Quiz

Correct answer to the quiz. Check your diagnosis

Case report

Primary anaplastic large T-cell lymphoma of the psoas muscle

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Lymphomas presenting and mimicking soft-tissue masses are important to recognize, to avoid unnecessary treatment delays or extensive surgery. We describe a case of primary anaplastic large cell lymphoma (ALCL) arising from a deep skeletal muscle in a middle-aged male. He presented with a two-month history of swelling of his right thigh and mild fever, which led to a diagnosis of abscess formation. Antibiotics were prescribed for two weeks, with little improvement of symptoms. Subsequently, an exploratory surgery, with excision of the mass, demonstrated a ALCL of the psoas muscle, ALK-1 positive.

Key words: anaplastic T-cell lymphoma, ALK, psoas muscle.

Solution to quiz

The histological findings are consistent with a skeletal primary anaplastic large cell lymphoma (ALCL), ALK-1+.

Our patient underwent extensive hematologic and radiological diagnostic workup, which failed to show further site involvement. Bone marrow aspiration revealed normocellular marrow (50%) with adequate trilineage hematopoiesis, and no evidence of lymphoma, immunoglobulin heavy chain gene rearrangements, or immunoglobulin kappa light chain gene rearrangements.

Aggressive adjuvant chemotherapy based on 6 cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) scheme was started. The patient achieved complete response and the follow-up PET scans up to two years postchemotherapy treatment showed no evidence of recurrence. He is presently disease free, at 28 months following diagnosis.

Commentary

Anaplastic large cell lymphoma is a rare lymphoproliferative T-cell disorder, which accounts for 2-3% of non-Hodgkin's lymphomas (NHL) of the adult. It is relatively more common in the first three decades of life, particularly in childhood, where it accounts for up to 20% of NHL. It usually arises from lymph nodes, while primary extranodal locations are considered to be extremely rare.

Skeletal muscle involvement by lymphoma is unusual, most often occurring as a result of hematogenous or lymphatic spread or contiguous spread from

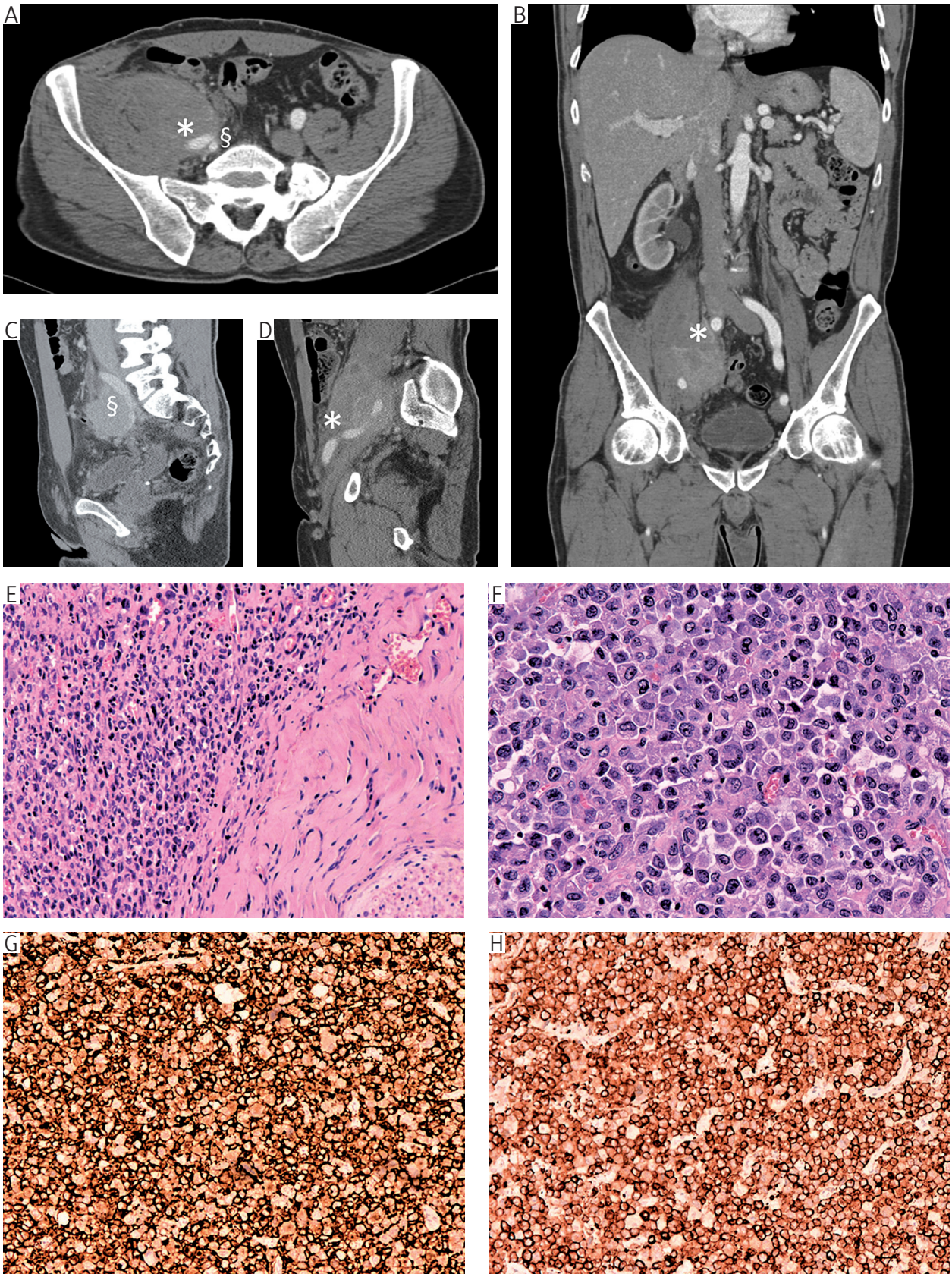

Fig. 1. Pre-operative CT scan axial view: A) showing the lesion encasing the right external iliac artery (*) at the level of common iliac artery bifurcation. The right internal iliac artery appears to be displaced (§); B) coronal view showing the encasement of the right external iliac artery (*); C and D) sagittal view showing the posteriously displaced right internal iliac artery (§) and the encased right external iliac artery (*) E) Microscopically, skeletal muscle fibers are infiltrated by large, pleomorphic lymphoid cell with prominent nucleoli and abundant cytoplasm. Marked cytological atypia, nuclear pleomorphism, and abundant eosinophilic cytoplasm can be noted. F) At higher magnification, occasional "doughnut cells", the hallmarks of ALCL, are observed (center). Note the background of lymphoid infiltrate (HE, 4× and 40×). G) Immunohistochemical staining of the lymphomatous cells for CD30 shows characteristic membrane and denser focal staining in the perinuclear, Golgi region of the cytoplasm. H) ALK-1 had an obvious diffuse cytoplasmic pattern of immunoreactivity in the tumor cells, as in the majority of the ALK+ ALCL

adjacent involved lymph nodes or bone [1]. The most commonly affected muscles are those of the extremities, pelvis, and gluteal regions. Lymphomatous involvement of muscles has been reported to occur in 0.3% of Hodgkin lymphoma and 1.1% of NHL (overall, 1.4% of cases) [1]. Primary skeletal muscle NHL (PSM-NHL) is an even rarer disease, accounting for only 0.5% of all extranodal lymphomas [2]. Using very stringent criteria in the selection of cases, Travis and coll demontrated that PSM-NHL accounted for only 0.11% of all lymphomas diagnosed at Mayo Clinic in a 10-year period of time [3].

An increased frequency of PSM-NHL (7%) is detected among AIDS-associated lymphomas [4].

The definition of primary extranodal lymphoma is controversial. Currently, an accepted definition is no or only minor nodal involvement associated with a clinically dominant extranodal component [5]. We reviewed the scientific literature for PSM-NHL. We chose to exclude cases of concurrent nodal, visceral or systemic disease, as well as instances with apparent direct extension from primary lymphoma of the bone on CT scans at presentation. In the selected published cases, diffuse lymphoma had been ruled out by CT of the thorax and abdomen, marrow aspirate, or at least 3-month follow-up reports. Cases with initial evaluation, not extensive enough to reasonably exclude disseminated disease were also discarded, as well as case series with no data on single patients. Using these inclusion criteria, our literature searches for PSM-NHL retrieved only 7 primary muscle ALCL and 51 other lymphomas (Table I).

Data show that PSM-NHL most commonly affects muscles of the lower extremities and pelvic region of elderly patients (6/8 ALCL; 32/51 other primary skeletal lymphomas; Table I). It usually presents as a localised mass [6], though cellulitis-like manifestations can be observed when involvement of the skin is present [7, 8]. Lymphoma may involve all or part of individual muscles and different degrees of involvement may be seen in different muscles in the same patient [9, 10]. A majority of patients show stranding in the subcutaneous fat, with a minority demonstrating overlying skin thickening. The age range is rather wide (6 to 93 years; mean 57.4 years), although PSM-ALCL included a younger patients'population (mean age 35,2 years vs. 60.8 years; Table I).

The present case illustrates a CD30+, ALK-1+, ALCL in the psoas muscle of an adult patient. Other subtypes include diffuse large B-cell lymphoma, peripheral T-cell lymphoma, natural killer T-cell lymphoma nasal type, follicular lymphoma and Burkitt lymphoma (Table I) [6]. Most reported cases (> 95%) are B-cell lymphomas, while our case was of T-cell lineage. In Chim's series of 17 cases of NHL with skeletal muscle involvement, 16 were of B-cell lineage and only 1 was an ALCL [11]. Overall, only few cases of PSM-ALCL have so far been described, and 62.5% of them arose in the first three decades of life (Table I).

Fig. 2. Gross appearance of the skeletal muscle infiltrated by a pinkish growth

ALCL, also known as Ki-1 (CD30+) lymphoma, is a non-Hodgkin lymphoma of T-cell origin, less often of null-cells type (younger presentation). It is predominantly an activated CD4+ T-cell tumor with an unusual cytotoxic TIA-1+, granzyme B+, perforin+, granulysin+, EMA+, punctate cytoplasmic clusterin+ phenotype. It frequently involves both lymph nodes and extranodal sites. The most common extranodal sites are skin, bone, soft tissues, lung and liver. Orbital, gastrointestinal and CNS involvement is occasionally seen. Marrow involvement is observed in 10% to 30% of cases [12]. Our case is peculiar in that no nodal involvement was present, and the mass appeared to arise within the psoas muscle. PSM-ALCL has also been described in dogs [13]. Three morphologic variants have been recognized: common, lymphohistiocytic, and small cell variant, all variants showing "hallmark" cells with eccentric horseshoe-shaped nuclei and an eosinophilic dense paranuclear region. Our case was of the common histological type.

Anaplastic large cell lymphoma is not EBV related, but can be associated with HIV, mycosis fungoides, pulmonary inflammatory pseudotumors. A subgroup of ALCL is characterized by recurrent t(2;5)(p23;q35) translocation, leading to the formation of a NPM-ALK fusion protein with proven oncogenic capacity. ALK-1+ ALCL is a clinically aggressive lymphoma that mostly occurs in young males [12], and carries a better prognosis than the negative ones after treatment with aggressive chemotherapy, with a 5-year survival as high as 80-90% [14]. So far no recurrent cytogenetic alterations have been described in ALK-1 negative ALCL. Fortunately, the present case showed immunohistochemical positivity for

Table I. Primary ALCL and other primary skeletal muscle lymphomas in the literature

Reference	Age	Sex	Muscle site	Spread	Size (cm)	Pathology/ALK status	Follow-up
[16]	16	♀	Sartorious	Fascial planes		ALCL/NR	NR
[11]	34	♂	R forearm	None			CHT; PR 4 years
[17]	8	♂	R gluteus	None	8	ALCL/ALK+	CHT, DF 7 years
[18]	14	♀	L major psoas and ileo-psoas	Skin	11	ALCL/ALK+	CHT, DF 4 years
[19]	51	♀	R gluteus maximus, iliopsoas, internal and external obturator muscle, biceps femoris, semimembranosus, semitendinosus	None	NR	ALCL/ALK–	Died 2 months
[20]	21	♂	R biceps femoris, vastus intermedialis, gluteus intermedius	None		ALCL/ALK–	CHT, died 11 months
[21]	83	♀	L psoas	None	2.5	ALCL/ALK–	NR
Study case	55	♂	R psoas	Iliac vessels, urether	9.5	ALCL/ALK+	DF at 16 months
[22]	84	♂	R psoas major muscle	None	10	DLBCL	Lost
[2]	60	♀	Gluteus maximus	Subcutaneous	3	MZL	RT; DF 3 years
	89	♂	L foot muscles	Subcutaneous	4	PTCL	CHT; died 13 months
[7]	55	♀	R hemisoma (shoulder girdle, intercostal muscles, latissimus dorsi, rhomboids, paraspinal muscles, psoas, iliacus muscles, muscles around the hip joint)	Rt pleural effusion, subcutis and dermis	NR	DLBCL	CHT Lost
[23]	56	♂	R sartorius	Sites of HM activity within abdominal wall, L vastus medalis, bilateral pelvic musculature, bilateral quadriceps at FDG-PET	5,6	PTCL, unspecified	CHT+stem-cell transplantation; DF 1 year

Table I. Cont.

Reference	Age	Sex	Muscle site	Spread	Size (cm)	Pathology/ALK status	Follow-up
[9]	66	♂	thigh muscles bilaterally	Subcutis	NR	IG centrocytic B-cell NHL	CHT, DF
	63	♀	R trapezius/ deltoid	Subcutis	NR	B-cell NHL	CHT
	68	♀	R glutei,	Pyriformis and obturator internus Enveloping the sciatic nerve and the ureter + subcutis	NR	DLBCL	CHT, DF
	31	♂	L & R glutei	Subcutis	NR	HG centroblastic B-cell NHL	HIV+, died 2 years (bil. pneumomonia)
	76	♂	R iliacus, psoas	None	NR	B-cell NHL	RT+CHT, lost
[24]	41	♀	R gracilis, adductor magnus, semitendinosus and sartorius muscles	Skin and subcutis	9 × 6.4	DLBCL	CHT, DF 1 year
[25]	72	♂	R gastrocnemius	None	10	DLBCL	CHT+RT, DF 16 months
[5]	17	♂	R paraspinal and gluteal musculature	Subcutis	NFM	DLBCL	Nr
[26]	60	♂	L pectoral muscle	Mediastinum and neck muscles	9	DLBCL	CHT, DF 6 months
[27]	61	♂	L masseter	Subcutis	9	B-cell, ingermediate grade	NR
[28]	42	♀	R soleus, lateral gastrocnemius	None	NR	PTCL, unclassified	CHT, DF 3 years
[6]	60	♂	Tight	NR	NR	DLBCL	NR
	71	♂	Trunk	NR	NR	BL	NR
	44	♂	Back	NR	NR	DLBCL	NR
	74	♀	Forearm	NR	NR	NK-T-cell, nasal type	NR
	57	♂	Forearm	Subcutis	NR	NK-T-cell, nasal type	NR
	70	♀	Hand	NR	NR	Peripheral T-cell	NR
	70	♂	Calf	NR	NR	Peripheral T-cell	NR
	37	♀	Foot	NR	NR	Peripheral T-cell	NR
	29	♂	Shoulder	NR	NR	DLBCL	NR
[29]	60	♀	Gluteus maximum	Subcutis	11	B-cell (BL?)	CHT, DF 18 months

Table I. Cont.

Reference	Age	Sex	Muscle site	Spread	Size (cm)	Pathology/ALK status	Follow-up
[30]	65	♀	Gluteus	NR	NR	DLBCL	CHT, died 14 months
	90	♂	Quadriceps	NR	NR	DLBCL	RT, Died 11 months
	61	♀	Quadriceps	NR	NR	DLBCL	CHT, DF at 46 months
	54	♀	Gluteus	NR	NR	DLBCL	CHT, DF 20 months
	90	♂	Biceps femuris	NR	NR	Indolent B-cell	Surgery, CR, 20 months
	52	♂	Popliteus	NR	NR	DLBCL	CHT, died 6 months
[31]	68	♂	L vastus lateralis	None	NR	DLBCL	CHT, DF 3 months
	29	♂	R biceps femoris, bilateral sartorious muscles	None	NR	Large cell follicular B-cell NHLin HIV+	CHT, DF 3 months
[32]	68	♂	R posterior tight, R posterior leg	Sciatic nerve, femural vessels	22 10	DLBCL	CHT, died 6 months
[33]	73	♀	Brachialis and biceps brachii	Subcutis	NR	IG B-NHL	NR
	41	♂	R obturator internus and externus, pettineus	None	NR	HG NHL	NR
[8]	77	♂	L adductor brevis	None	NR	DLBCL	Surgery, DF 1 year
[34]	84	♂	R tight	None	15		CHT, died 3 weeks (bronchopneumonia)
	44	♂	Back			DLBCL	
[35]	60	♀	Gluteal	NR	NR	Diffuse large T-cell	CHT+RT, DF
[36]	66	♀	Semitendineous, semimembranous	None	11.5	HG NH-B-cell	CHT, DF 3 years
[37]	31	♂	R leg	Soft tissues	19	DLBCL	CHT, DF 2 years
[38]	84	♀	3 masses in the anterior and L anterolateral abdominal muscles	None	12, 4, 4.3	DLBCL-GC	CHT, DF 10 months
[39]	65	♀	L gastrocnemius	Subcutis	15	Small, cleaved cells	RT
[40]	83	♀	R flexor digitorum longus	Subcutis	NR	B-cell	CHT

Table I. Cont.

Reference	Age	Sex	Muscle site	Spread	Size (cm)	Pathology/ALK status	Follow-up
[41]	77	♂	L triceps	Subcutis	9.5	DLC NHL(no IHC)	Incomplete excision
[42]	66	♂	Tight	NR	NR	Follicle centre cell	CHT, PR 30 months
	63	♀	Trapezius	NR	NR	Large B-cell	CHT, PR died 17 months
	93	♂	Biceps	NR	NR	Follicle centre cell	CHT, PR 3 years
[43]	6	♀	L pterygo-masseteric	None	NR	Lymphoblastic	CHT

ALCL – anaplastic large cell lymphoma; DLBCL – diffuse large B cell lymphoma; DLC – diffuse large cell; PTCL – peripheral T-cell lymphoma; NR – not reported, CHT – chemotherapy; DF – disease free; PR – partial response; RT – radiotherapy; CHT – chemotherapy; HG – high grade; IG – intermediate grade; NFM – no focal mass

ALK protein expression, and responded well to adjuvant chemotherapy.

Clinically, the most common presenting symptom is local pain, associated with a slow-growing or fast growing mass, or diffuse enlargement of the affected muscle. Lim *et al.* suggested that MRI is the most useful modality for assessment of muscular lymphoma, and the tumor will appear homogeneous and isointense to muscle signal on T1-weighted images, and diffusely hyperintense on T2 weighted images [15]. However, differentiation of skeletal muscle lymphoma from various neoplastic and inflammatory diseases is often difficult on the basis of clinical and imaging findings alone. On CT the masses can either be hypodense or isodense to normal muscle tissue, leading to confusion with muscle sarcomas. However, avid enhancement appears to be a universal feature [9]. Tumor biopsies are essential for definite diagnosis.

The treatment response and the prognosis of patients with PML are difficult to determine because of the low number of published cases and the lack of follow-up data. Our literature review shows that the three ALCL ALK+ patients were disease free at long-term follow-up (Table I).

In conclusion, although a rare tumor, primary skeletal muscle lymphoma should be considered in the differential diagnosis of a bulky skeletal muscle mass. As imaging cannot definitively establish the diagnosis of primary muscle lymphoma, a tissue biopsy with histological examination is required. When biopsy specimens are too difficult to acquire, fine-needle aspiration cytology becomes an acceptable alternative diagnostic procedure. Early recognition and correct diagnosis will allow the proper treatment protocol to be initiated.

The authors declare no conflict of interest.

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