

Chest radiological features of pulmonary histiocytosis X: a report based on 50 adult cases

J LACRONIQUE, C ROTH, J-P BATTESTI, F BASSET, J CHRETIEN

From the Clinique de Pneumo-Physiologie, INSERM U 214, Paris, Service de Pneumologie, Hôpital Avicenne, Bobigny, and INSERM U 82, Hôpital Bichat, Paris, France

ABSTRACT This study describes the chest radiographs of 50 adult patients with histologically verified histiocytosis X, proposes a radiological classification, and examines the role of radiology in assessing the prognosis of the disease. Radiologically the lesions predominate in the middle and lower lung fields, usually sparing the costophrenic angles, and are typically micronodular, reticular, or cystic. These features are especially suggestive of histiocytosis X if lung volume is normal or increased, there is an associated pneumothorax, they occur in a young male and there are no other intrathoracic changes (pleural or mediastinal). The three evolutionary patterns of improvement, stabilisation, and worsening are analysed with respect to the initial radiological features; one which carries a good prognosis is sparing of both costophrenic angles.

Pulmonary histiocytosis X (HX) is a chronic interstitial disease characterised by the presence of multiple specific granulomas which contain many Langerhans cells.

The radiological features of this disease comprise nodular, reticulonodular, or honeycomb patterns which classically appear "predominantly in the upper lung fields".¹ However, in our experience the radiographic findings often depart from the classic description.

The aims of this study, therefore, were: (1) to use a defined group of adults with HX to describe the chest radiological features of the disease; (2) to develop a qualitative method of analysing the chest radiographs; and (3) to determine whether the chest radiograph is useful in assessing the prognosis of this disease.

Patients and methods

SELECTION OF PATIENTS

The series consisted of 50 patients, six females and 44 males, followed in 11 French hospitals between 1965 and 1980. Their ages ranged from 15 to 59 (mean = 29.8) years.

They were selected on the basis of their referred pathological specimens which had been obtained by

open lung biopsy in 41 cases and by bronchoalveolar lavage in nine cases.² The diagnosis was confirmed by the ultrastructural demonstration of X bodies (or Langerhans cell granules) in all cases.

Follow-up information extending from one to 12 years was available for 37 patients; 26 of these were followed for over three years (mean = 5.4 years).

RADIOGRAPHIC STUDY

Only posteroanterior chest radiographs were considered; tomography was not included. In assessing prognosis, special attention was paid to the earliest and latest films.

To record the radiological changes, we used a method derived from the International Labour Organisation for Pneumoconiosis^{3 4} as shown in table 1: R = reticulation; p = micronodules up to 2 mm in diameter; q = micronodules from 2 to 5 mm in diameter; r = micronodules from 5 to 10 mm in diameter; M = macronodules over 10 mm diameter;

Table 1 *Symbols for radiological analysis*

| | |
|------|--|
| R: | reticulation |
| p: | micronodules up to 2 mm in diameter |
| q: | micronodules from 2 to 5 mm in diameter |
| r: | micronodules from 5 to 10 mm in diameter |
| M: | macronodules over 10 mm in diameter |
| k: | cysts up to 10 mm in diameter |
| K: | cysts over 10 mm in diameter |
| B: | bullae |
| Pno: | pneumothorax |

Address for reprint requests: J Lacronique, Hôpital Laennec, 42 rue de Sèvres, 75340 Paris Cedex, France.

k = cyst up to 10 mm in diameter; K = cysts over 10 mm in diameter; B = bullae.

The distribution of these features was analysed by dividing the two lung fields into four horizontal bands (numbered 1, 2, 3, 4 from the top), and into vertical zones (central and peripheral), the costophrenic angles (cpa) being treated separately (fig 1). The density of radiological changes per area was expressed quantitatively as a, b, or c, in increasing order.

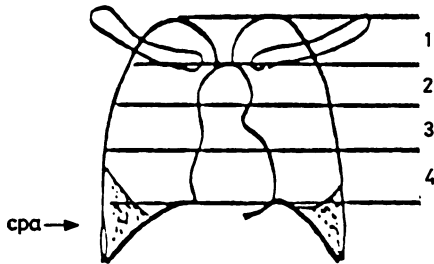


Fig 1 Distribution of the changes was analysed by dividing the two lungs into four horizontal bands numbered 1, 2, 3, 4. The costophrenic angles (cpa) were treated separately. Preliminary analysis showed that there was no significant difference in distribution between the right and left lungs or between the central and peripheral zones of each lung.

Results (figs 2-7)

INITIAL PATTERN

On the first radiograph, micronodular and reticular opacities were generally obvious, but occasionally larger nodules or cysts were also observed. The frequency of the abnormalities ranked in decreasing order was: R, p, k, q, K, r, M, and B (table 2); their density per area ranked: b, a, and c (table 3).

The distribution of each feature within the horizontal and vertical lung field subdivisions was analysed statistically by the χ^2 test, which showed that there was no significant difference between the right and left lungs, or between the central and peripheral zone of each lung, for any type of lesion. The analysis was therefore simplified by considering only the distribution of the lesions between the four horizontal bands and the costophrenic angles.

As shown in tables 4 and 5, the distribution of the changes generally involved three or four compartments (compartments 1, 2, 3; 2, 3, 4 or 1, 2, 3, 4). In 20% of the cases, only two compartments were involved. The changes were never restricted to a single compartment.

The costophrenic angles (cpa) were spared in 84% of the cases.

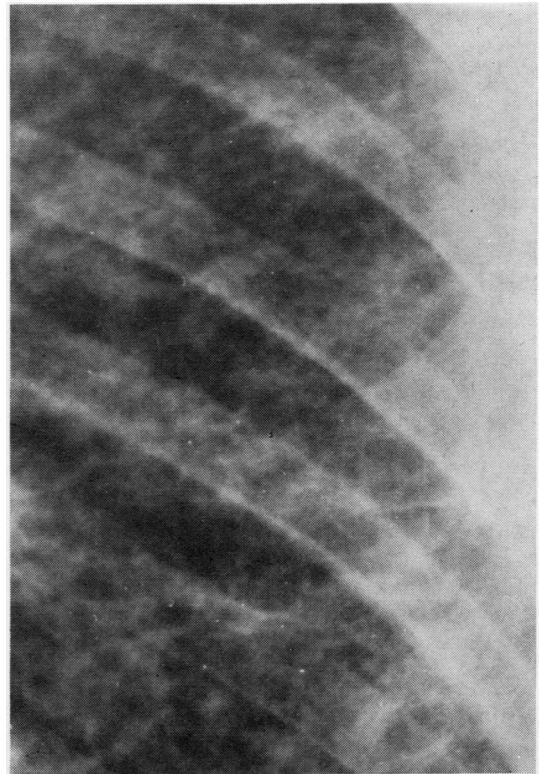


Fig 2 A high magnification of a chest radiograph showing r, p, q, k, K, changes usually described as honeycombing.

Table 2 Frequency of abnormalities

| Elementary changes | R | p | k | q | K | r | M | B | Pno |
|--------------------|----|----|----|----|----|----|---|---|-----|
| Patients | 47 | 46 | 25 | 20 | 8 | 6 | 4 | 2 | 7 |
| % | 94 | 92 | 50 | 40 | 16 | 12 | 8 | 4 | 14 |

Table 3 Density of radiological changes per area: frequency of the different degrees

| Density | a | b | c |
|----------|----|----|----|
| Patients | 15 | 21 | 14 |
| % | 30 | 42 | 28 |

The most frequent association of radiological abnormalities was: R p k (20%), and the most frequent distribution of lesions was 2, 3, 4 with sparing of the costophrenic angles (44%). The most typical initial pattern was expressed as: R p k (2, 3, 4) sparing cpa, although this was only seen in 8% of the cases.

Enlargement of the hilar lymph nodes, pleural

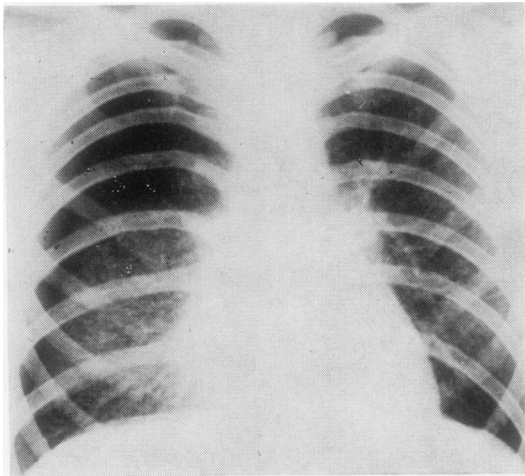


Fig 3 Radiograph very suggestive of the diagnosis of HX showing a pneumothorax on the right side and on the left typical reticulo-micronodular and cystic changes (R p k) the distribution of which (2 3 4 sparing cpa) is the most frequently encountered.

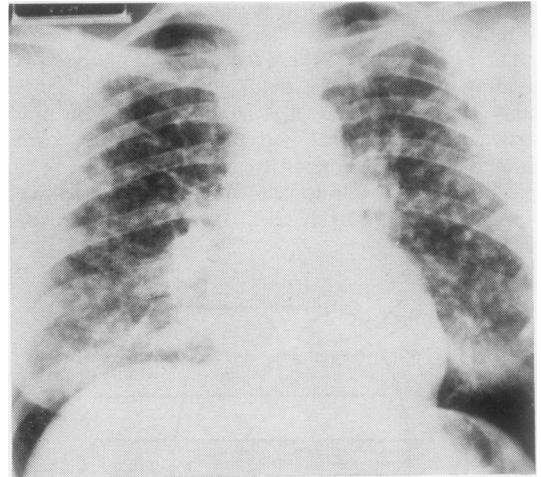


Fig 4 A very unusual case characterised by the presence of numerous macronodules (M) considered as alveolar opacities. However, the distribution of lesions is typical (2 3 4, sparing cpa). This case showed a dramatic improvement; four months later the pattern was only Rp.

Table 4 Frequency of involvement of each compartment (-cpa = cpa spared; +cpa = cpa involved)

| Compartments | 1 | 2 | 3 | 4 | -cpa | +cpa |
|--------------|----|----|-----|----|------|------|
| Patients | 13 | 49 | 50 | 37 | 42 | 9 |
| % | 26 | 98 | 100 | 74 | 84 | 18 |

effusion, significant cardiomegaly, solitary pseudotumoral opacities, and alveolar or ground-glass opacities were never found.

In contrast, pneumothorax was frequently observed: spontaneous pneumothorax was the presenting complaint in seven cases, and in four of these, it occurred on the opposite side within a short period of time.

PATTERN OF EVOLUTION

Of the 37 patients for whom follow-up data were available, three different patterns of evolution were observed. There was an improvement in 13 patients—four regained a normal radiograph and nine showed marked regression of the changes. Analysing this last group more closely, four patients had both reticular and micronodular shadows (Rp) but without cysts or bullae. The improvement generally

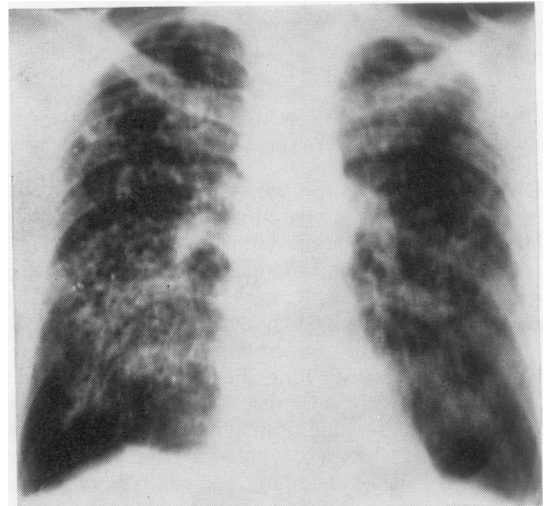


Fig 5 Radiograph showing severe lesions, predominantly fibrotic, with cystic (k, K) changes five years after presentation. Note that the lung volume does not appear to be diminished.

Table 5 Frequency of associations of several compartments

| Compartments | 234 -cpa | 234 +cpa | 1234 -cpa | 1234 +cpa | 23 | 123 | 34 +cpa |
|--------------|----------|----------|-----------|-----------|----|-----|---------|
| Patients | 22 | 4 | 7 | 3 | 9 | 4 | 1 |
| % | 44 | 8 | 14 | 6 | 18 | 8 | 2 |

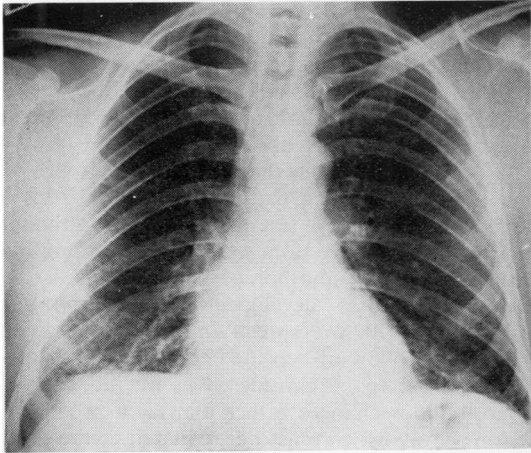


Fig 6

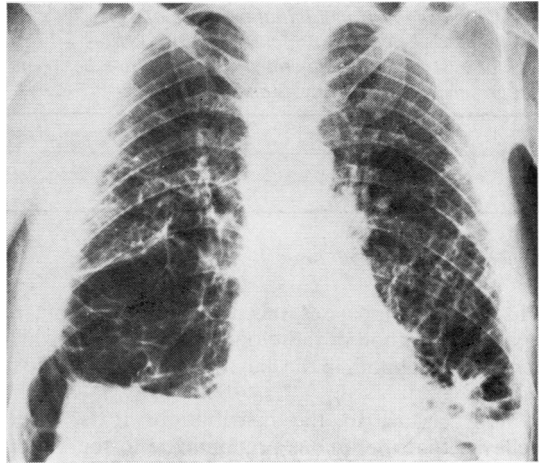


Fig 7

Figs 6, 7 A case showing evolution toward bullous and emphysematous deterioration which was associated with severe respiratory insufficiency. The initial radiograph shows slight changes predominating in the lower fields with involvement of both cpa. Notice the elevation of the right hemidiaphragm after pleurectomy for pneumothorax.

occurred over several years but in one case it was more dramatic: a young woman with widespread macronodules at the onset of her disease, had only reticular and micronodular lesions (Rp) four months later. In 11 patients the lesions persisted unchanged for at least three years. There was deterioration in 13 patients. In 10 of these, cystic changes became prominent (k, K). In the other three, bullous changes developed with hyperlucency and pulmonary distension and diffuse emphysema. Clinical and physiological data on these patients indicate that these radiological features represent a worsening course.

Regardless of the evolutionary pattern, it was observed that nodular opacities were much more numerous at the onset of the disease than a few months later.

The lung volume was never reduced during the course of the disease and even appeared increased in some cases. Pleural abnormalities related to pneumothorax or thoracotomy were noted in over half of the 37 patients, but abundant pleural effusions were never seen. In two cases, features of pulmonary tuberculosis were seen in association with those of HX, but these lesions improved with specific treatment. One patient developed an eosinophilic granuloma of a rib, and two patients developed signs of pulmonary hypertension.

Five patients died, three from deterioration of the lung lesions, which were predominantly fibrotic in two cases and predominantly emphysematous in the other. A fourth patient, with stabilised lesions, died of a perforated peptic ulcer. The last death was the result of a mediastinal tumour, probably lympho-

matous in nature, which developed in a man whose radiograph had returned to normal several years earlier.

PROGNOSIS

Attempts to correlate the different initial involvement and evolutionary patterns show that there is one radiological feature which carries a good prognosis: this is sparing of the two costophrenic angles. As shown in table 6, all the 24 patients who remained stable or improved showed sparing of their costophrenic angles. Of the 13 patients who deteriorated, four had costophrenic angle involvement at the onset. There is a statistically significant correlation between good prognosis and sparing of the two costophrenic angles ($p < 0.05$). In contrast, we were not able to find any significant statistical correlation between the degree of dissemination within the lungs, the presence or absence of cysts (k or K), the diameter of nodular opacities or the density of lesions, and the evolutionary pattern. For instance, of the 24 patients who improved or remained stable, 11 initially had cystic lesions (either k or K) (table 7).

Table 6 *Prognosis and involvement of cpa: + cpa = cpa involved; - cpa = cpa spared. There is a significant correlation ($p < 0.05$) between good prognosis (stabilisation or improvement) and the sparing of both cpa*

| | <i>Worsening</i> | <i>Stabilisation or improvement</i> |
|-------|------------------|-------------------------------------|
| + cpa | 4 | 0 |
| - cpa | 9 | 24 |

Table 7 *Prognosis and initial presence of cysts (k and/or K) k/K + = presence of cysts; k/K - = lack of cysts. There is no statistical correlation between the presence or lack of cysts and evolution*

| | Worsening | Stabilisation or improvement |
|-------|-----------|------------------------------|
| k/K + | 10 | 11 |
| k/K - | 3 | 13 |

Discussion

This study emphasises the advantage of using an analytical method of radiological observation, which can be helpful both in the diagnosis and the prognosis of HX.

With regard to the distribution, it is widely believed that the lesions predominate in the "upper lung fields".¹ In our experience, the most frequent distribution is: 2, 3, 4 sparing cpa (44%)—that is, the disease predominates in the middle and lower parts of the chest radiograph but spares the costophrenic angles.

Similarly, our results are not in agreement with other reports, with regard to some further radiological details. Pleural effusions, reported to occur rarely in both children⁵ and adults,⁶ were never found in our series, except for occasional small effusions after pneumothorax or thoracotomy. Neither was mediastinal lymphadenopathy observed in our series, although it has been reported as an occasional finding by others.^{7 8} Alveolar opacities have been described as early changes in two reports^{9 10} but in our series they were seen in only one patient who also had macronodular changes.

Our method of analysis appears to help in establishing the diagnosis of pulmonary HX on chest radiographs although the radiographic appearances are not diagnostic by themselves.

However, there is a strong probability of HX when the patient is a young man with abnormalities such as R, p, and k predominantly distributed in 2, 3, and 4 with sparing of the costophrenic angles, normal or increased lung volume and no other intrathoracic changes (pleural effusion, lymphadenopathy). The probability is even greater when pneumothorax is present. The frequency of pneumothorax in HX is well known.^{7 8}

The only conditions besides HX in which this combination of features may be encountered, are lymphangiomyomatosis,¹² and although much less frequently, sarcoidosis,^{13 14} and idiopathic pulmonary fibrosis.¹⁵

Our analytical method does not by itself allow prediction of the overall course of the disease. One element, the preservation of the two costophrenic angles, carries a favourable prognosis but the others

have no prognostic value. However the combination of several features may be helpful in this respect; all four patients in this series whose radiographs returned to normal had initially neither cysts, bullae, nor pneumothorax and their costophrenic angles were not involved.

It is usually stated that repeated episodes of pneumothorax carry a bad prognosis^{7 9} but this is not confirmed by the χ^2 test in our study even though most appear to have done very badly. Among five with repeated pneumothoraces two stabilised. The three other cases developed severe respiratory insufficiency with widespread emphysema. It seems that during follow-up repeated episodes of pneumothorax ought to be considered as an indicator of severe bullous changes rather than as a prognostic factor per se, which must be evaluated at the onset of the disease.

In conclusion, this study describes all the information that chest radiographs can provide on pulmonary HX in adults. It is based on a method of analysis which is helpful in diagnosis and, to a limited extent, in prediction of the evolutionary pattern of the disease.

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