GROWTH CONDITIONS OF HAMARTOMA OF THE LUNG
A STUDY BASED ON 22 CASES OPERATED ON AFTER RADIOGRAPHIC OBSERVATION FOR FROM ONE TO 18 YEARS

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(RECEIVED FOR PUBLICATION MARCH 17, 1958)

A hamartoma of the lung manifests itself radiographically as a "coin lesion," which demands thoracotomy because we cannot in such cases exclude the possibility of a malignant lung tumour (Husfeldt and Carlsen, 1950, among others). However, it is a matter of interest to know whether a hamartoma ought to be removed surgically, either on account of potential malignancy, or because of continuous growth. Numerous papers are available dealing with the morbid anatomy of hamartoma of the lung (Goldsworthy, 1934; Van Voorst Vader and Vossenaar, 1954), but investigations into the conditions of growth do not seem to have been published. The object of the present investigation has been to throw some light on this question on the basis of a review of 22 cases operated on after having been under radiographic control for from one to 18 years.

Several writers have given a rough estimate of the growth conditions of hamartomas, without having measured possible variations in size. McDonald, Harrington, and Clagett (1945), without referring to their own cases, state that a hamartoma grows slowly, whereas Hall (1948) found no increase in size in two cases radiographically controlled for 21 and five years respectively. Stein, Jacobson, Poppel, and Lawrence (1953) saw one case in which an increase of 0.5 cm. was measured after 12 years' observation, a slight increase which, for technical reasons, the authors regarded as uncertain. They wrote that hamartomas are characterized by remaining unchanged in shape and size for several years. Abeles and Chaves (1952) found appreciable growth in two hamartomas. Of Carlsen and Kjaer's (1950) examples, two were found to grow during the observation period, whereas two did not. Weisel, Glicklich, and Landis (1955) reported 10 cases of hamartomas which grew, but the authors do not consider the problem. The same can be said of Benninghoven and Peirce (1933), one of whose cases showed slow but marked growth through three years of radiological control. Edling's (1938) is a characteristic case, which displayed considerable growth radiologically during an observation period of 10 years (from \(4 \times 6.5\) cm. to \(7 \times 9-10\) cm.). Other reports on growing hamartomas of the lung have not been found in the literature. An instance of growth of an extrapulmonary hamartoma is Rasmussen's case (1955) of a liver hamartoma in an infant, aged 12 months, where the tumour "seemed to grow during the stay in hospital (37 days)." At necropsy and on histological examination the hamartoma showed no signs of malignancy.

Most writers take hamartomas of the lung to be benign (e.g., Bragg and Levene, 1950). However, Simon and Ballon (1947) report a case of a histologically verified hamartoma, in parts of which malignancy could not be excluded histologically, and Kuyjer (1955) reports a case of malignant hamartoma.

The series under review comprises all patients operated on for hamartoma of the lung in the Thoracic-Surgical Department of the Øresunds hospitalet, Copenhagen, during the period 1949 to the beginning of 1957. They number 22, of whom 14 were men and eight women. The age and sex incidences are shown in Fig. 1 (at the time of detection of the radiological shadow (1a) as well as at that of operation (1b)). The majority belonged to the age group 50–60 years at the time of operation; the age group under 20 is not represented. Fig. 1 shows the surprising fact that the oldest age groups are dominated by men and the younger by women.

In only one case was the tumour seen at operation to be endobronchial. In the remaining 21 it was found in the lung at the following sites: six in the right upper lobe, eight in the right lower lobe, one in the left upper lobe, and six in the left lower lobe.

The majority of the patients were referred for surgical treatment from the Tuberculosis Test Clinic, Copenhagen, where they had been sent for routine mass radiography. It was, in other words, a question of "accidental" findings of radiological
shadows in symptom-free patients. Most of the patients were followed radiographically through an observation period, i.e., the interval from the time when tumour was recognized as a shadow till operation. Another, smaller, proportion were followed by fluoroscopy and fluorography for shorter or longer periods before the tumour was recognized.

METHOD

The typical radiographic picture of a pulmonary hamartoma is one of a sharply demarcated, rounded (circular, slightly oval, or slightly lobulated) opacity, which may vary in diameter from 3 to 4 mm. to over 10 cm., and is surrounded by normal lung tissue (e.g., Hickey and Simpson, 1926; Hall, 1948). Hence, one has a fair chance of measuring the exact size of the shadow. In the present work this measurement was performed by tracing the hamartoma shadows in the earliest and the latest radiographs, and thereafter drawing with compasses on the tracing the smallest circle that could be inscribed in and the smallest circle that could circumscribe the outlines of the shadow. The area of the circle corresponding to the mean of these two diameters has been used as an expression of the shadow, and the volume of the corresponding sphere as an approximate measure of the volume of the hamartoma. Further, the largest and smallest diameters of the tumour shadow were measured in millimetres in as many suitable photographs as possible between the first and the last ones taken within the observation period. The area of the corresponding circle has been calculated on the basis of the mean of these diameters.

The radiographs under review have been taken under uniform conditions at two different institutions (at 1.5 m. distance in the phase of maximum inspiration). We must admit, however, that direct comparison of dimensions in different photographs, though of the same individual, may involve errors.

The most important error is variation in the distance from the tube to the tumour, and, in a lesser degree, to the film. These variations depend partly on the placing of the tube and film in relation to the patient, and partly on the site of the tumour in the lung under possible different conditions at two takings from the same individuals. The respiratory phase may influence the distance of the tumour from the tube. To evaluate this error we measured in the first and last pictures the distance between two as far as possible fixed osseous points so remote from each other as to be just within the range of reading. (The series comprises adults solely, so that growth of the bony system can be excluded.) These measurements showed negligible differences in extent compared with those of the tumour shadows in the same pictures. Exact localization of the hamartoma in all dimensions in the lung has not been possible. More particularly it has been impossible to get an impression of the variations with the respiratory phase of these most often peripheral tumours. Such variations are probably not important, because all the photographs were taken in the phase of maximum inspiration. The respiratory phase is unlikely to influence the volume of hard and unyielding hamartomas. Another source of error may be different times of exposure. This is unlikely to be important where sharply circumscribed shadows are concerned.

PATHOLOGY

The patho-anatomical sizes of all the hamartomas averaged 28.5 mm. in diameter; those of the women averaged 24 mm. and those of the men 31 mm. The tumours were distinct from the surrounding lung.

On microscopic examination a diagnosis of hamartoma of the lung was made in all cases on the basis of the current histological criteria in the literature, e.g., those of Carlsen and Kier (1950). In one case interstitial pneumonia was found in the lung beyond the limit of the hamartoma, which explains the difficult radiographic interpretation in this case (No. 19). In four the hamartoma contained no cartilage but was otherwise typical. In 15 of the cartilaginous hamartomas calcification was present.

None of the hamartomas were malignant, but the ruled out a malignant tumour which displayed certain signs of having developed from a hamartoma, though this opinion could not be proved.

RESULTS

The series may be divided into three groups:

GROUP I.—Eleven cases were followed radiographically through an observation period.
GROUP II.—Five cases were followed by fluoroscopy through a control period.

GROUP III.—Five cases were observed for too short periods or inadequately, and one case presented an atypical picture.

The cases of Group I are listed in Table I. The mean diameters of the first and last radiographic shadows are recorded (the total increase in millimetres) and the increase calculated per year within the observation period. The latter is seen to have ranged from 0.5 to 5 mm. Only in cases observed for more than three years was an increase in size of the shadow recognizable. Further, Table I shows the increase in area calculated as the difference between the areas of the circles corresponding to the mean diameters. By calculating the relative total increase in area (the growth of the shadow), this varies from one-fifth to five times the extent of the original shadow, in other words, an appreciable increase. To obtain an approximate expression of the proper growth of the pulmonary

**Table I**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age at Operation (Years)</th>
<th>First Radiograph (Mean Diam., mm.)</th>
<th>Last Radiograph (Mean Diam., mm.)</th>
<th>Increase (mm.)</th>
<th>Observation Period (Years)</th>
<th>Mean Growth (mm./Year)</th>
<th>Increase (sq. mm.)</th>
<th>Mean Increase (sq. mm./Year)</th>
<th>Percentage Increase of Area (&quot;Increase of Shadow&quot;)</th>
<th>Mean Increase (c.mm./Year)</th>
<th>Mean Increase (c.mm.)</th>
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**Fig. 2.**—Increase of area, being a graphic representation of Group I (Cases 6 and 13 excluded). For each curve the patient's sex and case number are indicated.
hamartomas, we have, with reference to their most often spherical shape, calculated the total as well as the annual increase in volume.

Fig. 2 is a graphic representation of the results set out in Table I. The patient’s age is the abscissa and the size in square centimetres the ordinate. The patient’s sex is also indicated. Included in the chart are also the results of measurements of shadows in radiographs taken at different times within the observation period between the first and the last pictures. (Cases 6 and 13 are ruled out for the sake of clarity.)

Table II illustrates the results for Group II, which comprises five cases controlled exclusively by fluoroscopy. In Table II are recorded the period during which the patient has been controlled without any abnormality having been noticed, as well as the number of fluoroscopic examinations within this period. Further, Table II shows the time of the first positive fluoroscopic finding, as well as the time of operation, and the tumour size in the photograph taken in direct relation to the positive fluoroscopic finding before operation. In Case 15 the film showed such blurred markings of the surrounding lung tissue, presumably due to atelectasis or chronic interstitial pneumonia, that the tumour shadow was impossible to measure. All five patients were controlled fluoroscopically at the tuberculosis clinic by an experienced medical staff. When, therefore, a patient controlled for a number of years without any abnormality having been found suddenly displays morbid changes which on operation prove to be of hamartomatous origin, we must be justified in supposing that the tumour has only gradually attained such a size as to be recognizable fluoroscopically. Table II shows that an unquestionable increase in size has been recorded in the five cases.

Group III comprises five cases observed for too short periods, i.e., less than 12 months. These patients could not be included in an estimate of the growth conditions of such a relatively slow-growing tumour. One patient (No. 19) had such blurred markings in the films that measurements could not be made.

**DISCUSSION**

Exact measurement of the growth of benign human tumours is generally difficult to carry through. The tumour may be inaccessible to direct measurement, such as a uterine fibromyoma, or its possible variations in size may have escaped recording, as is probably generally the case where benign skin tumours are concerned, whose growth most often must be roughly assessed, in part by the patient himself. The tumours that are fairly accurately measurable indirectly, i.e., especially by radiography, are chiefly osseous and cartilaginous tumours. Hamartomas of the lung, which are “isolated,” shadow-producing tumours in “translucent” tissue, are especially suitable for indirect recording of size. The question is therefor whether the variations in the size of the hamartoma observed in the present study represent similar variations in the size of the hamartoma itself. The sources of error mentioned under “Method” in comparing the picture are incorrigible, but we judge them to be of little importance, especially when we look at Fig. 2, which shows a gradual increase in size of the shadows where several measurements have been practicable within the observation period. Variations in size of tumours need not be indicative of growth, but may be due to oedema, congestion, or necrosis, for instance. These phenomena are not important in cases of hamartoma, which generally consist mainly of cartilage with little chance of oedema or necrosis.

We are thus of the opinion that the results achieved from our study bear evidence of growth of pulmonary hamartomas. Where we have recorded an increase in area it is actually an increase in volume that has taken place. Hamartomas being generally almost spherical in shape, we have calculated the increase in volume on the basis of the mean diameters of the measured frontal radiographic shadows (Table I).

The growth of the hamartomas was slow, having been demonstrable only after an observation period of more than three years, but it was marked, the tumour having attained a size of up to just over five times that in the earliest photograph. In a few instances the hamartoma was so large that the mere size was an indication for operation owing to a risk of pressure symptoms. Further, the tumours grew steadily, though with individual variations in the rate of growth. The speed of growth was a little more pronounced for the large hamartomas.
than for the smaller ones, without any constant relationship having been noticed. The growth curves give no explanation of the previously mentioned sex difference (the women were much younger than the men). At least the growth rate was not higher in the women than in the men. The series under review is selected, in as far as it comprises only patients who underwent an operation.

An attempt to find correlation between the growth rate and certain histological features, e.g., cartilage cell polymorphism or irregular cartilage cell arrangement, gave a negative result. On the contrary, Case 5, for instance, showed cartilage cell polymorphism, but a low growth intensity. There is accordance between the growth curves and the histological findings in respect of the fact that none of the growth curves suggest a sudden increase in growth indicating possible malignant proliferation, and none of the hamartomas have displayed histological signs of malignancy.

Summary

The growth conditions of hamartomas of the lung have been analysed in 22 cases operated on after having been under radiological observation for from one to 18 years. In 16 of these the growth could be followed radiographically (Groups I and II).

The result (Tables I and II) was that in nine cases observed for more than three years (Group I) unquestionable growth was demonstrated, with an increase in the size of the shadow of up to five times that in the earliest photograph, whereas two cases observed for one and two years respectively showed no growth. Another group (II) displayed positive findings on fluoroscopy after several negative fluoroscopic examinations. This has been interpreted as growth.

The increase in size of the radiological shadow is illustrated graphically (Fig. 2). The chart shows a relatively flat, gradually rising growth curve. The individual hamartomas varied in growth rate, this being generally the highest for the largest tumours, and independent of age and sex. The age and sex distribution (Fig. 1) showed a preponderance of men in the oldest age groups and of women in the younger.

None of the growth curves show sudden increases which might suggest malignant change, and histological examination of the hamartomas has not revealed malignancy. We ruled out a malignant tumour, which displayed certain signs suggesting development from a hamartoma, without this diagnosis having been established.

References