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Pulmonary manifestations of Hodgkin's disease: radiographic and CT findings

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Abstract The aim of this study was to assess the radiological and CT findings in patients with pulmonary Hodgkin's disease and to analyse to what extent CT provides more diagnostic information. In 37 patients with 41 episodes of pulmonary manifestation of Hodgkin's disease (histological diagnosis: 11, clinical diagnosis: 30) 39 radiographs and 33 CT scans were analysed by two readers in consensus. Pulmonary nodules were recorded in 77 % of radiographs (CXR) and 88 % of CT scans. Nodules were multiple in 67 % (CXR) and 86 % (CT) and bilateral in 43 % (CXR) and 66 % (CT) of cases, respectively. Nodule size ranged from 2 to 100 mm. Of the nodules, 83 % at radiography and CT, respectively, were ≤30 mm, and again 83 % at radiography and CT, respectively, were irregularly marginated. Diffuse infiltration with and without nodules was less common. With pulmonary manifestations at initial diagnosis of Hodgkin's disease there was always hilar or mediastinal lymphadenopathy. Of 20 episodes, in which radiograph and CT had been obtained within 8 days, CT demonstrated pulmonary involvement when chest radiography was normal in 3 cases and demonstrated more lesions in 12 cases. The typical appearance of pulmonary HD consisted of multiple, irregularly marginated pulmonary nodules. Diffuse infiltration was less common. Computed tomography was superior to radiography not only in characterization of lesions but could also demonstrate pulmonary involvement when the radiograph was normal and should, therefore, be used liberally in addition to radiography.

Keywords Pulmonary nodule · Hodgkin's disease · CT · Chest radiography · Lung disease

Introduction

Pulmonary involvement with Hodgkin's disease (HD) is not uncommon. Of all cases with HD, lung involvement has been diagnosed in up to 20 % at initial diagnosis (secondary pulmonary lymphoma) [1, 2, 3, 4], 40 % during the clinical course of the disease [5, 6] and 60 % at autopsy [7, 8] due to relapsing disease (recurrent pulmonary lymphoma). Isolated pulmonary manifestation (primary pulmonary lymphoma) with no extrapulmonary lesions, however, is rare with, to our knowledge, less than 100 reported cases [9, 10, 11].

Lung involvement in HD is believed to occur through direct or lymphangitic extension from adjacent lymph nodes or through hematogenous spread [4, 12].

In the Ann Arbor Classification involvement of one lymph node region or extralymphatic site represents stage I, two lymph node regions on the same side of the diaphragm stage II and lymph node regions on both sides of the diaphragm stage III. Diffuse organ involvement is classified as stage IV. Accordingly, pulmonary

lesions of HD are regarded as stage IE (primary pulmonary lymphoma), stages IE, IIE, IIIE (extension of disease from adjacent lymph nodes into the lung) or stage IV (diffuse pulmonary involvement) [13].

The radiographic findings of pulmonary HD have been classified into: (a) bronchovascular-lymphangitic; (b) nodular; and (c) alveolar [1, 14].

Computed tomographic findings have, to our knowledge, been reported in series of less than 20 patients, mostly as part of the analysis of overall thoracic findings in HD [3, 15, 16].

The differential diagnosis of pulmonary abnormalities in patients with HD includes a variety of diseases such as infection, bronchoalveolar carcinoma, bronchiolitis obliterans organizing pneumonia, Wegener's granulomatosis, drug toxicity, and effects of radiotherapy [12, 15, 17]. Differentiation of pulmonary HD from other abnormalities is usually important for adequate therapy but may be difficult without lung biopsy [14].

The purpose of our study was to assess radiographic and CT findings in patients with proven pulmonary HD and to identify characteristic appearances, thereby facilitating a non-invasive diagnosis without lung biopsy.

In particular, we wanted to assess to what extent CT provided additional information over chest radiography.

Patients and methods

The Radiology Information System of the Department of Radiology and the database of the Department of Oncology were searched for patients with findings suggestive of pulmonary manifestations of Hodgkin's disease by searching for the term "Hodgkin" in combination with the terms "lung," "pulmonary," and "stage IV." The records of 430 patients found by this search were then reviewed to assess whether a final diagnosis of pulmonary manifestation had been made at the time of the patient's treatment.

Thirty-seven patients were identified in whom pulmonary involvement was diagnosed confidently and chest radiographs and/or chest CT scans were available for analysis. Fourteen patients were women and 23 men; age ranged from 17 to 63 years (mean age 33.4 years).

Four of the patients had pulmonary involvement on two occasions during the course of their disease, resulting in a total of 41 episodes of lung manifestation of HD.

Pulmonary involvement was diagnosed histologically in 11 episodes of 10 patients (percutaneous CT-guided needle biopsy 4, open-lung biopsy 5, postmortem study 2 of 8 pulmonary nodules, and 2 diffuse micronodular infiltrates) and clinically in 30 episodes of 27 patients. A clinical diagnosis of pulmonary involvement with HD was made as previously described by other authors if lung lesions were identified in the absence of signs of infection, effects of therapy or other causes, and responded to chemotherapy like extrapulmonary histologically proven manifestations of HD [7, 14, 16].

Histologic type of HD was nodular sclerosis in 28 and mixed cellularity in 9 patients.

No patient was considered stage IE, 2 were stage IIE, 2 were stage IIIE, and 33 were stage IV according to the Ann Arbor Classification. In 18 patients pulmonary involvement was diagnosed at the initial diagnosis of HD (secondary pulmonary lymphoma) and in 19 patients after a disease-free interval following therapy for extrapulmonary HD (recurrent pulmonary lymphoma).

In patients with recurrent HD the time interval between initial diagnosis and pulmonary manifestation ranged from 4 to 138 months (mean 36 months; Table1). The most advanced stage of HD before the diagnosis of pulmonary involvement in the patients with recurrent HD had been stage II in 3, stage III in 9, and stage IV in 7 patients.

One patient was HIV positive (patient 13); otherwise, there were no previous serious illnesses in the patients' histories.

All patients had evidence of extrapulmonary HD at the time of pulmonary involvement (Figs. 1, 2, 3, 4, 5, 6, 7).

The most common extrapulmonary manifestation was lymphadenopathy (mediastinal/hilar: 35 of 41 (85%), cervical 18 of 41 (44%), supra-/infraclavicular 10 of 41 (24%), axillary 10 of 41 (24%), abdominal/pelvic 9 of 41 (22%), and inguinal 2 of 41 (5%). All 18 patients with lung manifestation at the time of initial presentation had mediastinal or hilar lymphadenopathy.

Extralymphatic manifestations at the time of pulmonary involvement were osseous: 8 of 41 (20%); hepatic: 8 of 41 (20%); splenic: 6 of 41 (15%); pericardial: 6 of 41 (15%); pleural: 3 of 41 (7%); thyroid: 2 of 41 (5%); and cerebral: 1 of 41 (2%).

Thirty-nine of 41 episodes of pulmonary manifestation of HD were treated with chemotherapy, in 18 cases in combination with radiotherapy. In two episodes patients with recurrent disease did not agree to therapy (patients 5b and 9). In 18 episodes this resulted in complete response, in 16 in partial response, and in 7 in progressive disease.

Fifteen patients died during follow-up, including all 7 patients with progressive disease. Survival in these individuals ranged from 13 to 186 months (mean 57.2 months) following initial diagnosis of HD, and 3 to 65 months (mean 20.5 months) following diagnosis of pulmonary involvement.

Eighteen patients are alive with follow-up ranging from 24 to 168 months (mean 70.0 months) after initial diagnosis and 3 to 168 months (mean 65.6 months) after diagnosis of lung involvement.

Four patients who had responded to therapy with complete remission were subsequently lost from follow-up. The patients' characteristics are presented in Table 1.

Image analysis

Of the 41 episodes of pulmonary involvement with HD in 37 patients, chest radiographs could be assessed in 39 (34 conventional, 5 digital, ≥120 kVp, automatic exposure; posteroanterior and lateral: 37; posteroanterior: 1; anteroposterior supine: 1) and CT scans in 33 episodes. Computed tomography had been performed at different institutions with various CT scanners using sequential technique (collimation 8–10 mm, spacing 8–10 mm) in 25 and spiral technique (collimation 8–10 mm, pitch 1–2) in 8. Additional high-resolution images (collimation 2 mm, spacing 10 mm) had been obtained in 2 cases. Intravenous contrast (50–200 ml with different injection/infusion protocols) was administered in 26 CT scans. Seven scans were unenhanced.

Two board-certified radiologists reviewed chest films and CT scans and assessed the findings in consensus, recording pulmonary abnormalities as well as axillary, hilar, or mediastinal lymphadenopathy, pleural effusion or thickening, and skeletal and upper abdominal pathology in a standardized form.

During analysis of each episode findings at the chest film were always recorded first without knowledge of the CT findings. Sub-

Table 1 Clinical features of patients with pulmonary manifestations of Hodgkin's disease. *M* male; *F* female; *H* histology; *C* clinical diagnosis; *CT* CT-guided percutanous biopsy; *OLB* open-lung biopsy; *PM* postmortem; *FOB* fibreoptic bronchoscopy; *NS* nodular sclerosis; *mixed* mixed type; *E* extralymphatic site; *A* alive; *D* dead; *L* lost from follow-up; *ID* initial diagnosis, (1–4)/*RD* (1–4 episodes of) recurrent disease; *C* chemotherapy; *R* radiotherapy; *M* mediastinal; *S* supraclavicular; *I* infraclavicular; *AX* axillary; *C* cervical; *ABD* abdominal; *I* inguinal lymphadenopathy

Patient no.	Age (years)	Gender	Type	Modality of diagnosis	Stage of hd	ID/RD	Time interval between initial diagnosis of HD and pulmonary manifestation (previous therapy)	Extrapulmonary manifestations at time of pulmonary involvement	Outcome (follow-up in months)
Initial diagnosis, pulmonary manifestation diagnosed clinically									
1	25	F	NS	C	IV B	ID	–	M, C, S, AX, ABD, spleen, skeletal	A, 91
2	46	M	Mixed	C	IV B	ID	–	M, S, C, liver	A, 84
4	43	M	Mixed	C	IV B	ID	–	M, S, C, ABD spleen, liver, skeletal pericardium	D, 13
6	53	F	NS	C	IV B	ID	–	M, C, AX	D, 65
8	38	F	NS	C	IV B	ID	–	M, C, AX, I	A, 105
10	41	M	NS	C	IV B	ID	–	M, C, AX, I, pleura	A, 47
12	59	M	Mixed	C	IV B	ID	–	M, soft tissue	A, 30
13	30	M	Mixed	C	IV E	ID	–	M, C	A, 96
14	17	F	NS	C	IV BE	ID	–	M, AX, pleura, pericardium	A, 108
15	28	M	NS	C	IV B	ID	–	M, C, ABD, S, thyroid	A, 55
16a	39	M	NS	C	IV BE	ID	–	M, S	A, 41
23	33	M	NS	C	IV B	ID	–	M, spleen, liver, pericardium	A, 38
24	34	M	NS	C	IV B	ID	–	M, S, skeletal	A, 81
32a	22	M	NS	C	IV B	ID	–	M, C, pleura	A, 39
34	19	M	NS	C	IV B	ID	–	M, C, S, AX,	A, 114
35	28	M	Mixed	C	IV BE	ID	–	M, C, I, ABD, liver pericardium	A, 16
37	54	M	NS	C	IV B	ID	–	M, C, S,	L
Initial diagnosis, pulmonary manifestation diagnosed pathologically									
28	24	F	NS	H/CT	II AE	ID	–	M, C, S	A, 168
Recurrent disease, pulmonary manifestation diagnosed clinically									
3	24	F	NS	C	IV B	1. RD	11 months, CTx	S	D, 8
5a	61	F	NS	C	IV B	1. RD	40 months, Rx	C, liver, skeletal	D, 48
5b	63	F	NS	C	IV B	2. RD	70 months, Rx	AX	D, 18
9	24	M	Mixed	C	IV B	1. RD	26 months, Rx/CTx	M, spleen, liver skeletal, soft tissue	D, 20
11	33	F	NS	C	IV A	1. RD	20 months, Rx/CTx	M, H, ABD	A, 3
16b	40	M	NS	C	IV A	1. RD		M, S	A, 24
18	36	F	Mixed	C	IV B	4. RD	138 months, Rx/CTx	M	D, 34
19	39	F	NS	C	IV B	1. RD	14 months, Rx/CTx	M, C, thyroid	D, 14
20	19	M	NS	C	IV A	2. RD	39 months, Rx/CTx	M, ABD, pericardium	D, 20
26	18	M	NS	C	IV A	1. RD	10 months, Rx/CTx	M, C, ABD, spleen, liver, skeletal	A, 54
27	47	F	NS	C	III AE	4. RD	96 months, Rx/CTx	M, C	L
30	36	F	NS	C	IV B	3. RD	97 months, Rx/CTx	M	D, 3
36	31	M	NS	C	IV B	4. RD	71 months, Rx/CTx	M	D, 33
Recurrent disease, pulmonary manifestation diagnosed pathologically									
7	19	F	NS	H, PM	IV A	1. RD	17 months, Rx/CTx	M, ABD, spleen, liver, cerebral	D, 33
17	20	M	Mixed	H, PM	IV B	1. RD	16 months, Rx/CTx	AX, ABD, soft tissues	D, 5
21	42	M	NS	H, OLB	IV A	1. RD	9 months, Rx/CTx	M, C, skeletal	D, 5
22a	29	M	NS	H, CT	IV A	1. RD	24 months, Rx/CTx	M	D, 18
22b	30	M	NS	H, FOB	IV A	2. RD	36 months, Rx/CTx	M, C, H	D, 5
25	23	M	NS	H, OLB	IV B	2. RD	50 months, CTx	M, C	A, 9
29	27	M	Mixed	H, OLB	IV A	1. RD	4 months, CTx	M, C, skeletal	L
31	35	F	NS	H, CT	III BE	2. RD	14 months, Rx/CTx	M	D, 6
32b	24	M	NS	H, OLB	IV A	1. RD	22 months, Rx/CTx	M	A, 17
33	30	M	NS	H, OLB	II BE	1. RD	39 months, CTx	M	L

Two episodes of pulmonary manifestations in 4 patients each (patients 5a,b; 16a,b; 22a,b; 32a,b)

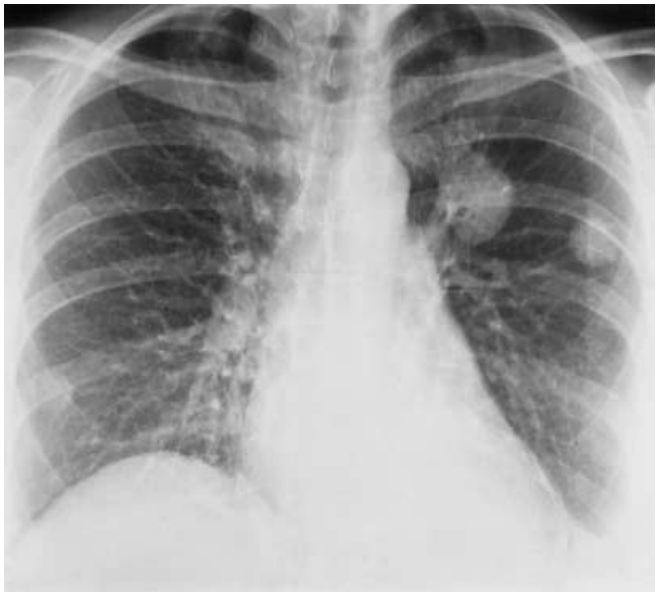


Fig. 1 A 39-year-old female (patient 19) with recurrent nodular sclerosing Hodgkin's disease (HD) and clinical diagnosis of pulmonary involvement. Chest radiograph: two smoothly marginated nodules in left mid-lung zone, one smoothly marginated nodule in right lower lung zone

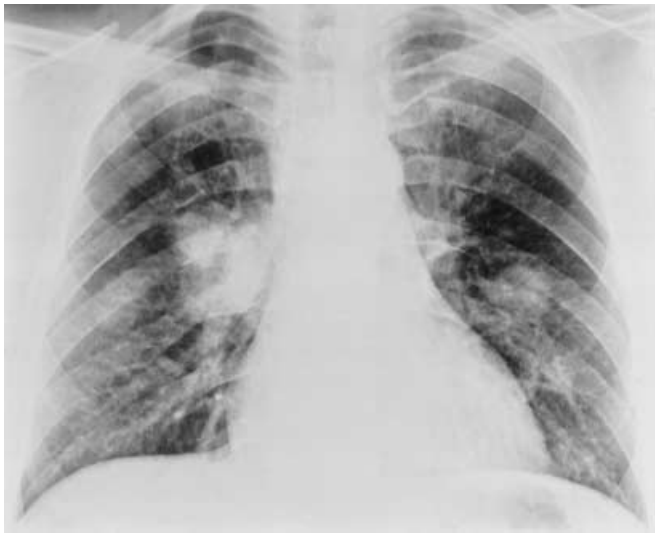
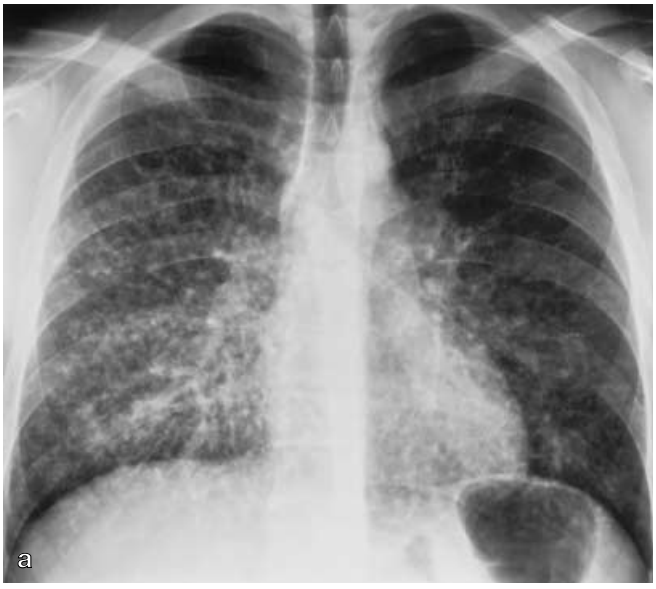


Fig. 2 A 30-year-old male (patient 33) with recurrent nodular sclerosing HD and histological diagnosis of pulmonary involvement. Chest radiograph: bilateral irregularly marginated nodules, right hilar lymphadenopathy



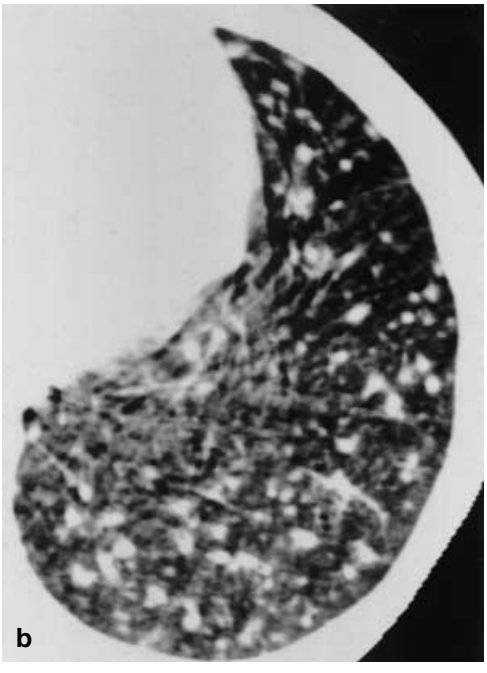


Fig. 3 a, b A 23-year-old male (patient 25) with recurrent nodular sclerosing HD and histological diagnosis of pulmonary involvement. **a** Chest radiograph. **b** CT scan, magnified view at level of left lower lobe obtained within 48 h: diffuse micronodular infiltration

sequently, the CT scan was analysed. Finally, the additional information obtained from CT only was recorded.

Always the earliest chest film or CT scan available demonstrating the pulmonary abnormality diagnosed as manifestation of HD before initiation of therapy was analysed. However, due to the retrospective design of our study, the interval between chest radiographs and CT scans available for analysis ranged from 0 to 63 days and was 8 days or less in only 20 episodes. In 18 episodes the radiograph had been obtained before the CT scan, in 8 episodes the CT scan had been obtained before the radiograph, and in 5 episodes both examinations had been performed on the same day. In 10 episodes only chest radiograph (8 episodes) or only CT scan (2 episodes) were available for analysis.

We did not assess the findings of pulmonary HD during therapy because complications, such as infection, haemorrhage, or drug

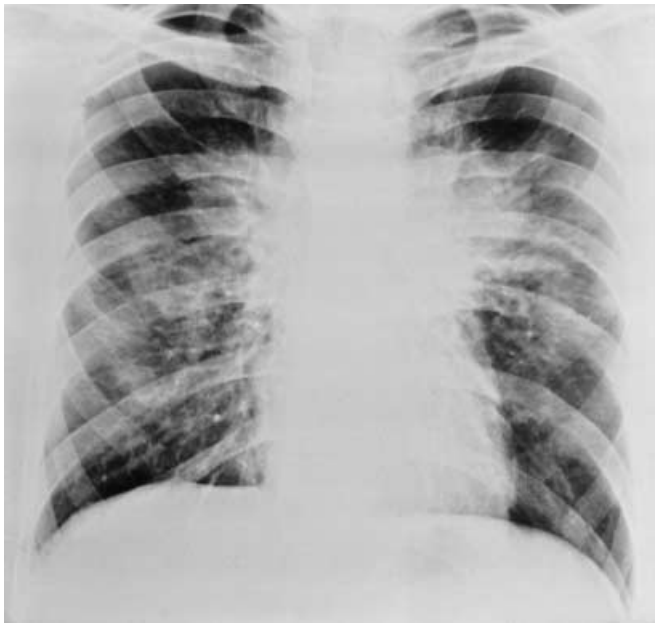


Fig. 4 A 19-year-old female (patient 7) with recurrent nodular sclerosing HD and histological diagnosis of pulmonary involvement. Chest radiograph: diffuse bilateral bronchovascular infiltration extending peripherally from bilateral hilar lymphadenopathy

toxicity, could not be reliably differentiated from pulmonary lymphoma, and repeat histological confirmation was usually not obtained during therapy.

In all cases hard copies were analysed using window settings that had been selected at the time of the examination. The CT window widths ranged from 1200 to 1500 Hounsfield units (HU), and window centers ranged from –530 to –600 HU. Measurements were made using a ruler in conventional radiographs. In digital chest films and CT scans the electronic caliper provided on the film was transferred to cardboard which could be held against the lesion.

If pulmonary nodules were present, their number was recorded if possible; if nodules were too numerous for reliable assessment, they were recorded as diffuse nodules. The nodules' size was measured in less than five lesions, and in five or more the range of nodule size was recorded. The nodules' location was described with regard to lobar distribution (left and right upper and lower lobes, right middle lobe) on CT scans. At chest radiography the lesions' location was recorded with regard to right or left upper, middle, or lower zones as lobar location could not be definitely determined in many nodules.

If diffuse pulmonary densities were present, their location was recorded again with regard to lobes or lung zones, respectively, and their extent was recorded in four categories (involving ≤25 %, 26–50 %, 51–75 %, > 75 % of the lung).

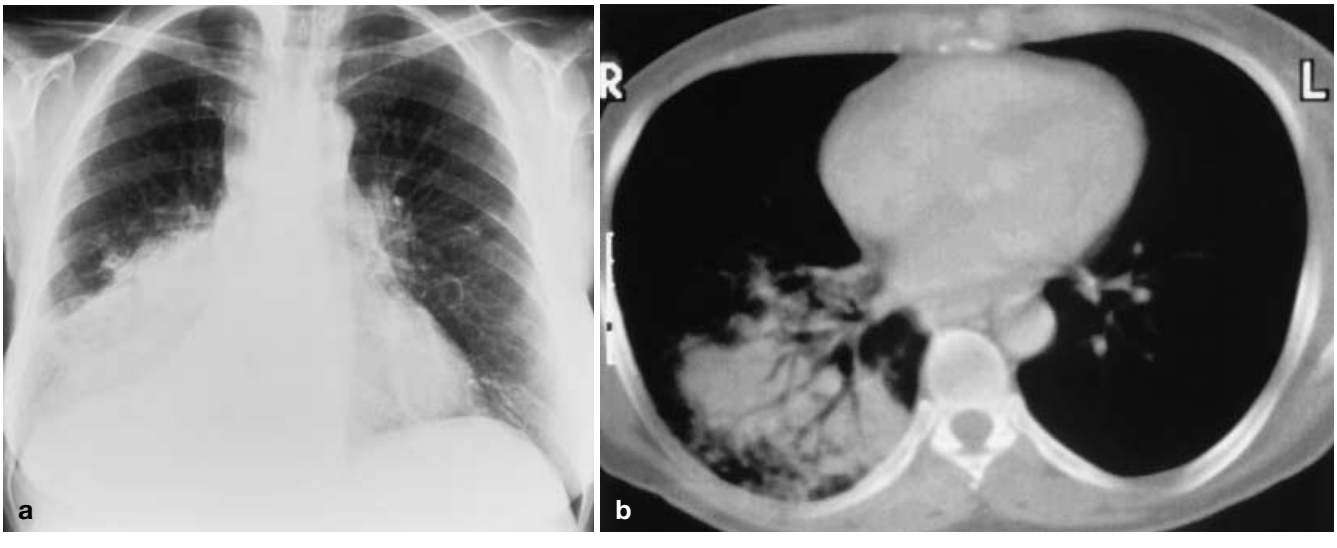
Results

The two predominant findings at both chest radiographs and CT scans were pulmonary nodules and diffuse infiltration.

Of the 39 radiographs, pulmonary nodules were observed in 21 of 39 cases (54 %), in 6 of 39 cases (15 %) infiltration was recorded and in 9 of 39 cases (23 %) there was a combination of nodules and infiltration. In 3 of 39 (8 %) radiographs no pulmonary abnormality was seen. Pleural effusion was recorded in 7 of 39 cases (18 %) and atelectasis in 3 of 39 cases (8 %).

Of the 33 CT scans, 24 (73 %) showed pulmonary nodules, 4 of 33 (17 %) exhibited infiltrative changes

Fig. 5 a, b A 53-year-old female (patient 6) with secondary nodular sclerosing HD and clinical diagnosis of pulmonary involvement. **a** Chest radiograph: dense consolidation of right lower lobe, irregularly marginated nodule left mid lung zone. **b** CT scan at level of right inferior pulmonary vein: diffuse alveolar consolidation with air bronchogram



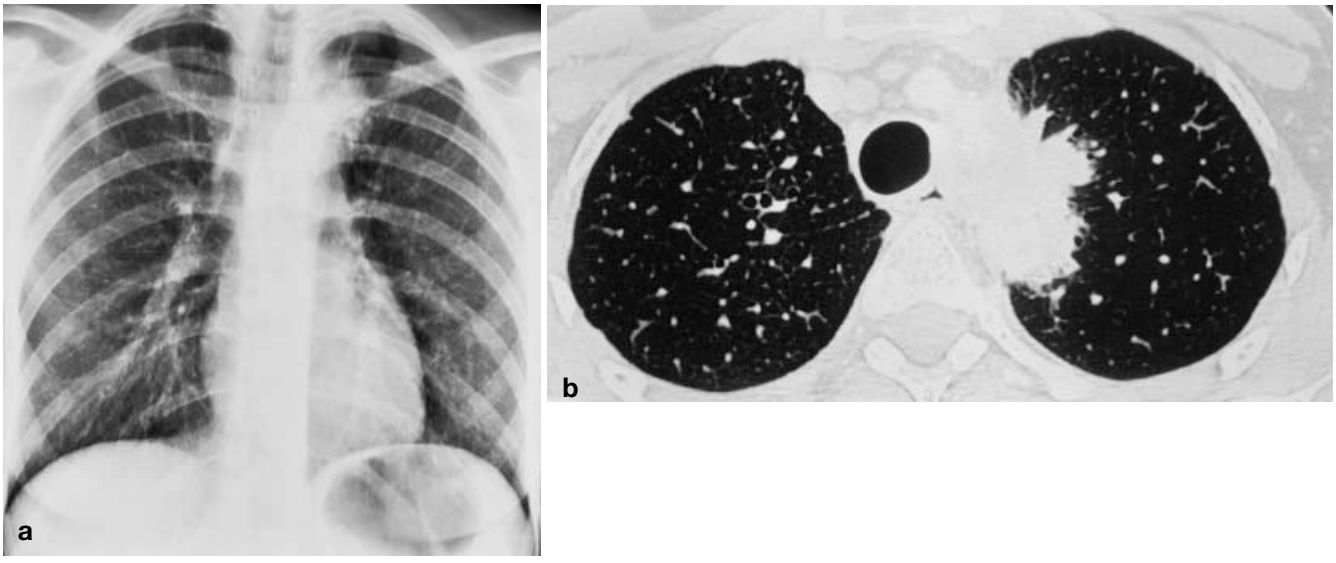


Fig. 6a, b A 36-year-old female (patient 30) with recurrent nodular sclerosing HD and clinical diagnosis of pulmonary involvement. **a** Chest radiograph. **b** High-resolution CT scan at level of aortic arch: lung manifestation by direct extension from left upper mediastinal mass

and 5 of 33 (15 %) showed a combination of nodules and infiltration. In 1 case a large nodule extended into the pericardium. In 8 of 33 cases (24 %) pleural effusion, and in 1 case of 33 (3 %) atelectasis, were observed. The findings at chest radiography and CT are presented in Table 2.

Nodules

Nodules were observed in 30 of 39 (77 %) of chest radiographs and 29 of 33 (88 %) CT scans. They were bilateral in 13 of 30 (43 %) radiographs and 19 of 29 (66 %) CT scans, respectively. There was no particular predominance of the nodules' location with regard to right or left lung, different lobes or lung zones.

The total number of nodules was 146 at radiography and 309 (and 4 cases of diffuse nodules) at CT. The

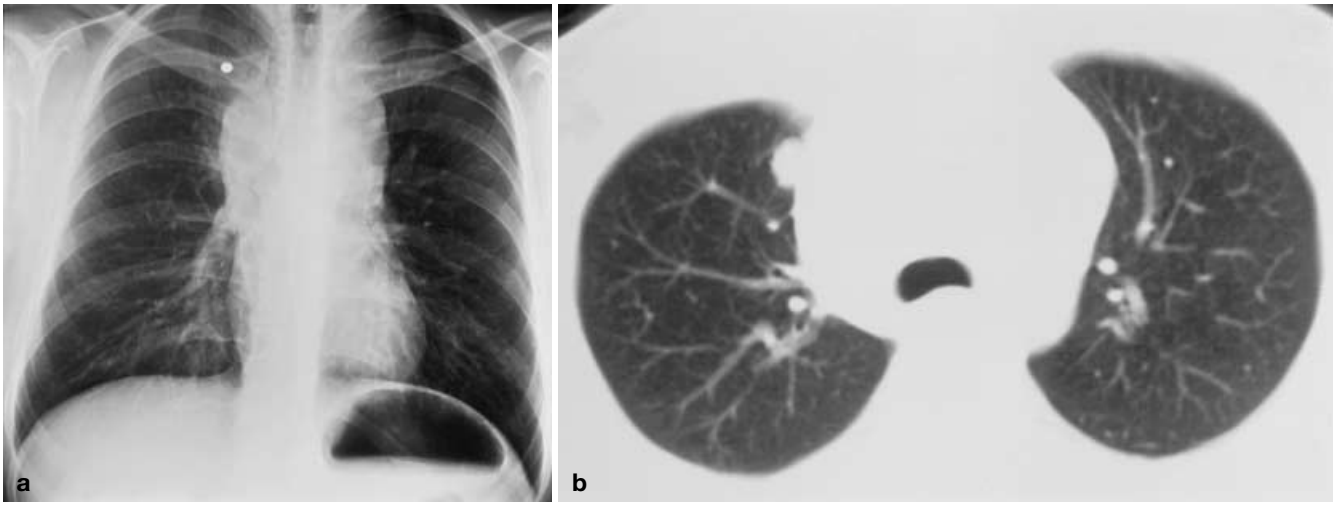


Fig. 7a, b A 34-year-old male (patient 24) with secondary nodular sclerosing HD and clinical diagnosis of pulmonary involvement. **a** Chest radiograph: extensive bilateral mediastinal lymphadenopathy. Lungs appear normal. Lead marker of intracutaneous suture projected on right clavicle following supraclavicular lymphadenectomy. **b** CT scan at level of tracheal bifurcation: right pulmonary nodule adjacent to mediastinum

Table 2 Radiographic and CT findings of patients with pulmonary manifestation of Hodgkin's disease

Patient no.	Interval between CXR and CT (first study)	CXR						CT					
		Nodules				Infiltration		Nodules				Infiltration	
		Uni-/ bilateral	*N*	Size (mm)	Border	Morphology	Extent (%)	Uni-/ bilateral	*N*	Size (mm)	Border	Morphology	Extent (%)
1	28,CXR	Bilateral	5	10–40	Ill-defined	–	–	Bilateral	30	3–30	Ill-defined	–	–
2	6, CXR	Bilateral	3	6–8	Ill-defined	–	–	Bilateral	21	4–15	Ill-defined	–	–
3	4, CXR	Bilateral	12	10–30	Ill-defined	Broncho-vascular	26–50	Bilateral	61	3–50	Ill-defined	broncho	≤ 25
4	3, CT	Bilateral	19	8–19	Ill-defined	Nodular	≤ 25	Bilateral	> 140	2–30	Ill-defined	–	–
5a	–	Unilateral/R	1	17	Ill-defined	–	–	–	–	–	–	–	–
5b	–	Bilateral	5	6–12	Ill-defined	–	–	–	–	–	–	–	–
6	15,CXR	Unilateral/l	1	15	Ill-defined	Alveolar	≤ 25	Unilateral/l	1	22	Ill-defined	alveolar	≤ 25
7	–	Unilateral/l	3	7–9	Ill-defined	Broncho-vascular	≤ 25	–	–	–	–	–	–
8	17,CXR	Bilateral	11	8–45	Ill-defined	–	–	Bilateral	> 90	5–45	Ill-defined	–	–
9	0	Bilateral	3	4–8	Ill-defined	–	–	Bilateral	> 80	2–8	Ill-defined	–	–
10	7, CXR	Unilateral	1	53	Ill-defined	–	–	Bilateral	2	5, 50	Ill-defined	–	–
11	–	Bilateral	16	10–30	Ill-defined	–	–	–	–	–	–	–	–
12	–	–	–	–	–	–	–	Bilateral	2	7, 8	Ill-defined	–	–
13	8, CXR	Unilateral/R	1	6	Ill-defined	Broncho-vascular	≤ 25	Unilateral/R	4	10–20	Ill-defined	–	–
14	–	–	–	–	–	Alveolar	≤ 25	–	–	–	–	–	–
15	8, CT	Bilateral	7	5–24	Ill-defined	–	–	Bilateral	20	3–20	Well-de-fined	–	–
16a	–	–	–	–	–	Broncho-vascular	26–50	–	–	–	–	–	–
16b	0	Unilateral/l	2	12, 18	Ill-defined	Broncho-vascular	≤ 25	–	–	–	–	Broncho-vascular	≤ 25
17	23, CT	Unilateral/R	1	60	Ill-defined	–	–	Unilateral/R	1	100 × 70 × 50	Ill-defined	–	–
18	1, CXR	Unilateral/R	1	10	Ill-defined	Broncho-vascular	≤ 25	Unilateral/R	9	3–19	Ill-definedr	Broncho-vascular	≤ 25
19	–	Bilateral	5	8–30	Well-defined	–	–	–	–	–	–	–	–
20	4, CXR	Bilateral	20	7–28	Ill-defined	–	–	Bilateral	39	3–30	Well-defined	–	–
21	45,CXR	Bilateral	2	10, 20	Ill-defined	–	–	Bilateral	21	3–21	Ill-defined	–	–
22a	65,CXR	Unilateral/R	3	5–6	Well-defined	Broncho-vascular	≤ 25	Unilateral/R	7	10–12	Ill-defined	Broncho-vascular	≤ 25
22b	0	Unilateral/L	4	7–11	Ill-defined	–	–	Bilateral	18	4–10	Well-de-fined	–	–
23	4, CXR	–	–	–	–	Nodular	≤ 25	–	–	–	–	nodular	≤ 25
24	1, CT	–	–	–	–	–	–	Unilateral/R	1	18	Ill-defined	–	–
25	5, CXR	–	–	–	–	Nodular	> 75	–	–	–	–	nodular	> 75
26	5, CXR	Unilateral/L	2	7, 9	Well	–	–	Bilateral	9	2–10	Well-de-fined	–	–
27	27,CXR	Unilateral/R	1	14	Well	–	–	Bilateral	6	12–24	Ill-defined	–	–
28	2, CT	Unilateral/R	1	40	Ill-defined	–	–	Unilateral/R	1	30	Ill-defined	–	–
29	63,CXR	–	–	–	–	Nodular	> 75	–	–	–	–	nodular	> 75
30	0	–	–	–	–	–	–	Bilateral	20	2–12	Ill-defined	broncho	≤ 25
31	7, CT	Unilateral/R	1	23	Well-defined	–	–	Bilateral	> 33	2–23	Well-de-fined	–	–
32a	0	–	–	–	–	–	–	Bilateral	4	3–7	Ill-defined	–	–
32b	–	–	–	–	–	–	–	Bilateral	5	3–12,	Ill-defined	–	–
33	32,CT	Bilateral	6	10–30	Ill-defined	–	–	Unilateral/R	2	19, 45	Ill-defined	–	–
34	5, CXR	–	–	–	–	Nodular right lung	≤ 25	Unilateral/R	5	8–16	Ill-defined	atelectasis right upper lobe	
35	12,CXR	Unilateral/R	1	23	Ill-defined	–	–	Bilateral	8	3–10	Ill-defined	-	–
36	142,CT	Unilateral/R	4	7–12	Ill-defined	Nodular	≤ 25	Unilateral/R	12	2–12	Ill-defined	–	–
37	–	Unilateral/R	4	9–11	Ill-defined	–	–	–	–	–	–	–	–

Size of nodules was measured individually when < 4 nodules per right or left lung; otherwise, the range of nodule size was recorded. In 31 episodes in which both chest radiograph and CT scan were available for analysis intervals between both studies ranged from 0 to 63 days; in 18 episodes the chest radiograph and in 8 episodes the CT scan had been obtained first, in 5 episodes both examinations had been performed on the same day

Table 3 Additional findings at CT in patients with pulmonary manifestation of Hodgkin's disease

Patient no.	Interval between chest radiograph and CT scan	Additional findings from CT scan
2	6	More bilateral nodules
3	4	More bilateral nodules, less extent of infiltration
4	3	More bilateral nodules
9	0	More bilateral nodules
10	7	One additional nodule, thus demonstrating bilateral (one each side) instead of unilateral nodule
13	8	More unilateral nodules, bronchovascular infiltration not confirmed
15	8	More bilateral nodules
16b	0	Two Ill-defined unilateral nodules not confirmed
18	1	More unilateral nodules
20	4	More bilateral nodules
22b	0	More nodules, thus demonstrating bilateral instead of unilateral nodules
23	4	No additional information
24	1	Solitary nodule (18 mm) only seen at CT
25	5	No additional information
26	5	More nodules, thus demonstrating bilateral instead of unilateral nodules
28	2	No additional information
30	0	Small bilateral nodules and bronchovascular infiltration (≤25 %) only shown at CT
31	7	More nodules, thus demonstrating bilateral instead of unilateral nodules
32a	0	Four bilateral small (< 8 mm) nodules only shown by CT
34	5	Less unilateral nodules shown due to development of right upper lobe atelectasis in interval between chest radiograph and CT

Comparison only of patients with chest radiograph and CT obtained within 8 days

number of nodules observed in an individual patient ranged from solitary (chest radiograph and CT scan) to 20 (radiograph) and > 140 (CT), respectively.

At radiography and CT, respectively, there were solitary nodules in 10 of 30 (33 %) and 4 of 29 (14 %), 2–5 nodules in 13 of 30 (43 %) and 7 of 29 (24 %) cases, 6–10 nodules in 2 of 30 (7 %) and 5 of 29 (17 %), and > 10 nodules in 5 of 30 (17 %) and 13 of 29 (45 %) cases, respectively.

At radiography, in 30 episodes a total of 146 nodules was observed, the nodules' size ranged from 4 to 60 mm. In 25 of 30 (83 %) episodes nodules were ≤30 mm, in 17 of 30 (57 %) ≤20 mm and in 7 of 30 (23 %) ≤10 mm.

At CT, pulmonary nodules were recorded in 29 episodes. Of these, in 4 episodes nodules could not be reliably counted (recorded as > 30, > 80, > 90, > 140); these were described as diffuse nodules. In the 25 episodes in which lesions could be counted a total of 309 nodules were observed. In 24 of 29 episodes (83 %) nodules were ≤30 mm, in 16 of 29 (55 %) ≤20 mm and in 6 of 29 (21 %) ≤10 mm (range 2 to 100 mm).

All the nodules exhibited soft tissue density at chest radiographs as well as CT scans. No calcification of nodules was observed. The nodules were classified as irregularly marginated in 25 of 30 (83 %) of cases at chest radiography, and 24 of 29 (83 %) at CT.

Cavitation was observed at chest radiography in one nodule and at CT in 4 nodules. Air bronchogram or the "open bronchus sign" was not recorded at radiography but was observed in 2 cases at CT.

Infiltration

At chest radiography diffuse infiltration was recorded in 15 of 39 (38 %) cases; in 9 of 39 (23 %) also pulmonary nodules were present. The morphology of infiltration was bronchovascular in 7 of 15 (47 %), nodular in 6 of 15 (40 %) and alveolar consolidation in 2 of 15 (13 %). It involved ≤25 % of the lung in 11 of 15 (73 %), 26–50 % in 2 of 15 (13 %) and > 75 % in 2 of 15 (13 %); these two cases exhibited a nodular pattern.

At CT diffuse infiltration was recorded in 9 of 33 (27 %) cases; in 5 of 33 cases (15 %) also pulmonary nodules were present. The morphology of infiltration was bronchovascular in 5 of 9 (56 %), nodular in 3 of 9 (33 %) and alveolar in 1 of 9 (11 %) cases. It involved ≤25 % of the lung in 7 of 9 (78 %), and > 75 % in 2 of 9 (22 %); these two showed a nodular pattern with nodule size ranging from 3 to 6 mm.

Other findings

Pleural effusion was recorded by radiography in 7 of 39 (18 %) and by CT in 8 of 33 (24 %) cases. Radiographs demonstrated hilar (15 of 39, 38 %) or mediastinal (15 of 39, 38 %) lymphadenopathy in 22 of 39 (56 %) cases; at CT hilar (17 of 33, 52 %) or mediastinal (26 of 33, 79 %) lymphadenopathy were observed in 27 of 33 (82 %) cases.

Additional findings demonstrated by CT

In 20 episodes of pulmonary manifestation of HD a chest radiograph and CT scan had been obtained within 8 days. Only in these cases were findings of the two examinations compared (Table 3). In 17 of these 20 (85 %) cases CT provided additional diagnostic information: In 15 of 20 (75 %) cases more pulmonary nodules were recorded, thus demonstrating bilateral nodules in 4 of 20 (20 %) cases, which had been regarded as unilateral nodules by chest radiography. In 2 of 20 cases (10 %) nodules, and in 1 case of 20 (5 %) both nodules and infiltration, were shown by CT when chest radiography had been interpreted as normal. Computed tomography demonstrated cavitation not demonstrated on the radiograph in three nodules and air bronchogram in two lesions.

In 1 patient CT obtained 8 days after chest radiography did not confirm bronchovascular infiltration, and in 1 patient CT performed on the same day as the radiograph did not confirm two irregularly marginated nodules but confirmed infiltration.

Also unilateral (five episodes) or bilateral (five episodes) mediastinal lymphadenopathy was demonstrated only by CT. In one episode each pleural effusion, pericardial effusion and pleural thickening were only appreciated by CT.

Discussion

Radiographic findings in patients with pulmonary manifestations of HD have been reported most commonly as thickening of bronchovascular bundles and interlobular septa due to lymphangitic spread of disease and discrete pulmonary nodules, and less commonly as consolidation and disseminated micronodules. Cavitating masses and endobronchial lesions have also been described. Lymphadenopathy and pleural effusion were regarded as common [1, 4, 12, 14].

In our series of 37 patients with pulmonary HD the spectrum of findings was somewhat different, particularly at CT.

The most common finding at both CT and radiography were irregularly marginated soft tissue density pulmonary nodules or masses with size ranging from 2 to 100 mm.

In patients examined with CT nodules were demonstrated in 88 % of episodes of which 86 % had multiple and 66 % bilateral nodules. In 83 % of episodes with pulmonary nodules their maximum size was 30 mm. In patients who underwent radiography nodules were observed in 77 % of cases, of which 67 % had multiple and 43 % had bilateral nodules. Again, in 83 % of episodes with nodules their maximum size was 30 mm.

Cavitation was seen in less than 1 % of nodules at both radiography and CT.

Diffuse infiltration was less commonly observed both at CT and radiography. In subjects who underwent radiography diffuse infiltration was observed in 38 % of cases mostly involving ≤25 % of the lung. In individuals in whom CT was performed, 27 % of cases showed infiltration again usually involving ≤25 % of the lung.

At both CT and plain film bronchovascular and nodular patterns were present in approximately equal proportions. Alveolar infiltration was reported on the chest radiograph in 2 patients and at CT in 1 patient.

Pleural effusion was equally well detected on radiographs and CT scans, and in 1 case pleural thickening possibly representing lymphoma was seen only at CT. Hilar and mediastinal lymphadenopathy was demonstrated more commonly at CT than radiography. Axillary lymph node enlargement, pericardial effusion and splenomegaly were seen only at CT.

The differences between CT and radiographic findings are certainly partially due to the superior detection and characterization of lesions by CT as shown by direct comparison.

Computed tomography can detect nodules and infiltration not seen on radiography, exhibit more nodules than the plain film and demonstrate bilateral disease when the radiograph shows only unilateral lesions. Computed tomography can also demonstrate separate nodules that are regarded as consolidation on radiography due to superimposition. This is particularly true for large nodules [15].

Our findings correspond well to those from other reports on CT findings of pulmonary HD. In a CT study of 15 patients with pulmonary manifestation of HD by Lewis et al., 40 % of cases represented secondary and 60 % recurrent pulmonary lymphoma. In 47 % of the cases the diagnosis was confirmed histologically [16]. In these patients "masses or mass-like consolidation > 1 cm" (80 %) and "nodules < 1 cm" (67 %) were the most common findings. These lesions exhibited soft tissue density and shaggy borders (93 %), their size ranging up to 8 cm. Of the masses, 32 % had air bronchograms, particularly when large. Nodules < 1 cm did not exhibit air bronchograms. Cavitation was not observed in the series of Lewis et al. [16]. Less common findings in their series were pleural effusion (40 %) and pleural masses (33 %), infiltrates (40 %) and peribronchial thickening (40 %). Lymphadenopathy (53 %) was observed less commonly than in our series; however, the authors noted that pulmonary HD with no thoracic lymphadenopathy in newly diagnosed disease is very uncommon.

Similarly, all of our patients with lung involvement at initial diagnosis had hilar or mediastinal lymphadenopathy; therefore, a diagnosis of pulmonary involvement in the absence of hilar or mediastinal lymphadenopathy in patients with untreated HD seems very unlikely [4].

Cobby et al. reported radiographic and CT findings of 15 patients with HD relapsing in the lung; in five the

diagnosis was confirmed histologically [15]. Again, pulmonary nodules (80 % of cases) were the commonest finding; consolidation (27 %) and direct extension from the mediastinum (20 %) were observed less frequently. Forty-seven percent had new mediastinal adenopathy, 40 % pleural effusion or masses, and 7 % had pericardial involvement. Cavitation of nodules (20 %) and consolidation (7 %) was less common.

In our series pulmonary manifestation was only detected on CT whereas the radiograph was recorded as normal in 15 % of cases in which both CT and chest radiography had been obtained within 8 days. In 10 % of cases demonstration of pulmonary lesions by CT altered the stage from stage III to stage IV. Computed tomography demonstrated additional findings of pulmonary involvement in 85 % of cases when compared with radiography. In 60 % of cases more pulmonary nodules were detected, and in 20 % of cases bilateral disease was shown when radiographs suggested unilateral lesions. In these cases demonstration of additional pulmonary abnormalities did not, however, alter stage or treatment.

The superiority of CT over radiography is also reported by Cobby et al. [15] and Hopper et al. [3]. Castellino et al., however, found no additional benefit from CT in 17 patients with pulmonary HD, although CT detected additional lesions elsewhere in the chest (lymphadenopathy, pleura, pericardium, chest wall) [2].

In general, it is recommended to perform chest CT routinely in patients with HD, not only for precise staging but also for assessment of the effects of therapy [17].

Limitations

There are several limitations of this study. Due to its retrospective design, we cannot be sure to have identified all cases with pulmonary manifestations of HD. Therefore, we cannot comment on the proportion of patients with pulmonary HD as compared with the total number of patients or the patients with stage IV treated for HD at our institution.

As pulmonary HD was diagnosed clinically in 30 of 41 episodes, some cases may have represented other disease misinterpreted as pulmonary HD despite our efforts to exclude other causes of pulmonary abnormalities. This limitation, however, to our knowledge, also applies to the other series in the literature. Also, examination technique was not standardized particularly with CT, which may cause inaccuracy in the proportion of the different radiological findings.

We did not analyse the course of pulmonary HD with or without therapy in our study because complications, such as infection or haemorrhage were common, and no further histological confirmation of lung involvement was obtained in our patients once the diagnosis of pulmonary HD had been established.

Conclusion

In our study typical findings of pulmonary HD consisted of solitary or multiple irregularly marginated soft tissue density nodules with or without diffuse bronchovascular or nodular infiltration. Most of the nodules had a maximum size of 30 mm, although lesions as large as 100 mm were observed. Cavitation or air bronchogram as described in other series, particularly of pulmonary manifestations of non-Hodgkin's lymphoma, were uncommon.

In patients with pulmonary involvement at initial diagnosis of HD there was always hilar or mediastinal lymphadenopathy present which was not always found in patients with recurrent pulmonary HD.

Computed tomography was superior in detection and characterization of pulmonary lesions, and even more so of extrapulmonary manifestations. We believe that with typical radiological findings in the appropriate clinical context a diagnosis of pulmonary manifestation of Hodgkin's disease has to be considered. As there are, however, several conditions that can mimic pulmonary manifestations of Hodgkin's disease, biopsy remains required in many cases.

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