Joint Pain And Pulmonary Disease

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JOINT PAIN AND PULMONARY DISEASE*

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Dr. Geoffrey Brinkman: Before presenting today's case, I would like to discuss a rather uncommon but interesting and important physical sign of pulmonary disease.

This man (Figure 1) complained of severe arthritis, the pain of which immobilized him. His hands looked spatular due to severe edema extending to the fingertips. He had clubbing, and the wrist joints were swollen. In the feet the same changes were noticed; he had thick ankles and clubbing of the toes, all of which are very suggestive of pulmonary osteoarthropathy. These physical signs immediately give a lead as to the underlying condition. I have asked Dr. Friedman to tell us a little more about it.

Dr. Ivan Friedman: The significance of pulmonary hypertrophic osteoarthropathy lies in the fact that in the majority of cases, it is associated with bronchogenic carcinoma. It has been variously reported to occur in 5 to 10 per cent of cases of bronchogenic carcinoma. Much less frequently, it may be associated with pleural mesothelioma. It also occurs infrequently with such intrathoracic lesions as dilatation or neoplasm of the esophagus, neurofibroma of the mediastinum, and mediastinal cysts. Very occasionally, it has also been reported in metastatic lung cancer.

The syndrome of pulmonary hypertrophic osteoarthropathy should be distinguished from clubbing of the digits. Osteoarthropathy consists of an overgrowth of vascular connective tissue of the distal limbs resulting in new growth of periosteal bone and may, or may not, include clubbing. In the majority of cases hypertrophic pulmonary osteoarthropathy is associated with bronchogenic carcinoma or some other type of intrathoracic lesion, whereas simple clubbing may be associated with non-pulmonary disease, e.g.:

*Edited by W. S. Haubrich, M.D., Chairman, Tuesday Morning Medical Clinic Committee.
Figure 1

Swelling of the hands and wrists with clubbing of the fingers typical of pulmonary osteoarthropathy.

1) Congenital, cyanotic, cardiac lesions with right-to-left shunt;
2) Acquired cardiac lesions such as subacute bacterial endocarditis;
3) Digestive system disorders such as sprue, ulcerative colitis, regional enteritis, cancer of the colon, polyps of the colon, tumors of the small bowel, and cirrhosis, especially of the biliary type;
4) Chronic myelogenous leukemia, chronic pyelonephritis, and such toxic conditions as phosphorus, arsenic, and beryllium poisoning; and finally,
5) It also has been reported in syphilis and syringomyelia.

Rarely, idiopathic hypertrophic osteoarthropathy may occur in the absence of underlying disease. The distinguishing features of these idiopathic cases is that all
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have occurred in males; usually the onset is at puberty or soon after. It has no influence on the life span or general health of the patient. The growth of the acral parts is usually painless which distinguishes it from the pain associated with the secondary type of hypertrophic pulmonary osteoarthropathy.

Dr. Brinkman: Dr. Friedman, what is the treatment of the painful osteoarthropathy if the patient has incurable bronchogenic carcinoma?

Dr. Friedman: Several methods of treatment have been used. Of course, the best and most efficient treatment is removing the actual lesion in the thorax. This is usually associated with relief of the arthropathy, even though it might not cure the underlying disease. If this is not feasible, vagotomy will relieve the pain even though it has no influence on the underlying condition. On some occasions, simple thoracotomy has been reported to relieve the pain. If none of these procedures is possible, then symptomatic relief may, on occasion, be obtained with corticosteroids or phenylbutazone.

Dr. Brinkman: Now, we will proceed to the case presentation. In addition to Dr. Coates and Dr. Bower, of our staff, we have a guest panelist this morning, Dr. Paul Chapman, who is Tuberculosis Controller for the City of Detroit and Chief Physician at Herman Kiefer Hospital. It may surprise some of you who believe that tuberculosis is a disease of the past to know that at present there are 1000 patients at Herman Kiefer Hospital undergoing treatment for tuberculosis.

Dr. Friedman: Our patient is a 62 year-old truck driver who was quite well until January, 1962, at which time, following a "flu"-like episode, he began to complain of pains in his hips and his ankles. Since then, he has had arthralgias in most of the other joints, but these were transient. In October, 1962, he came to the Emergency Room complaining of inability to walk because of pain in his hips and swelling of his ankles. He did not have any chest complaints except for the chronic cough which was an incidental complaint and had been present for many years.

Dr. Brinkman: On examination he had severe clubbing with osteoarthropathy.

Dr. Friedman: There was also a weight loss of about 30 lbs in the past 6 months.

Dr. Brinkman: In his chest x-ray (Figure 2) there are large infiltrates in the upper left lobe and in the right lower lung area with a suggestion of a large cavity at the apex of the right lower lobe. Dr. Friedman, in view of your dissertation a minute ago, what would you think was the most likely diagnosis in this man?

Dr. Friedman: I would certainly say bronchogenic carcinoma.

Dr. Brinkman: Yes, I agree; about 10 per cent of patients with bronchogenic carcinoma have joint pain, and in about 3 per cent this is actually the presenting symptom. He had a bronchoscopy which was negative. Bronchial washings were
Figure 2

Chest roentgenogram showing bilateral infiltration. The cavity at the apex of right lower lobe is faintly discernible.

done, and these were normal. Dr. Eyler, you saw these x-rays originally. Do you remember your initial impression?

Dr. Eyler: Yes, I thought it hard to put everything together with a diagnosis of bronchogenic carcinoma because of the diffuse involvement and the character of the infiltrations. I thought he had chronic inflammatory disease.

Dr. Brinkman: The x-ray, then, was not characteristic of lung cancer, and so far we hadn't established a diagnosis. Sputum examinations were obtained. On Papanicolaou smear, one of these was definitely positive for malignant cells. Another specimen was positive on smear for acid fast bacilli. We now had a double diagnosis. He had bronchogenic carcinoma, which accounts, I expect, for his osteoarthropathy and, as well, he had pulmonary tuberculosis, which accounts for the rather atypical x-ray appearance. Dr. Chapman, would you say these two diseases form an increasingly common association?

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Dr. Chapman: I think they do. In our experience, and in that recorded by others, the association of cancer in tuberculous patients seems to be more evident than it was a while back. I think it always was a little more than most people gave it credit for. Of course, the patient population with tuberculosis is older and this, in part, may account for the association. Some people think it runs as high as 7 per cent. Sometimes the cancer occurs in the presence of active tuberculosis; others have been treated for tuberculosis and returned with what appears to have been a relapse, and then have been found subsequently not to have had a relapse but carcinoma.

Dr. Brinkman: In your experience, does the carcinoma occur in the same area of lung as the tuberculosis, or elsewhere in the lungs?

Dr. Chapman: Usually it is in the same area of disease.

Dr. Brinkman: I was wondering, Dr. Coates, is there any way we can get an indication on admission that a patient may have bronchogenic carcinoma as well as tuberculosis? Is there any clue we might look for?

Dr. Osborne Coates: The most obvious clue in this particular patient was the osteoarthropathy, but the location of the lesion in the lung is important. Tuberculosis usually occurs in a posterior segment of the upper lobe or in the superior segment of the lower lobe. If, on the other hand, the lesion is predominantly in the anterior segment, we should first consider some other diagnosis than tuberculosis.

From the Audience: In this case you established the diagnosis of bronchogenic carcinoma on the basis of tumor cells in the sputum. Is this a reliable test?

Dr. Brinkman: In our laboratory, a report of malignant cells in the sputum has been very reliable.

From the Audience: For a primary tumor only?

Dr. Brinkman: I would say for a primary tumor. I don’t think we have had much experience with sputum examination in metastatic disease.

Now, how about the reverse situation? How often do we see patients with primary bronchogenic carcinoma who have been treated and subsequently develop tuberculosis?

Dr. Chapman: I have seen it occasionally. I feel certain that the tumor was the primary disease and, as it progressed, the tuberculosis, otherwise latent, became sufficiently active to produce a positive sputum.

Dr. Brinkman: I would like to ask Dr. Bower a question. We blame cigarettes for bronchogenic carcinoma. Is there any evidence that people who have tuberculosis...
smoke more, and if so, could it be the cigarette smoking that gives them bronchogenic carcinoma? Is there anything to support that theory?

_Dr. G. C. Bower:_ I am not sure. I think if we were to do careful studies of people with tuberculosis, we might find that at least up to the time that they were found to have active tuberculosis, perhaps their smoking habits might be different from the rest of the non-tuberculous population. Perhaps, tuberculous patients, before they get active disease, are heavier than average smokers, so that, by inference, if one wants to implicate smoking with carcinoma, this might be a factor.

_Dr. Brinkman:_ Another theory that has been put forth is that the tuberculosis patients get a lot of x-rays over the course of their lifetime, and it has been suggested that repeated chest roentgenograms predispose to lung cancer. What do you say about that, Dr. Eyler?

_Dr. Eyler:_ Nonsense.

_Dr. Brinkman:_ This is the chest roentgenogram (Figure 3) of a woman of 44 who was a tuberculosis contact, and who came in with hemoptysis. She had a right apical lesion containing a 2 cm. cavity and a small cavitory lesion at the left apex as well. She was sent here as a case of tuberculosis. Repeated PPD skin tests up

**Figure 3**

Chest roentgenogram showing the right apical paramediastinal lesion which contains a 2 cm. cavity. There is a 1 cm. cavity behind the first rib on the left.
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to second strength, were negative. Dr. Chapman, would you think the negative skin tests were significant or not?

Dr. Chapman: Yes, I would think they are if she is a relatively healthy woman. This would make me suspicious of some other etiology.

Dr. Brinkman: Well, the histoplasmosis skin test was strongly positive. Dr. Coates; could this account for the x-ray appearance?

Dr. Coates: I think it could. Histoplasmosis can mimic almost any chronic lesion in the lung.

Dr. Brinkman: Well, this certainly proved to be a red herring. Because of the strongly positive histoplasmin skin test, we delayed further investigation while awaiting sputum cultures for histoplasmosis. These take 3 or 4 weeks. After obtaining several negative sputums, it was felt that she should be explored, and this cavitary lesion turned out to be bronchogenic carcinoma.

There is one advantage to being the quizmaster, and that is knowing ahead of time the questions to be asked.

I would like to bring to your attention an Australian report. Campbell\(^1\) reviewed 6,500 patients who had had pulmonary tuberculosis and compared them with a comparable group of men who had not had pulmonary tuberculosis. During a 5 year follow-up, there was 3 times as much bronchogenic carcinoma in the group who had tuberculosis, and a majority of the cancers occurred in close proximity to the original tuberculous lesion. This is certainly strongly in favor of an association between the two diseases. Has anyone any questions they would like to ask at this point?

From the Audience: Would you comment on the pathophysiology of the hypertrophic pulmonary osteoarthropathy as it relates to relief by vagotomy?

Dr. Coates: There is some interesting recent work\(^2\) on dogs which may answer that question. It appears that dogs are one of the few animals that do get true pulmonary osteoarthropathy, and they get it with metastatic lesions as well as with primary lung cancer. It has been shown by blood flow measurements in the limbs of these dogs that the bony changes of pulmonary osteoarthropathy are preceded by a marked increase in the blood flow to the limbs. When the lung lesion is removed, the blood flow drops off within 24 to 48 hours, but the bony changes regress much more slowly. The reason for this appears to be a reflex mechanism carried over the afferent fibers of the vagus nerve. If you atropinize the dog thus blocking the motor fibers of the vagus, the osteoarthropathy is not relieved; as a result the swelling persists and the increased blood flow is unchecked. If you cut the vagus (it has to be cut in most dogs on both sides), the increased blood flow is immediately relieved and the tissues recede. Cross-circulation experiments, matching an affected dog with a normal dog, have shown no humoral agent influencing osteoarthropathy.

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From the Audience: Why are we seeing more lung cancer and pulmonary tuberculosis occurring together?

Dr. Chapman: Generally, the younger people are not being affected by tuberculosis which is now appearing more in those of middle and older age. These are patients in the carcinoma age group.

Dr. Brinkman: What would the panel feel about irradiating a lesion which is surrounded by active tuberculosis? Is that a dangerous thing to do or not?

Dr. Coates: I haven't had the occasion to have this particular treatment carried out in my own patients. The only report I can recall offhand concluded that there was no danger in the concomitant treatment of carcinoma and tuberculosis.

Dr. Chapman: I wanted to ask if any of you had considered the use of a bronchogram in a case like this to further elucidate the nature of the lesion. Andrews and Nelson in Columbus, Ohio, have done a lot of work on this in trying to demonstrate bronchial cutoff, as contrasted to a rat tail type of bronchi which would be indicative of an infectious process. This may be helpful in differentiating a lesion of unknown type.

Dr. Brinkman: Thank you.

REFERENCES