Hong Kong J Radiol. 2012;15:15-20

ORIGINAL ARTICLE

Clinical Presentation and Radiological Features of Intrathoracic Non-Hodgkin's Lymphoma in Paediatric Patients: an Institutional Review

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ABSTRACT

Objective: *Non-Hodgkin's lymphoma is the most common tumour causing the superior mediastinal syndrome and superior vena caval obstruction in paediatric patients. Our objective was to review the clinical parameters, radiological features and outcomes of children presenting with intrathoracic non-Hodgkin's lymphoma and superior mediastinal syndrome in a tertiary cancer centre over a period of 11 years.*

Methods: *Retrospective review of clinical and radiological features of 11 patients with intrathoracic non-Hodgkin's lymphoma admitted to a tertiary children's cancer centre between 1999 and 2010 was undertaken.*

Results: *Most patients presented with superior mediastinal symptoms, including dyspnoea (n = 9, 82%) and neck swelling (n = 3, 27%). All the tumours were located within the anterior mediastinum. Their most common radiological features included heterogeneous enhancement (n = 7, 64%) and necrosis (n = 7, 64%). Neither abnormal fat/calcium nor chest wall invasion was evident in these patients. Associated complications included superior vena caval obstruction (n = 6, 55%) and tracheobronchial compression (n = 7, 64%). Correlation between clinical oxygenation status and radiological evidence of tracheobronchial compression was poor (Fisher's exact test, p = 0.49).*

Conclusion: *Data from this large patient cohort of paediatric intrathoracic non-Hodgkin's lymphoma in Hong Kong are presented. Non-Hodgkin's lymphoma is the most common tumour causing superior mediastinal syndrome in children, who usually present late in the course of the disease. This study illustrates the spectrum of clinical manifestations and associated findings in such children. Clinicians should have high awareness of these mediastinal symptoms and assess the risk of airway compromise by computed tomographic quantification.*

Key Words: *Child; Lymphoma, Non-Hodgkin*

中文摘要

胸部非何杰金氏淋巴瘤小兒患者的臨床症狀及影像特徵：一所機構的報告

梁凱瑩、黎家攸、成明光、李志光、朱昭穎

目的：非何杰金氏淋巴瘤是導致小兒縱隔綜合症及上腔靜脈阻塞一種常見病因。本研究回顧一所機構在11年內，患有上縱隔綜合症及胸部非何杰金氏淋巴瘤的小童的臨床症狀、影像特徵及治療結果。

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Submitted: 16 Nov 2011; Accepted: 14 Dec 2011.

方法：回顧1999年至2010年間，因胸部非何杰金氏淋巴瘤而到一所提供專科醫療服務的小兒腫瘤中心應診的11名病人的臨床症狀及影像特徵。

結果：大部分患者出現上縱隔綜合症的症狀，包括呼吸困難（9例，82%）及頸部腫脹（3例，27%）。所有腫瘤的位置均在前縱隔內。最常見的影像特徵包括不均勻強化（7例，64%）及壞死（7例，64%）。患者均無異常脂肪/鈣質或胸壁受侵的徵狀。有關的併發病包括上腔靜脈阻塞綜合症（6例，55%）及氣管支氣管狹窄（7例，64%）。臨床氧合狀態和氣管支氣管狹窄影像結果並無相關（Fisher確切檢驗，$p = 0.49$）。

結論：這是一項對於香港小兒胸部非何杰金氏淋巴瘤的大型研究。非何杰金氏淋巴瘤是導致小兒縱隔綜合症及上腔靜脈阻塞一種常見病因。患者通常在上縱隔綜合症晚期才到診。本研究顯示小兒上縱隔綜合症廣泛的病變臨床表現。醫生應對這些縱隔綜合症的症狀有高度警惕，應根據CT來量化評估呼吸道風險。

INTRODUCTION

Lymphoma constitutes approximately 15% of childhood malignancies and is the third most common cancer in children.[1-4] For those younger than 15 years, non-Hodgkin's lymphoma (NHL) is more frequent than Hodgkin's lymphoma.[2,3] NHL is also the most common tumour causing the superior mediastinal syndrome (SMS) in children.[5]

SMS and superior vena cava syndrome (SVCS) are often used synonymously to indicate the compression of vital structures of the superior mediastinum. Strictly, SVCS refers to compression, invasion, or thrombosis of the superior vena cava precluding venous blood return, while the term SMS is used when additional tracheal compression occurs leading to clinical symptoms such as cough, wheezing, or respiratory distress. Delayed diagnosis can be fatal, as these patients usually have compromised airway and / or a compromised circulation at presentation. Our objective was to review the clinical parameters, radiological features, and outcomes of children presenting with intrathoracic NHL and SMS in a tertiary paediatric cancer centre over an 11-year period.

METHODS

We retrospectively reviewed the database of the cancer centre from the period of 1999 to 2010, to identify patients aged 18 years or below at diagnosis, with radiological features of a mediastinal mass with histological confirmation of NHL. Corresponding medical records were reviewed to retrieve patient's age at presentation, gender, presenting symptoms and signs, oxygen requirement, treatment and outcome, diagnostic chest radiography, computed tomography (CT) findings, and pathology reports. On the CT, the radiological characteristics of the tumour, its size, the presence and degree of vascular and tracheal compression were recorded. Associations between clinical use of oxygen supplement and radiological evidence of tracheobronchial compression were analysed, using Fisher's exact test. A two-tailed significance level of 5% was used. Statistical analyses were performed using the Statistical Package for the Social Sciences (Windows version 19.0; SPSS Inc, Chicago [IL], US).

RESULTS

Fifteen paediatric patients with a mediastinal mass histologically proven to be NHL were identified, of whom 11 (8 males and 3 females) with full medical records were included in the analysis. Their mean age at presentation was 10 (range, 3-17) years. Histological diagnoses (T-cell lymphoblastic lymphoma in 8 and large cell lymphoma in 3) were retrieved from the electronic database (Table 1).

The presenting symptoms and signs of all 11 subjects are summarised in Table 2; most presented with mediastinal symptoms, including dyspnoea with or without orthopnoea (n = 9, 82%) and neck swelling (n = 3, 27%). Other symptoms were cervical lymphadenopathy (n = 4, 36%) and constitutional disturbance (n = 5, 45%). One patient presented with sudden cardiac arrest preceded by neck swelling for three days. These symptoms had evolved over 2 to 60 (mean, 12) days. The patients received oxygenation supplementation if the oxygen saturation (SaO_2) was lower than 95% on room air. Two patients required oxygen at presentation.

Table 1. Patient demographics and clinical outcome.

Patient No.	Gender / age (years)	Pathological diagnosis	Follow-up time (years)	Outcome
1	F / 16	Diffuse large B cell lymphoma	6	Clinical remission
2	M / 14	T cell lymphoblastic lymphoma	12	Clinical remission
3	M / 4	T cell lymphoblastic lymphoma	3	Deceased due to disease relapse
4	F / 5	T cell lymphoblastic lymphoma	-	Cardiac arrest during sedation for imaging-guided percutaneous biopsy
5	M / 9	T cell lymphoblastic lymphoma	7	Clinical remission
6	M / 17	Diffuse large B cell lymphoma	1	Deceased due to local disease progression
7	F / 11	T cell lymphoblastic lymphoma	-	Cardiac arrest on presentation
8	M / 3	T cell lymphoblastic lymphoma	3	Clinical remission
9	M / 14	Anaplastic large B cell lymphoma	5	Clinical remission
10	M / 3	T cell lymphoblastic lymphoma	4	Clinical remission
11	M / 11	T cell lymphoblastic lymphoma	1	Deceased due to disseminated disease

Table 2. Presenting signs / symptoms of patients with intrathoracic non-Hodgkin's lymphoma.

Sign / symptom	No. (%) of patients
Dyspnoea / cough	9 (82)
Stridor / wheeze	2 (18)
Neck swelling	3 (27)
Hoarseness of voice	1 (9)
Chest discomfort	2 (18)
Cervical lymphadenopathy	4 (36)
Fever	5 (45)
Sudden cardiac arrest	1 (9)

Table 3. Imaging features of mediastinal non-Hodgkin's lymphoma.

Imaging feature	No. (%) of patients
Location	
Anterior mediastinum	11 (100)
Superior mediastinum	10 (91)
Enhancement pattern	
Homogeneous	4 (36)
Heterogeneous	7 (64)
Necrosis	7 (64)
Fat	0
Calcium	0
Chest wall invasion	0
Pericardial effusion	1 (9)
Pleural effusion	4 (36)
Vascular encasement / compression	
Superior vena cava syndrome	6 (55)
Other major mediastinal vessels/pericardium	11 (100)
Tracheobronchial compression	7 (64)

The radiological features of these patients are summarised in Table 3. All the tumours were located within the anterior mediastinum, while superior mediastinal extension was noted in 10 (91%) of the patients. The average size of the tumours was 11.5 cm x 7.7 cm (trans-section x anteroposterior). Their most common radiological features included heterogeneous enhancement (n = 7, 64%) and necrosis (n = 7, 64%). Neither fat, calcium, nor chest wall invasion were evident in any of the lesions.

Superior vena caval obstruction was identified in six (55%) of the patients, with the mean smallest luminal diameter of 2.4 mm, ranged from 1 cm to complete occlusion. Tracheobronchial compression was identified in seven (64%) of the patients, with the mean smallest luminal diameter of trachea being 8 (range, 3-10) mm. Tracheobronchial compression was defined as decrease in luminal calibre compared to more normal luminal areas in other parts of the patient's trachea. Other identified complications were pleural effusion (n = 4, 36%) and pericardial effusion (n = 1, 9%).

Despite six patients demonstrating radiological evidence of superior vena caval obstruction and seven demonstrating tracheobronchial compression, only two (with SaO_2 <95%) were deemed to require oxygen. There was no statistically significant difference in the apparent need for oxygen in seven patients who demonstrated radiological evidence of tracheobronchial compression and four patients who did not (Fisher's exact test, p = 0.49).

In this cohort, two patients (18%) died of acute respiratory failure (one reaching the emergency department and one during sedation for ultrasound-guided percutaneous biopsy). Table 1 shows that six patients (55%) achieved disease remission after chemotherapy (mean survival, 4.6 years; standard deviation, 3.9 years), and three (27%) died of relapse/ disease progression (mean survival, 1.7 years; standard deviation, 1.2 years).

DISCUSSION

T cell lymphoblastic lymphoma was the most common histological subtype of NHL presenting with a mediastinal mass in our patient group, which is also consistent with the literature.[6] In our cohort, the majority of patients had a subacute onset of dyspnoea or cough followed by symptoms such as fever, lymphadenopathy, and neck swelling. Sudden deterioration is not infrequent. Therefore, high vigilance is needed when assessing paediatric patients who present with such symptoms and early chest radiography is crucial for initial management. In paediatric patients with isolated symptoms such as lymphadenopathy or neck swelling, intrathoracic pathology also needs to be excluded.

Most of the patients presented with a large anterior mediastinal mass, in which neither fat / calcium nor chest wall invasion was evident. These characteristics were also consistent with previous report,[6] and could help differentiate NHL from other mediastinal

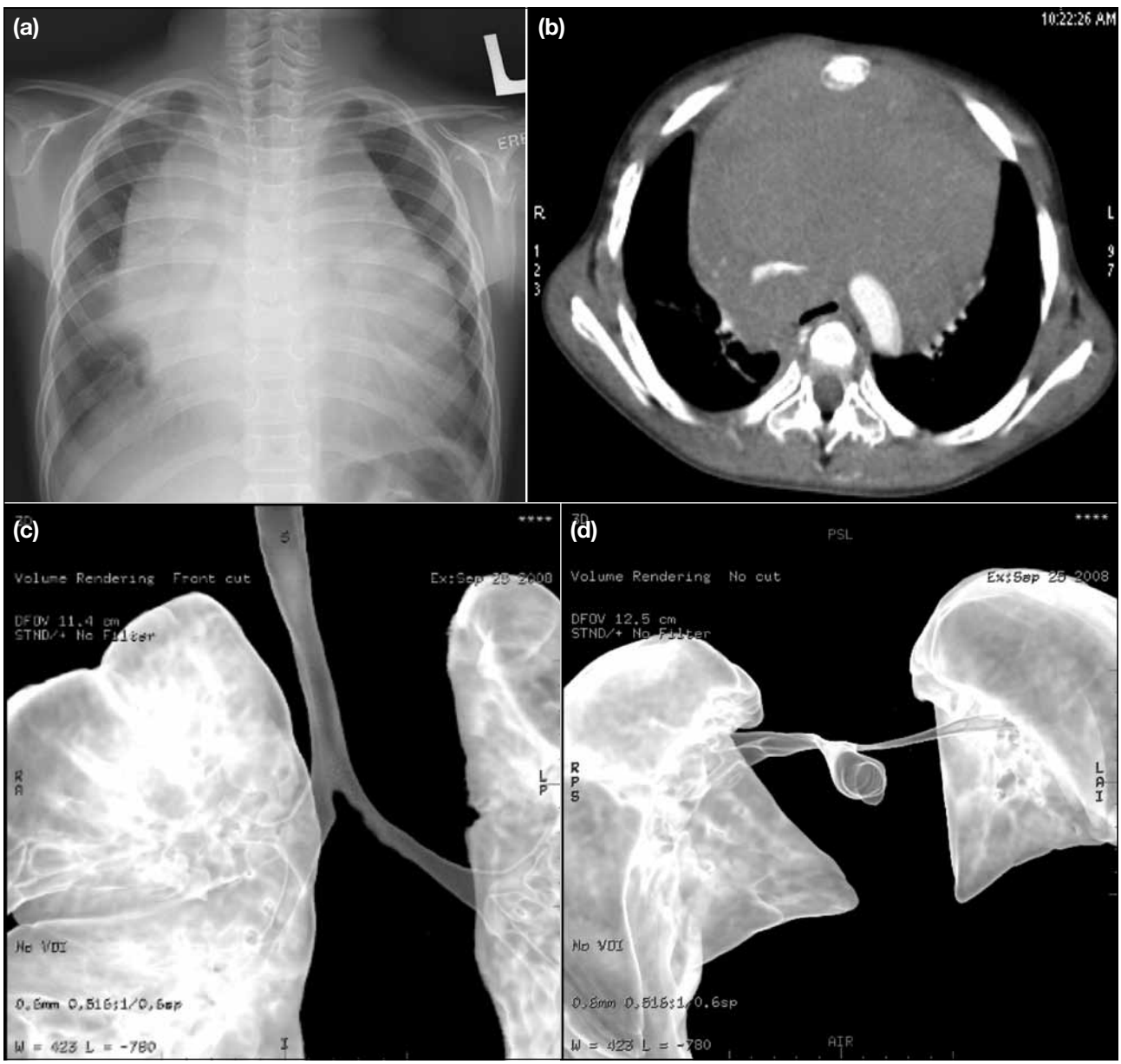

Figure. A 5-year-old patient presented with dyspnoea and developed cardiac arrest upon sedation for percutaneous biopsy. (a) A chest radiograph reveals a large mediastinal mass at presentation. (b) Contrast-enhanced computed tomographic thorax reveals a large anterior mediastinal mass compressing onto the trachea. (c and d) Volume-rendering reformatted images demonstrate severe compression onto the distal trachea and proximal left main bronchus (significant decrease in tracheobronchial area and diameter).

tumours. In other mediastinal tumours (e.g. germ cell tumour), calcifications and internal fat density are more frequently observed.

In our cohort, the majority of patients presented with superior mediastinal extension and encasement of the major vascular structure, leading to features of clinical SMS; 64% actually had demonstrable tracheobronchial compression. This high frequency of airway obstruction can be accounted for by the softer tracheal and proximal bronchial tissues in children being prone to compression by enlarged nodes.[7,8] However, oxygenation status was a poor clinical indicator for tracheobronchial compromise. Moreover, clinical symptoms are generally not predictive of the degree of airway compromise.[9] CT assessment of tracheobronchial status is therefore essential to identify children at risk for life-threatening airway compression whenever chest radiography shows a large mediastinal mass.[9,10]

Patients with compromised airways should be under close observation and intensively being monitored. A pathological diagnosis should always be reached using the least invasive approach and most readily accessible sites, such as the bone marrow or where there are superficial lymph nodes, and any necessary sedation should be undertaken with extreme care. Biopsy of the mediastinal mass should always be avoided, as airway compromise can be exacerbated by the supine position needed for the induction of general anaesthesia.[11-14] Moreover, such biopsy carries the risk of haemorrhage into mediastinum, which could lead to further compression of the soft trachea. If percutaneous mediastinal biopsy becomes necessary, for older children it is generally feasible to perform ultrasound-guided biopsy without sedation. For younger children, special measures and precautions should be implemented to assess anaesthetic risk. The literature indicates that children with mediastinal masses and associated severe tracheobronchial compression (>1/3 decrease in luminal cross-sectional area) are at high risk for total airway obstruction during general anaesthesia.[15] Regrettably, one patient in our series developed acute respiratory failure and cardiac arrest when sedated for ultrasound-guided percutaneous biopsy; the luminal cross-sectional area of her trachea was reduced by two-thirds (Figure). CT quantification of tracheal cross-sectional area has been suggested as a guide to the surgical and anaesthetic management of children with anterior mediastinal masses.[15,16] Radiologists should quantify the smallest dimensions (diameter and area) of the compressed trachea and stratify the severity with reference to normal non-compressed tracheas. For patients with severe tracheobronchial compression (>1/3 decrease in luminal area), the airway must be protected (by intubation or stenting) before any anaesthetic drug is to be given or biopsy to be taken. If the patient is not stable enough and no other alternative biopsy site is available, empirical treatment should be started. Biopsy can be performed as soon as the patient is stabilised.

CONCLUSION

Here we describe one of the largest cohorts of paediatric intrathoracic NHL in Hong Kong. NHL is the commonest tumour causing SMS in children, who usually present late in the course of the disease. Our report illustrates the spectrum of clinical manifestations and associated findings in such children. Clinicians should have high awareness of the clinical presentations in children with such mediastinal pathology and assess the risk of airway compromise quantitatively by CT.

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