The Diagnosis and Management of Solitary Circumscribed Lesions of the Lungs

CORRIN H. HODGSON, M.D.* and JOHN R. MCDONALD, M.D., F.C.C.P.**
Rochester, Minnesota

Advances in diagnosis and therapy quite naturally stimulate interest in medical subjects and such is certainly true of the isolated pulmonary nodule. The more hopeful outlook justifies the placing of emphasis on this problem.

There is a trend toward pulmonary resection as a simple solution to the complex problem of solitary lesions of the lungs. The fact that a great many of such lesions should be treated by pulmonary resection does not diminish the physician's responsibility to those patients whose lesions should not be so treated; therefore, we should like to introduce this subject by emphasizing that the final decision regarding every patient with a solitary lesion of the lungs should be based on judicious individual consideration and not on a rule of thumb.

The great importance of this subject, the solitary pulmonary lesion, is well recognized by those of us interested in diseases of the chest. One of the chief reasons it is important is that some of the lesions are malignant. The proportion of circumscribed undiagnosed densities of the lung that represent malignant lesions is variously given as 20 to 55 per cent. Grow, Bradford and Mahon in a series of 86 circumscribed, undiagnosed lesions, found 23 per cent to be malignant tumors and 49 per cent granulomas. Abeles and Ehrlich, in New York City, explored 21 lesions, 33 per cent of which were found to be malignant and 20 per cent "tuberculomas." Watson of Memorial Hospital found 40 per cent of 104 silent intrathoracic tumors to be malignant. Overholt performed an exploratory operation on 145 patients for abnormalities discovered in roentgen-ray surveys and found that 24 per cent had malignant tumors. Harrington reviewed a series of 52 cases of asymptomatic intrathoracic lesions in which he had carried out exploration and reported that 23 per cent represented malignant growths. Hood, Good, Clagett, and McDonald recently studied 158 consecutive cases of solitary circumscribed lesions which were totally removed surgically. Of these lesions, 35.5 per cent were malignant, 16.5 per cent of the total series being primary bronchogenic carcinoma, 11.4 per cent metastatic lesions, and 7.6 per cent bronchial adenoma. Granulomas constituted 41.8 per cent of the entire group. Others have reported the total rate of malignancy for resected solitary pulmonary lesions as follows: Davis and Klepsor, 55 per cent; O'Brien, Tuttle and Ferkayne, 42.9 per cent; Fink, 33 per cent; and Sharp and Kinsella, 27.3 per cent.

Although the foregoing figures do not represent comparable series of cases, the implication is the same for all of them, namely, that a signif-

*Division of Medicine, Mayo Clinic, Rochester, Minnesota.
**Division of Surgical Pathology, Mayo Clinic, Rochester, Minnesota.
icant percentage of the clinically undiagnosable lesions of the lungs are malignant. It would seem unlikely, however, that as high a percentage of all solitary lesions of the lung are malignant as is represented by the figures just given. It is reasonable to assume that each of these series included cases in which there was a high degree of suspicion that the lesion was malignant, this being the reason for surgical removal and, therefore, inclusion in the report, whereas other cases were excluded by an equally high suspicion that they were benign. Too, malignant lesions are more apt to cause symptoms and therefore bring the patient to the physician, while benign lesions await accidental detection.

A second, and not insignificant, reason for this being an important subject is the high incidence of granulomas, as indicated by some of the foregoing figures. While many of the granulomatous lesions either heal or remain stationary, others break down, disseminate their contents and often spread the infection which has caused them. For this reason surgical extirpation is to be recommended for many such pulmonary lesions. Thus, it would seem that somewhere between 50 and 75 per cent of the solitary circumscribed lesions of the lungs are either granulomas or malignant tumors which should be removed. The remainder, not an insignificant number, are important because they cannot be distinguished from the above-mentioned lesions as a rule, and are treated by pulmonary resection because of the physician's inability to separate clinically the nonsurgical from the surgical lesions.

**Difficulties in Diagnosis**

Many factors are responsible for the difficulty in establishing the cause of most of these circumscribed lesions. Most such lesions are peripherally

---

**Figure 1A**

**Figure 1B**

*Figure 1 (A and B): Pigmented mole causing a shadow that was thought to represent tuberculosis.*
placed, beyond the limits of bronchoscopic visualization. In the case of
tuberculomas, smears of sputum seldom demonstrate the organisms, and
cultures of sputum and gastric contents for tubercle bacilli do not often
give positive results. The long delay in obtaining the final culture report
destroys the value of the procedure when one must act promptly because
of the possibility that the lesion is malignant. Cultures for fungi take less
than do cultures for tubercle bacilli, fortunately. The necessity of haste
is a troublesome factor, yet prompt action is essential, for if the lesion is
cancerous, delay of a few weeks may prove fatal. Malignant cells can be
demonstrated in the sputum of only about 10 to 15 per cent of the cases of
peripherally placed cancerous lesions, thus limiting the value of cytologic
examination. The skin sensitivity tests for various pathogens are of limited
value, as will be seen later. Roentgenographically, there are few distin-
guishing characteristics by which these shadows can be differentiated. In
the majority of cases, these limitations are sufficient to prevent the making
of a diagnosis except after surgical removal of the solitary nodule.

Intrathoracic Lesions Which Do Not
Cause Circumscribed Shadows

Before discussing the lesions which do cause circumscribed solitary shad-
ows we wish to mention a number of intrathoracic conditions which do
not. Such shadows are not due to teratoids, dermoids, thymomas, intra-

![FIGURE 2: Unilateral shadow of the nipple resembling an intrapulmonary tumor.](image-url)
thoracic thyroids, pleuropericardial cysts or diaphragmatic hernias and are rarely, if ever, due to arterial aneurysms or tumors of the lymphoma group.

**Extrapulmonary Shadows Simulating Intrapulmonary Masses**

The superimposition of roentgenographic shadows of lesions not actually within the lungs may resemble those of intrapulmonary masses and unless we localize every one of these lesions accurately, embarrassing errors in diagnosis will result. Lesions of the skin, such as tumors and moles, not uncommonly cast shadows that resemble nodules in the lung (Figure 1). The nipple shadow, when only one breast is present, may prove confusing (Figure 2). Tumors of the thoracic wall, such as osteochondromas of the

---

**FIGURE 3A**

*Figure 3*: Cardiac decompensation with interlobar pleural effusion. There was an interval of four days between A and B.

**FIGURE 3B**

**FIGURE 4A**

*Figure 4 (A and B)*: Fibrous mesothelioma of the interlobar pleura.
ribs or intercostal neurofibromas, have been interpreted as being intrapulmonary. Stereoscopic roentgenograms taken in the postero-anterior projection plus those taken in the lateral projection usually suffice to localize the process roentgenographically.

Certain pleural lesions such as encapsulated fluid (Figure 3) or empyema, fibrous mesothelioma (Figure 4), and pleural plaques may simulate lesions of the parenchyma of the lung, especially when they occur in the interlobar pleura.

**FIGURE 5A**

*Figure 5: Aneurysm of the inferior pulmonary vein. Circumscribed lesion discovered on routine survey. A, Roentgenographic appearance. B, Gross appearance at operation.*

**FIGURE 6A**

*Figure 6: A. Acute pneumonitis resembling tumor. B, Disappearance in ten days.*
Pulmonary Lesions Causing Circumscribed Shadows

Vascular Abnormalities: Very few vascular lesions are solitary and circumscribed. Arterial aneurysms probably always are contiguous with the hilum and therefore are not discrete lesions. We have seen one aneurysm of the inferior pulmonary vein (Figure 5) which was a discrete lesion within the substance of the lung, but it is mentioned here only to emphasize the rarity of its occurrence.

Pneumonitis, Abscess, Infarction and Hydatid Disease: Acute pneumonitis may, on occasion, give a circumscribed density as seen on the roentgenogram (Figure 6). In such a case, however, the history of recent respiratory symptoms should lead one to repeat the roentgenographic examination after an interval, and in all likelihood there will be a definite change in the appearance of the lesion. Acute and chronic (Figure 7) abscesses of the lung often produce a discrete tumefactive lesion within the lung, and in such cases the history again should give the proper clue to their identity. Not to be overlooked is the common condition, pulmonary infarction (Figure 8), which may adopt a freakish nature and resemble an intrapulmonary neoplasm. Should such a situation occur and thoracic exploration be carried out, the patient would be subjected to a procedure performed under hazardous conditions and with no hope of benefit. Such cases emphasize the importance of the history and the need for individual consideration of every patient who has a pulmonary lesion. The case illustrated (Figure 8) also brings to mind the value of obtaining previously taken roentgenograms, which were available in this case and were of paramount importance in arriving at the correct diagnosis. On that rare occasion when one sees echinococcosis of the lung it is most likely to present as a well-defined, circumscribed mass, probably solitary.

Granulomas (Figures 9, 10, 11 and 12): As seen from the previous discussion, the granulomatous lesions are numerically the largest group under consideration here. They are clinically significant because of the pos-
solubility of dissemination of the infection causing them. Pathologically, the different types of granuloma can be distinguished from each other only by identifying the causative organism or substance. From microscopic examination of the tissues identification is possible only in some cases of histoplasmosis, coccidioidomycosis and actinomycosis, and in oil granuloma. One cannot be sure of the identity of tubercle bacilli because they may be simulated by other acid-fast organisms and debris, and their identity must be confirmed by culture and guinea pig inoculation in any event. It is, therefore, a waste of time to search for acid-fast organisms in tissue sections.

Bacteriologic examination of granulomatous tissue removed at operation is fully as important as the microscopic examination of excised tumors and should consist of (1) microscopic examination of direct smears and fixed sections to search for and identify fungi and other causative agents, (2) culture for routinely encountered organisms, tubercle bacilli and fungi, and (3) guinea pig inoculation. If structures suggestive of tubercle bacilli or fungi are found in the histologic sections, the interpretation should be confirmed or corrected by cultures. Dr. L. A. Weed \(^1\) of the Mayo Clinic conducted such a study of the specimens removed from 81 patients with granulomas of the lung and was able to identify tubercle bacilli in 13, Coccidioides in three, and Brucella suis, Streptococcus faecalis, Escherichia coli, Staphylococcus and Micrococcus in one case each. The remaining 60 failed to yield causative organisms. The cause of these 60 bacteriologically

![Image](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21238/)

FIGURE 9: Tuberculoma. Tissue positive for tubercle bacilli on culture and guinea pig inoculation.
negative granulomas is unknown. However, many of these have been referred to as a Ghon tubercle in the past, a lesion which has been commonly regarded as the residuum of primary tuberculosis. Such a concept has a number of fallacies. These lesions are frequently inactive histologically (no giant cells or epithelioid cells) and it is likely that they do represent a “burned out” granulomatous infection. The nature of that infection is conjectural, however. We have seen “typical” Ghon tubercles which yielded

FIGURE 10A  FIGURE 10B
Figure 10 (A and B): Granuloma. Tissue culture yielded Coccidioides immitis.

FIGURE 11: Granuloma removed surgically. Tissue culture was positive for Brucella suis.
a few colonies of Coccidioides immitis on culture. We believe that no granuloma in the lung should be regarded as tuberculous when bacteriologic proof is lacking, and we feel that the word "tuberculoma" should be reserved for those granulomas proved bacteriologically to be due to the tubercle bacillus.

One should not conclude a discussion of granulomatous lesions of the lung without consideration of the specific skin tests and their value as diagnostic tools. The authors of one article stated that if a patient with a circumscribed pulmonary lesion had a positive skin reaction with coccidioidin or histoplasmin, they did not then recommend thoracic exploration. Their reasoning is difficult to understand, and we mention this here only to condemn it. The skin tests are very helpful diagnostic aids, but the

**FIGURE 12**

*Figure 12*: Oil granuloma, right lower lobe, proved at necropsy. The patient had ingested mineral oil for many years and the lesion had been present for eight years.—**FIGURE 13**: Hamartoma showing evidence of calcification.

**FIGURE 14A**

**FIGURE 14B**

*Figure 14 (A and B)*: Bronchial adenoma showing increase in size over a four-year period.
results should never influence one in making the decision to explore or not to explore a thoracic lesion of unknown cause. It should be pointed out that if a localized lesion proves to be a manifestation of coccidioidomycosis or histoplasmosis, resection is good treatment. Among the multitude of people in the United States who are positive reactors to one or another of the specific antigens, a large number will ultimately have malignant lesions and the reaction to skin testing will not be altered or related in any way to such a lesion. The high degree of specificity of the tuberculin test is not yet substantiated for the other antigens.

**Benign Tumors:** Some of the peripheral lesions will prove to be benign tumors such as bronchogenic cysts or hamartomas (Figure 13). The former may on occasion undergo malignant changes, but the latter would never warrant resection if its absolute identity could be established preoperatively. Unfortunately, however, accurate identification of hamartomas is almost never possible until they are removed. They may even slowly enlarge while under observation, thus simulating other expanding types of tumors. When calcification is demonstrated within a hamartoma on roentgen-ray examination, as it frequently is, one cannot even then distinguish it from a calcifying granuloma. Thus, the majority of benign tumors will need removal in order to prove their innocence.

**Adenoma of the Bronchus** (Figure 14): When compared with other types of carcinoma of the lung, adenomas of the bronchus are relatively benign and definitely a distinct entity. Nevertheless, between 5 and 10 per cent of them will metastasize and therefore all of them are a menace and must be removed when found. As they are covered with mucous membrane they do not shed tissue and consequently no cells are present in the sputum. Most adenomas are centrally placed and within the range of bronchoscopic visualization and biopsy, but an occasional one will be peripheral, making

---

**Figure 15:** The initial diagnosis was tuberculosis. After observation in a sanatorium the patient underwent left pneumonectomy for carcinoma. Death resulted from metastasis. Three years elapsed between A and B.
removal the only means of recognition. Moersch and McDonald\textsuperscript{12} found that 91 per cent could be visualized bronchoscopically.

\textit{Malignant Tumors} (Figure 15): The chief reason for concern and haste in the management of solitary lesions of the lung is the frequency with which they prove to be malignant and the disaster that befalls the patient when these tumors are not promptly recognized and removed. True enough, some of these solitary carcinomas are metastatic growths from tumors arising in other organs, but others are primary and curable and the two cannot be separated clinically. Malignant cells can be demonstrated in the sputum in only about 10 to 15 per cent of the cases of peripheral carcinoma, which is about the same percentage as is found in cases of metastatic lesions. Almost all the truly peripheral carcinomas are of the large cell or adenocarcinoma type.

There has been much discussion as to the size a nodule should be before it becomes clinically significant; this seems to be a rather hollow argument in view of the fact that every large, clinically important lesion was tiny during one period of its growth, and this would have been the time to eliminate it. The chance that a small nodule is significant is not as great as that of a large one, and yet none of them can be ruled insignificant on a basis of size alone.

If carcinoma is a possibility, one must not lose time with slow diagnostic methods such as cultures for tuberculosis. The practice of sending patients to the sanatorium for weeks or months in an effort to confirm a suspicion of tuberculosis must be abandoned. Unfortunately, many of our tuberculosis sanatoria are far removed from centers of population and are necessarily limited in their clinical and laboratory facilities for general diagnosis. Such institutions should not be considered diagnostic hospitals and patients should be sent to them only when a diagnosis of tuberculosis has been substantiated by acceptable procedures, but never when there remains a reasonable doubt.

The former practice of taking roentgenograms at intervals, waiting for some alternation in the size of a tumor, must also be condemned. Cancer of the lung may remain the same size for many months and to wait for some change may be the fatal delay. A "period of observation" is an obsolete tool in our diagnostic kit.

The factor of age as a guide to the diagnosis of carcinoma of the lung is proving to be unreliable as more and more malignant lesions are being recognized in younger people in their early thirties. Carcinoma of the lung occurs much more frequently in men than in women, but this difference is not sufficient to be of diagnostic significance.

\textit{Solitary Metastatic Lesions:} The problem of solitary metastatic growths in the lungs raises a number of interesting and important questions. As mentioned above, it is rarely possible clinically to differentiate between primary and secondary cancerous lesions when dealing with solitary nodules, and in a rather high percentage of cases the pathologist may not be able to tell even after examining the surgical specimen whether a growth at its site of origin or merely a metastatic lesion has been removed. These
**Figure 16**: The patient underwent resection for an annular carcinoma of the rectosigmoid in 1922 and right hemicolec- tomy for adenocarcinoma in 1948, when the presence of a metastatic lesion in the lung was suspected. In 1951 resection of the lung for bronchial adenoma was performed.—**Figure 17 (A and B)**: Granuloma. The value of tomography in demonstrating calcification is illustrated.
limitations to discernibility should be emphasized because the final results in any study of patients with such lesions will be considerably influenced by the number of patients with metastatic lesions included in the group—patients for whom there is no hope of ultimate cure.

When metastasis is a possibility one should make a reasonable search for the primary tumor. The word "reasonable" is used advisedly. The method and extent of any investigation to be conducted depend on the history and findings in the individual case and will vary accordingly. Surely any clue to the source of trouble should be carefully studied. On the other hand, one is not justified in going to extremes because the yield is poor when one is searching blindly for primary tumors and there are no symptoms or findings to point the way.

When a patient has or has had a known malignant condition and a solitary pulmonary lesion develops, we are not justified in jumping to the conclusion that the pulmonary affair represents metastasis of a malignant growth. It must be remembered that he is still subject to other unrelated disorders or may even have a second malignant tumor. When this situation prevails, individualization is of the utmost importance and many factors must be considered: the location and type of the first tumor, the extent and speed of its growth, its invasive characteristics, the time interval between removal or discovery of the original tumor and the appearance of the supposed metastatic tumor, the evidence of metastasis elsewhere, and the age and general condition of the patient. Under favorable conditions, exploration may be justified because (1) of the possibility that the pulmonary lesion may not be metastatic from the known original tumor (Figure 16) or (2) the removal of known metastatic tumors at times may be worth while as a palliative procedure. Obviously, the latter will be exceptional.

The Significance of Calcification

Before closing this discussion it is well to consider the significance of calcification within a pulmonary lesion. If the physician is to use this sign as a guide in the management of the lesion in question he must be absolutely sure that what he sees is calcium and that it lies within the mass. Often, tomography will demonstrate the presence of calcium in a lesion when it is not clearly shown on ordinary types of roentgenograms (Figure 17). Calcification may occur in a number of pulmonary conditions such as in old tuberculous foci, hematomas and hamartomas, around foreign bodies, within parasites, in thyroid and thymic tissue or tumors, in teratoma and dermoids, in granulomas, notably coccidiodomycosis and histoplasmosis, in pleural plaques, in metastatic osteogenic sarcoma, and perhaps rarely in a case of adenoma of the bronchus. Therefore, the presence of calcification is not specific. The presence of calcification indicates that the lesion is not a carcinoma, except in those rare instances in which a carcinoma has developed around a stone in the lung or as a secondary change in an otherwise benign condition such as teratoma. In spite of the comforting assurance that the presence of calcium gives, there are
some calcific lesions which should be removed. Granulomatous lesions may evacuate and spread the infection causing them. Many of them will yield positive cultures even though they may seem well calcified. Mahon and Forsee\textsuperscript{13} have stated that the laminated or target lesions are always sterile, however. The calcification within a hamartoma or other neoplasm would not have the laminations seen in some granulomas. For the most part, lesions containing calcium may be left alone, but the clinician must exercise his judgment in determining those to be removed.

As seen from the foregoing, the problem of the solitary lesion of the lung is a complicated one imposing great responsibility on the physician. We cannot escape that responsibility by generalizations, but must individualize each case as it comes to us.


\textbf{SUMMARY}

1) Solitary circumscribed lesions of the lung are significant because of the frequency with which they are malignant and the potential danger when granulomatous.

2) In the majority of cases the diagnostic limitations are sufficient to prevent making a diagnosis except after surgical removal.

3) Complete bacteriologic study of granulomatous tissue is as important as microscopic examination of tumor tissue.

4) The results of specific skin tests are of limited diagnostic value and are never conclusive in themselves.

5) The presence of a known extrapulmonary malignant lesion is not incontestable proof that an intrapulmonary nodule in the same patient is metastatic.

6) Slow diagnostic methods and prolonged periods of observation have no place in the management of the patient with a possible malignant tumor of the lung.

7) Most intrapulmonary nodules containing calcium need not be removed.

8) Careful individual consideration must be given each patient with a solitary lesion of the lung.

\textbf{RESUMEN}

1) Las lesiones circunscritas del pulmón son significativas por qué con frecuencia son malignas y cuando son granulomatosas, potencialmente peligrosas.

2) En la mayoría de los casos las limitaciones del diagnóstico obligan a llegar a él sólo por la extirpación quirúrgica.

3) Un estudio bacteriológico completo del tejido granulomatoso es tan importante como el examen microscópico de tejido tumoral.

4) Los resultados de las pruebas cutáneas específicas son de limitado valor diagnóstico y por sí solos nunca son concluyentes.

5) La presencia de una lesión maligna extrapulmonar comprobada no
es una prueba indiscutible de que un nódulo intrapulmonar en el mismo enfermo sea una metástasis.

6) No hay lugar para los métodos lentos de diagnóstico y los prolongados periodos de observación, al tratarse a un enfermo de posible tumor maligno del pulmón.

7) La mayoría de los nódulos intrapulmonares que contienen calcio no necesitan ser extirpados.

8) Debe estudiarse cuidadosamente cada caso cuando hay una lesión solitaria del pulmón.

RESUME

1) Les lésions isolées circonscrites du poumon ont une valeur particulière à cause de la fréquence avec laquelle elles se montrent malignes, et leur danger en puissance lorsqu'elles sont granulomateuses.

2) Dans la plupart des cas, les possibilités de diagnostic sont telles qu'on peut le porter sans attendre l'exirpation chirurgicale.

3) L'étude bactériologique complète du tissu granulomateux a une importance aussi grande que l'examen macroscopique du tissu tumoral.

4) Les résultats des tests cutanés spécifiques sont de valeur limitée au point de vue diagnostique, et ne sont jamais suffisants à eux seuls.

5) L'existence d'une altération maligne extra-pulmonaire déjà connue n'est pas une preuve incontestable qu'il s'agit de métaastases pour la masse intra-pulmonaire constatées chez le même malade.

6) Il n'y a pas place pour des méthodes de diagnostic lents et de longues périodes d'observation quand il s'agit d'un malade chez lequel existe la possibilité d'un cancer du poumon.

7) La plupart des nODULES intra-pulmonaires comprenant des parties calcifiées doivent être excisés. Une observation attentive est nécessaire pour chaque malade atteint d'une lésion isolée du poumon.

REFERENCES

3 Watson, W. S.: Quoted by Overholt, R. H.
6 Hood, R. T. Jr., Good, C. A., Clagett, O. T. and McDonald, J. R.: Personal communication to the authors.
11 Weed, L. A. Personal communication to the authors.