Med & Health 2008; 3(1): 69-74

CASE REPORT

Anaplastic Large Cell Lymphoma Presenting as a Soft Tissue Mass – A Case Report

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ABSTRAK

Limfoma sel besar anaplastik (ALCL) adalah tumor yang jarang berlaku. Limfoma ini terdiri daripada kira-kira 3% daripada limfoma bukan-Hodgkin dewasa. Kerapkali ALCL sistemik primer melibat pada kedua-dua nodus limfa dan tapak ekstranodus. Seorang wanita berumur 44 tahun menampilkan dengan massa padat di bahagian fosa iliak kiri. Penemuan *ultrasound* menunjukkan massa tisu lembut *inhomogenous* yang agak berbatas jelas, berukuran 4x4x2.6cm di bahagian subkutanus dalam. Pemeriksaan histopatologi menunjukkan sel limfoid yang besar dengan nukleus yang atipikal, termasuk nukleus berbentuk ginjal. Sel neoplastik ini mengekspres ALK (pewarnaan pada kedua-dua sitoplasma dan nuklues), CD30 dan EMA tetapi penanda bukan pada sel-T (CD45RO dan CD3) dan sel-B (CD20 dan CD79α). Analisis hibridisasi in situ fluoresens (*FISH*) menunjukkan translokasi kromosom, t(2;5)(p23;q35). Berikutnya pesakit mengalami kesesakan nafas yang mendadak dan skan tomografi berkomputer torasik (CT) menunjukkan massa mengelilingi bronkus lobus atasan kanan. Pesakit juga mempunyai nodus limfa aksilari bilateral, berukuran 1 sm diameter (biopsi tidak dilakukan). Kawasan mediastinum dan endobronkus tidak menunjukkan sebarang keabnormalan. Pesakit menerima rawatan kemoterapi CHOP sebanyak 6 pusingan (*cycle*) dan pesakit ini sembuh daripada penyakit ini. ALCL jarang menampil sebagai tumor tisu lembut dan adalah disyorkan supaya penyakit ini dimasukkan dalam senarai sebagai diagnosis diferensial pada sebarang massa tisu lembut.

Kata kunci: limfoma anaplastik sel besar, massa tisu lembut

ABSTRACT

Anaplastic large cell lymphoma (ALCL) is a rare tumour, accounting for approximately 3% of adult non-Hodgkin lymphomas.[1] Primary systemic ALCL frequently involves both lymph nodes and extranodal sites. A 44-year-old woman presented with a firm, mobile mass in the left iliac fossa region. Ultrasound findings showed a well defined inhomogenous soft tissue mass, measuring 4x4x2.6cm in the deep subcutaneous region. Histopathological examination revealed that the mass was infiltrated by large lymphoid cells with marked nuclear atypia including kidney-shaped nuclei. These neoplastic cells expressed anaplastic

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lymphoma kinase (ALK) (both nuclear & cytoplasmic staining), CD30 and EMA but not for T-cell (CD45RO and CD3), and B-cell (CD20 & CD79α) markers. Fluorescence *in situ* hybridization (FISH) analysis showed a t(2;5)(p23;q35) chromosomal translocation. Subsequently the patient developed shortness of the breath and a thoracic computed tomography (CT) scan showed a mass encasing the right upper lobe bronchus. She also had bilateral axillary lymph nodes, measuring 1 cm in diameter (biopsy was not done). The mediastinum and endobronchial region did not show any abnormalities. She received 6 cycles of CHOP chemotherapy and remained disease free 2 years after diagnosis. ALCL, rarely present as a soft tissue tumour and this disease should be included as a differential diagnosis of any soft tissue mass.

Key Words: Anaplastic large cell lymphoma, soft tissue mass

INTRODUCTION

Anaplastic large cell lymphoma (ALCL) is a rare tumour, accounting for approximately 3% of adult non-Hodgkin lymphomas (Delsol et al. 2001). Three entities of ALCL have been identified: primary systemic ALK+ ALCL, primary systemic ALK- ALCL, and primary cutaneous ALCL (Stein et al. 2000). Primary systemic ALCL frequently involves both lymph nodes and extranodal sites. Extranodal sites commonly involve the skin (21%), bone (17%), soft tissues (17%), lung (11%) and liver (8%). Other rare sites include gut, central nervous system, parotid gland, pancreas and kidney (Delsol et al. 2001; Stein et al. 2000; Yamamoto et al. 2003; Cohen et al. 2003 & Venizelos et al. 2003).

The majority of soft tissue lymphomas are of non-Hodgkin B-cell type, including diffuse large-cell lymphoma, small lymphocytic cell lymphoma and follicular lymphoma (Knowles et al. 2003). Anaplastic large cell lymphoma is a T-cell or null cell phenotype, but shows evidence of T-cell genotype (Delsol et al. 2001).

We report a case of a 44-year-old female presenting with ALCL in the soft tissue.

CASE REPORT

A 44 year-old lady presented with a left iliac fossa mass of 3 weeks duration which was rapidly increasing in size recently. For the past 3 years she had constipation but she was otherwise asymptomatic. She had no other medical history or previous surgery.

On initial examination, there was a superficial soft to firm swelling which was slightly tender, measuring 4 x 4 cm in the abdomen. Ultrasound showed a fairly well defined inhomogenous soft tissue mass, measuring 4 x 4 x 2.6cm in the deep subcutaneous region in the left iliac fossa (Figure 1). Some posterior echo enhancement was present.

The following week the overlying skin was reddish in colour, associated with mild pain which became much worse later. She was afebrile, conscious and alert. The mass was slightly larger, measuring 5 x 6 cm. It was firm, mobile, fluctuant, slightly tender and the overlying skin was inflamed. The impression at this time was an anterior abdominal abscess and the patient was given a course of antibiotics. Aspiration yielded blood stained serous fluid.

Two weeks later she was readmitted to another hospital for shortness of breath and cough. A computed tomography (CT) scan showed a solitary right broncho-pulmonary mass in the upper lobe suggestive of bronchogenic carcinoma.
There was no mediastinal lymph node or endobronchial tumor seen but there were bilateral axillary lymph nodes, measuring one cm in diameter (no biopsy was available).

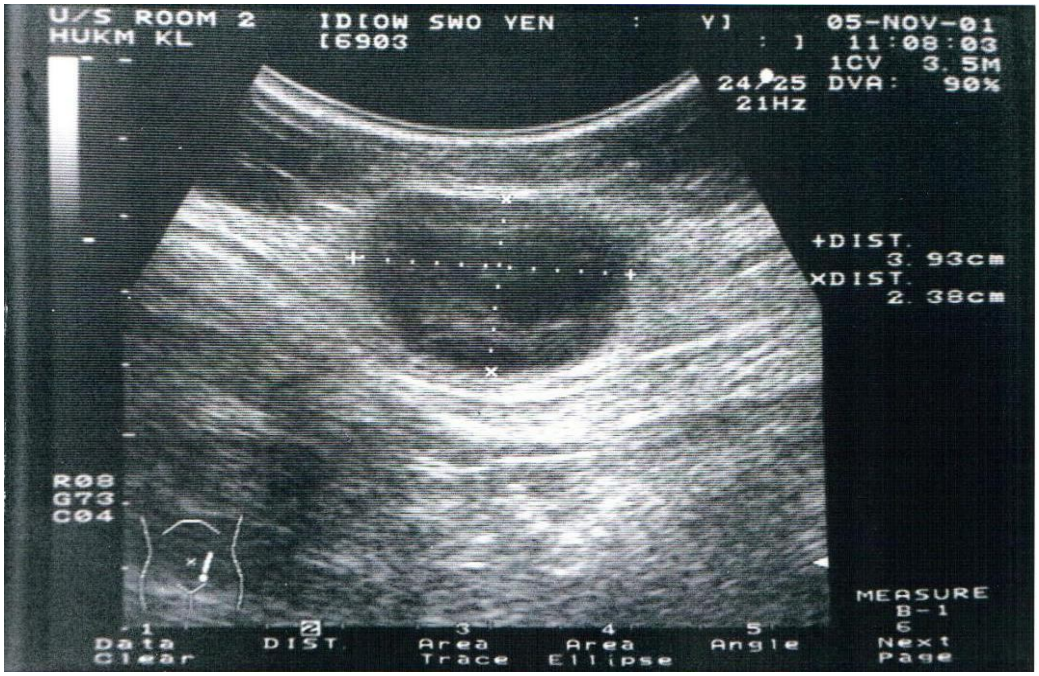


Figure 1: Ultrasound showed a fairly well defined inhomogenous soft tissue mass, measuring about 4x4x2.6cm in the deep subcutaneous region in left iliac fossa

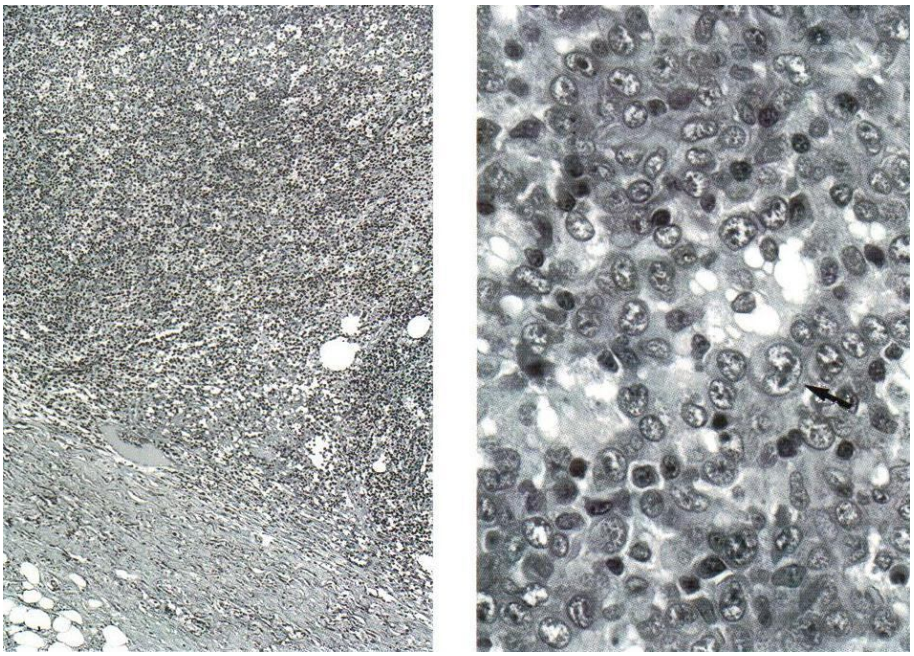
Excision biopsy of the anterior abdominal mass was performed and diagnosed histologically as lymphoplasmacytic lymphoma by the pathologist in the other hospital. The patient returned to Hospital universiti Kebangsaan Malaysia (HUKM) for further treatment. We received a block of the paraffin-embedded specimen and 4 µm thick sections were made. Histologic examination showed a circumscribed tumour mass infiltrated by large pleomorphic lymphoid cells displaying marked nuclear atypia, vesicular nuclei, and kidney-shaped and abundant cytoplasm (Fig. 2) in a background of macrophages, lymphocytes and plasma cells. Mitotic figures and areas of necrosis were present. Immunohistochemistry performed on formalin-fixed, paraffin-embedded sections using the avidin-biotin complex technique (Vector, Burlingame, CA) showed that the neoplastic cells expressed ALK protein in the nuclei and cytoplasm, and EMA. The neoplastic cells were negative for CD45RO, CD3, CD20 and CD79α (Table 1). The diagnosis was of ALK-positive anaplastic large cell lymphoma (common variant).

Fluorescence *in situ* hybridization (FISH) analysis was performed using the LSI ALK breakpoint-spanning and flanking dual-colour DNA probes (Vysis, Inc., Downers Grove, IL) (Bridge et al. 2001). A t(2;5) or other chromosome rearrangement at the 2p23 ALK breakpoint region would be indicated by one orange and one green signal, while the native ALK region will remain as an orange/green fusion signal (1O1G1F), [Fig.3].

She was at Stage IIA of the disease. The lactate dehydrogenese was raised to 535 U/l (Normal = 211-423 U/L) but there was no bone marrow infiltration. She was treated with CHOP (cyclophosphamide, vincristine, allopurinol and prednisolone) chemotherapy. One year later she deve-

Table 1.: Antibodies used in the immunohistochemical staining

Antibody	Source	Clone	Dilution
1. Alkaline protein (**ALK**)	DAKO	ALK1	1:100
2. CD30 (**Ki-1 antigen**)	DAKO	Ber-H2	1:25
3. Epithelial membrane antigen (**EMA)**	DAKO	E29	1:400
4. CD 45 RO	DAKO	UCHL-1	1:200
5. CD 3	DAKO	-	1:400
6. CD 20cy	DAKO	L26 Ab-1(L26)	1:1000
7. CD 79α	DAKO	JCB117	1:200



(A) (B)

Figure 2.: (A) Histologic examination showed the tumour mass is surrounded by fibrous tissue and adipocytes (Haematoxylin and Eosin, magnification x100). (B) These cells are large exhibiting pleomorphic and vesicular nuclei and abundant cytoplasm. Some of the nuclei are kidney in shaped Anaplastic large cell lymphoma showing large cells with eccentric kidney shape nuclei [(↑) H & E, x400]

loped pulmonary tuberculosis and was treated with anti-tuberculous drugs. She completed six cycles of CHOP chemotherapy and remains healthy at follow-up.

DISCUSSION

Lymphoma presenting as a soft tissue mass is rare and may thus be confused with the more common soft tissue sarcoma (STS) (Knowles et al. 2003 & Damron et al. 1999).

Damron et al (1999) reported that clinical and radiographic features that favor extranodal soft tissue lymphoma over sarcoma include pain and tenderness, lymphadenopathy (particularly when confluent radiologically), ipsilateral extremity

swelling and elevated lactate dehydrogenese (Damron et al. 1999). Another recent article suggested computed tomography scanning and core biopsy for such cases where the latter established a diagnosis in 13 out of 17 patients (sensitivity 93%) (Knowles et al. 2003). Our patient had pain, and tenderness. Lactate dehydrogenese was elevated.

Clinically, ALK-positive lymphoma mostly occur in children and young adults with a male predominance. It usually present as an aggressive, stage III-IV disease, frequently associated with systemic symptoms and extranodal involvement (Falini et al. 1999). In contrast, ALK-negative cases occur in older individuals (mean age, 44.33 years) and show lower male/female ratio (0.9) as well as a lower incidence of stage III-IV disease and extranodal involvement at presentation. Our patient was in the older age group and was ALK-positive.

The commonest sites for STS and extranodal lymphomas are the lower limbs, especially in the thigh (25%), retroperitoneum (16%), and upper limb (11%) (Knowles et al. 2003). Other unusual sites include the erector spinae muscle, the supraclavicular fossa and surrounding the wing of the ileum. Our patient presented in the left iliac fossa.

There was no confirmation of nodal involvement by histology in this patient, but the expression of ALK in an extranodal site favours systemic ALCL with (primary) nodal involvement (ten Berge et al. 2000). The definition of primary extra-nodal soft-tissue lymphoma is the presence of soft tissue lymphoma in a region not typically considered to be rich in lymph nodes (Knowles et al. 2003).

ALCL contain cells with eccentric, horse shoe- or kidney-shaped nuclei often with an eosinophilic region near the nucleus, referred to as hallmark cells (Delsol et al.

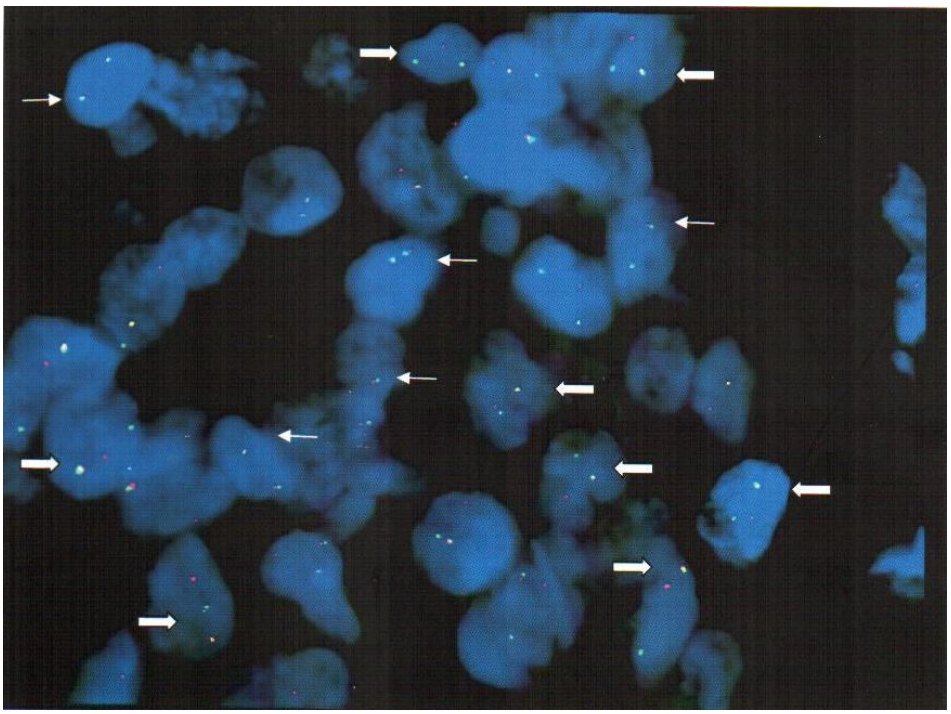


Figure 3: FISH showing nuclei with three signals are positive with the rearrangement (thick arrows) while nuclei with two fusion signal pattern lack the ALK gene rearrangement (thin arrows)

2001). The application of these stains, CD30 and ALK immunostaining is helpful in the diagnosis of ALCL. ALK expression can also be detected in inflammatory myofibroblastic tumours (IMT) and a variety of other non-inflammatory myofibroblastic tumours and soft tissue tumours (Li et al. 2004). Most cases, except the inflammatory myofibroblastic tumours, display low-level expression of ALK.

The most important prognostic indicator is ALK positivity, which has been associated with a favourable prognosis (Delsol et al. 2001). This patient is well till today.

The most frequent alteration of ALCL is the translocation, t(2;5)(p23;q35)), between the ALK gene on chromosome 2 and the nucleophosmin (*NPM*) gene on chromosome 5 (Delsol et al. 2001). The classic t(2:5) leads to positive staining for ALK in both the nucleolus and the cytoplasm. Similar findings have been reported in other studies (Delsol et al. 2001).

CONCLUSION

ALCL presenting as a soft tissue tumour is rare and it is important that it be included in the differential diagnosis.

ACKNOWLEDGEMENTS

The authors thanked Professor H.K. Muller Hermelink of the Institute of Pathology, University of Wurzburg, Germany, for confirmation of the diagnosis during the Precongress tutorial; a comprehensive course 'lymph node diagnosis' at the Third IAP Asia Pacific Meeting, Bangkok, Thailand, January, 2003, and also Encik Rosli Nasir of Hospital Universiti Kebangsaan Malaysia for the photographs.

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