

Ninety of the 202 (45%) soft tissue sarcomas were found to express CD10. Sixty-five of these CD10-positive cases showed diffuse strong positivity, however, other 23 cases showed focal positivity (Fig. 1). Staining intensity and percentage of the soft tissue sarcomas are summarized in Table 3. Twenty-eight of the 39 (72%) malignant fibrous histiocytomas expressed CD10, and all of these cases displayed a diffuse and strong immunoreaction except for two cases. Eighteen of the 40 (45%) fibrosarcomas, 9 of the 26 (34%) rhabdomyosarcomas, 17 of the 34 (50%) leiomyosarcomas, 5 of the 23 (22%) liposarcomas, and 8 of the 11 (72%) MPNSTs were positive for CD10 (Fig. 2). All positive cases of MPNST displayed focal immunopositivity. Two cases (2/3) of alveolar soft part sarcoma, one case (1/6) of synovia1 sarcoma, one case (1/4) of epithelioid sarcoma, and one case (1/1) of angiosarcoma were found to be positive for CD10. None of the 14 PNET cases and only one clear cell sarcoma showed CD10 expression (Table 4).

Table 2
CD10 expression and parameters of the soft tissue grading scheme.

	CD10 positive	%	CD10 negative	%	Total
Differentiation					
1	1	9	10	91	11
2	29	37	50	63	79
3	60	54	52	46	112
Mitotic count					
1	33	33	66	67	99
2	28	51	27	49	55
3	29	60	19	40	48
Necrosis					
0	36	39	56	61	92
1	50	51	49	49	99
2	4	36	7	64	11
Grade					
1	11	26	31	74	42
2	38	42	53	58	91
3	41	59	28	41	69

Table 3
Staining intensity and percentage of the CD10-positive sarcomas.

		Staining intensity		
		Weak	Strong	Total
Percentage of the CD10 positive tumor cells	Focal (<50%)	13	10	23
	Diffuse (≥50%)	2	65	67

Tumor grade and CD10 expression

Tumor grade and CD10 expression correlate; 26% of the G1 tumors, 42% of the G2 tumors, and 59% of the G3 tumors showed CD10 expression (Fig. 3). Comparing the grades with one another, the *p*-values were as follows: G1 versus G2, 0.121; G2 versus G3, 0.038; G1 versus G3, 0.001.

Parameters of the sarcoma grading scheme were evaluated in correlation with CD10 expression. In terms of tumor differentiation,

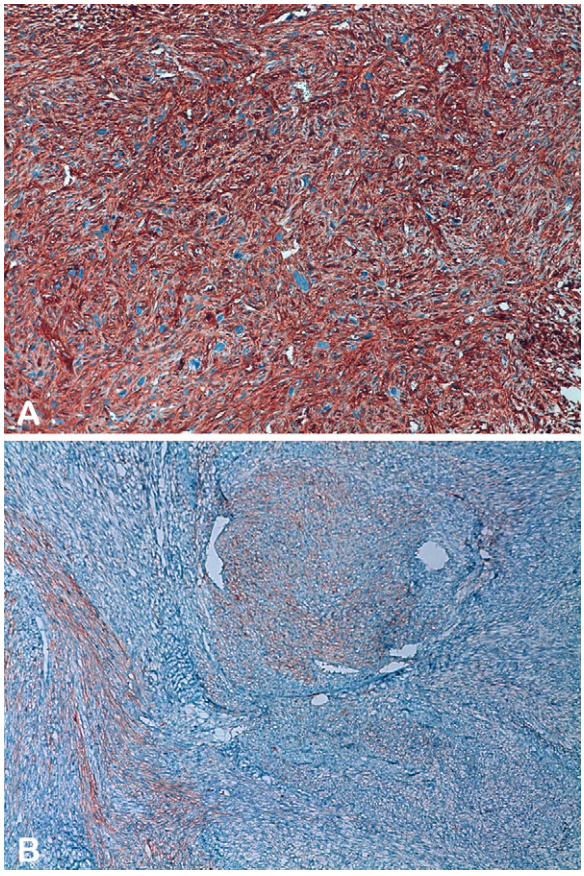

Fig. 1. Diffuse (A) and focal (B) CD10 expression (100×).

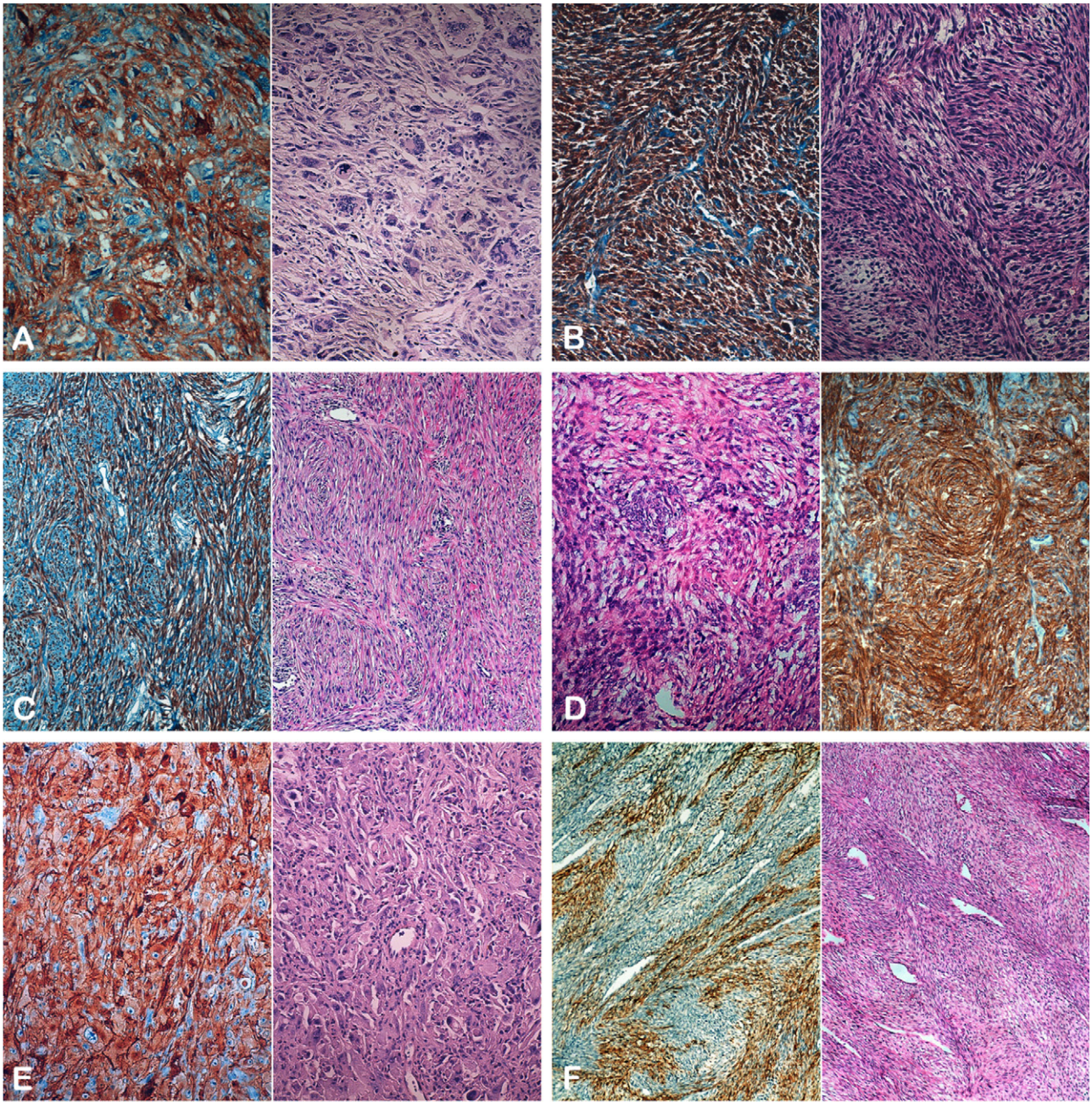

Fig. 2. CD10 expression in (A) malignant fibrous histiocytoma (200×), (B) leiomyosarcoma (200×), (C) fibrosarcoma (100×), (D) synovial sarcoma (200×), (E) rhabdomyosarcoma (200×), and (F) malignant peripheral nerve sheath tumor (100×). Hematoxylin and eosin histology of the same tumor was shown next to the immunohistochemistry image.

Table 4
CD10 expression in subtypes of 202 soft tissue sarcomas.

Tumor type	CD10 positivity	%
Fibrosarcoma	18/40	45
Malignant fibrous histiocytoma	28/39	72
Leiomyosarcoma	17/34	50
Rhabdomyosarcoma	9/26	34
Liposarcoma	5/23	21
Primitive neuroectodermal tumor	0/14	0
Malignant peripheral nerve sheath tumor	8/11	72
Synovial sarcoma	1/6	17
Epithelioid sarcoma	1/4	25
Alveolar soft part sarcoma	2/3	67
Clear cell sarcoma	0/1	0
Angiosarcoma	1/1	100
	90/202	45

10% (1/10) of score 1 tumors, 37% (29/79) of score 2 tumors, and 54% (60/112) of score 3 tumors were CD10-positive. There was a gradual decrease in CD10 expression in correlation with tumor differentiation. *p*-Values regarding the comparison of tumor differentiation scores with one another were as follows: score 1 versus score 2, 0.092; score 2 versus score 3, 0.027; score 1 versus score 3, 0.008. In terms of mitotic count, 33% (33/99) of score 1 tumors, 51% (28/55) of score 2 tumors, and 60% (29/48) of score 3 tumors were CD10-positive. There was a gradual increase in CD10 expression in correlation with mitotic count. *p*-Values regarding the comparison of the mitotic count scores with one another were as follows: score 1 versus score 2, 0.040; score 2 versus score 3, 0.427; score 1 versus score 3, 0.002. There was no significant difference in CD10 expression between the necrosis of score 0, score 1, and score 2.

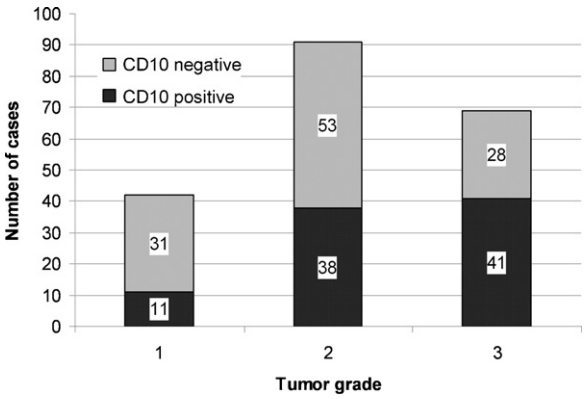

Fig. 3. CD10 expression and tumor grade.

Table 5
CD10 expression and tumor cell pleomorphism.

	CD10 positive	%	CD10 negative	%	Total
Pleomorphism-positive	56	75	19	25	75
Pleomorphism-negative	34	27	93	73	127

The tumor cell pleomorphism has shown a correlation with CD10 expression. Fifty-six of the 75 pleomorphic sarcomas showed CD10 immunopositivity, whereas only 34 of the 127 non-pleomorphic sarcomas were CD10-positive (Table 5). The difference between two groups was statistically significant ($p = 0.000$). In the univariate analysis, pleomorphism was the strongest predictive factor for CD10 expression, followed by tumor differentiation, tumor grade, and mitotic rate.

Discussion

CD10 immunohistochemistry has initially been used for the diagnosis of acute lymphoblastic leukemia, follicular lymphoma, and Burkitt lymphoma [9,16]. Thereafter, it was found to be a useful marker for renal cell carcinoma [1] and endometrial stromal cell tumors [12]. Chu and Arber tested a large number of non-hematopoietic neoplasms by using immunohistochemistry for CD10 expression, but they included only 46 soft tissue sarcomas in their study [3]. They found positive reaction in 9 of 46 (20%) cases of sarcoma (four cases of epithelioid sarcoma, three cases of rhabdomyosarcoma, one case of liposarcoma, and one case of leiomyosarcoma). However, malignant fibrous histiocytoma, PNET, MPNST, liposarcoma were not included in their study. The number of cases they studied was too small to comment on CD10 expression in soft tissue sarcomas. In our study, regardless of tumor type, soft tissue sarcomas showed CD10 expression in 45% of the tumors, which is higher than the rate reported by Chu and Arber (20%) [3]. Different types of soft tissue sarcomas, except PNET and CSS, express CD10 in varying percentages. Among the sarcomas, MFH expressed CD10 more frequently than the other types of sarcoma.

Previous studies on CD10 expression in soft tissue tumors predominantly focused on atypical fibroxhantomas (AFX) and uterine sarcomas. Mirza and Weedon were the first to report CD10 expression in 20 atypical fibroxanthoma cases [7]. Hultgren and DiMaio confirmed the expression of CD10 in a high percentage of AFXs (95%) [5]. They suggested using CD10 immunohistochemistry as a marker for the diagnosis of AFXs. However, in our study, we found lower expression of CD10 in MFHs (72%) compared to previously reported AFX case series (95–100%) [5,7]. It is difficult to conclude that CD10 is a diagnostic marker for AFX as suggested earlier. We believe that CD10 is not a lineage-specific antigen for AFX/MFH because other sarcomas can also display CD10 expression. CD10 expression in AFX/MFH is probably related to an aggressive tumor phenotype rather than to a tumor type. We found strong expression (50%) of CD10 in soft tissue leiomyosarcomas in contrast to the uterine counterparts. CD10 has been considered as a marker for normal and neoplastic endometrial stromal cells, which typically express CD10 [12]. CD10 has been reported as a useful marker for differentiating endometrial stromal sarcomas from uterine leiomyosarcomas [4]. Although CD10 has been considered as a marker for ESS, some studies have shown that uterine smooth muscle tumors may also express CD10 [8]. This study shows that the soft tissue leiomyosarcomas tend to have strong CD10 expression especially in pleomorphic cases. Half of the fibrosarcomas showed CD10 expression. CD10-positive fibrosarcomas were more cellularly and mitotically active than the CD10-negative cases. Approximately one third of the rhabdomyosarcomas were CD10-positive. Embryonal rhabdomyosarcomas with small undifferentiated cells tend to be CD10-negative, however, pleomorphic rhabdomyosarcomas tend to be CD10-positive. We found that CD10 expression was lower in liposarcomas than in the other common types of soft tissue sarcoma. Liposarcomas included in this study were mainly low grade tumors (well-differentiated liposarcomas, myxoid liposarcomas), and they did not show CD10 positivity. All PNETs were CD10-negative, similar to the embryonal rhabdomyosarcomas composed of small round blue cells. Eight of the 11 MPNSTs were found to be CD10-positive. Interestingly, all CD10-positive MPNSTs showed a focal expression pattern. Our data do not provide sufficient results on uncommon types of sarcomas, such as alveolar soft part sarcoma, epithelioid sarcoma, angiosarcoma, and clear cell sarcoma. However, CD10 positivity was found in some of these tumors.

We observed that strong CD10 expression in MFH is related to higher tumor grade rather than to the type of tumor. We also observed that the pleomorphic subtypes of rhabdomyosarcoma, leiomyosarcoma, and liposarcoma show stronger CD10 expression than the non-pleomorphic tumors. Our data revealed that higher tumor grade and tumor pleomorphism directly correlate with CD10 expression. Pleomorphic tumor cells displayed stronger immunopositivity than the non-pleomorphic cells in the same tumor. This observation also supports that CD10 expression may be related to aggressive phenotype.

CD10 had a key role for the differential diagnosis of renal cell carcinoma, and it has been reported to be positive in 94% of the classic renal cell carcinoma [1]. Renal cell carcinomas may undergo a sarcomatoid transformation, and the sarcomatoid component usually displays histological features closely resembling soft tissue sarcomas. CD10 positivity in sarcomatoid renal cell carcinoma is often conserved, similar to the classic renal cell carcinoma [6,14]. Our results show that CD10 cannot be used for the differential diagnosis of sarcomatoid variants of CD10-expressing tumors, such as sarcomatoid renal cell carcinoma, because high grade sarcomas may also express CD10. A recent study by Vennapusa et al. showed that sarcomatoid carcinomas display strong CD10 expression (82%), similar to soft tissue sarcomas (68%). They also demonstrated that stronger expression of CD10 was found in higher grade tumors, similar to the results of our study [13].

In conclusion, approximately half of the soft tissue sarcomas express CD10. CD10 is frequently expressed in pleomorphic and aggressive soft tissue tumors. CD10 is an unreliable tool to distinguish and differentiate high-grade soft tissue sarcoma and sarcomatoid tumors (e.g. sarcomatoid renal cell carcinoma). CD10 expression should be interpreted with caution since it is frequently expressed in soft tissue sarcomas.

Conflict of interest

All authors have no conflict of interest.

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