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Primary atypical pneumonia clinical picture and diagnosis

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PRIMARY ATYPICAL PNEUMONIA

CLINICAL PICTURE AND DIAGNOSIS

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INTRODUCTION AND HISTORY

Primary atypical pneumonia is one of the many terms used to designate an acute respiratory infection which has been widely prevalent in recent years. The illness is characterized by gradual onset, with constitutional, as well as respiratory signs, and pulmonary changes more manifest in roentgenograms than by physical examination. The course of the illness varies considerably in duration and severity. Complications are uncommon, and although convalescence is frequently protracted, the illness almost invariably terminates with complete recovery.

There is little evidence that this is a new disease entity, since reports of a similar pneumonia extend back into the nineteenth century. Stansfield, in 1923, discussed the pulmonary involvement in twelve cases of grippe. Cole and MacCallum, summarizing data on pneumonia occurring in military camps in 1918, mentioned one type of bronchopneumonia with pathological changes similar to those of primary atypical pneumonia. Interstitial penumonia has been detected in preserved lungs of soldiers of the Civil War (Wall).

Perhaps the first report of what we have come to know as primary atypical pneumonia came from Bowen in Hawaii in 1935.

This condition was thought to be similar to that reported by Allen from Texas in 1936, by Rieman from Philadelphia in 1938, and in 1939, a report of a new disease entity came from Cornell University via Smiley, et al.

All of these reports described a single disease entity and emphasized the importance of the roentgenogram.

During the following years this disease received much attention. Its importance increased when many millions of young men were assembled in military camps, for it attacks young adults more frequently than other age groups (Moore, Wightman and Showacre). The vast majority of reported cases have occurred in adolescents and young adults (Finland and Dingle). Because of the considerable temporary disability occurring among those afflicted, the disease created much interest among the medical officers of the armed forces. The Surgeon General assigned a special commission to study the cause as well as the clinical problem. Through the many reports on the subject, a clinical picture of the disease is now well established. The clinical course has been repeatedly described, prognosis has been reported generally good, the treatment advocated has been largely symptomatic, and the complications few (Moore).

ETIOLOGY

The exact etiology of primary atypical pneumonia is unknown. A great variety of animals and special technics have been employed, but no single agent has been found clearly established and confirmed by others as the cause of primary atypical pneumonia (Dingle).

Eaton and his co-workers have found pulmonary lesions in cotton rats and hamsters inoculated intranasally with tissue from chick embryos which had been previously inoculated with sputum or macerated lung tissue from patients with primary atypical pneumonia.

Viruses capable of causing penumonia in animals have been suspected to be causative also of pneumonia in man. Among these are the viruses of influenza, lymphocytic-choriomeningitis, and measles. It remains to be proven, however, whether the pneumonia which may occur during infection with these diseases is caused by the virus of results from a concomittant or secondary invader (Finland and Dingle, and Curnen).

The question of the transmission of primary atypical pneumonia with bacteria-free filtrates of sputa and throat washings from patients with the disease was not easily answered. The results of an experiment, in which atypical pneumonia was

According to the literature, cough is the most constant complaint being present in most cases reported. The cough usually begins as a dry, nonproductive type, gradually developing into the productive type. The sputum produced is usually copious and may at times be blood tinged. A rusty or frankly bloody sputum is only occasionally observed (Curnen, 1946).

Sore throat is occasionally present. Von Ravenswaay, in his study of 1,860 cases, found sore throat to be present in about one half of those studied. This soreness was oftentimes a scratchy kind of soreness. This author also found chest pain to be present in over two thirds of the cases. About half of the cases showed some pleural pain on motion. In the series reported by Tansey, Culver and Frost, the chest pain was described as a substernal pressure or a "heaviness". Rarely was there severe pleuritic pain.

Dyspnea was present in about one quarter of the patients studied by Goodrich and Bradford. Von Ravenswaay et al seems to agree with these findings. Dyspnea with or without cyanosis occurs mostly in the more severly ill.

Primary atypical pneumonia produces various general symptoms---the most frequent being malaise and feverishness. Malaise is, according to many workers, the only symptom when the patient presents himself to the physician. Bahlke reports

that frank chills are not as common in this disease as they are in pneumococcal pneumonia. Nevertheless, chills, or a sense of chilliness do occur (Von Ravenswaay et al). Goodrich and Bradford report that while not always present at the onset of the disease, headache often became an important feature and assumed distressing proportions after the second or third day of the disease. Anorexia was present in about one third of the patients. Niedles and Gilbert reported anorexia in 68% of patients studied.

Nausea and vomiting are reported as being rare by some authors, but both were present in about one fourth of the series of cases studied by Curnen and his workers.

Physical Signs: Curnen, who has made several studies of virus pneumonia, thinks the physical signs are many times minimal even though the disease process is well advanced. In 1945, he and others presented the clinical picture of 106 patients studied, and found the physical signs to be as listed below:

Fever	101
Nasal congestion	60
Pharyngitis	73
Cervical adenopathy	25
Bradycardia	72
Tachycardia	8
Pulmonary signs	
Dullness	57
Altered breath sounds	74
Rales	99
Friction rub	7
Fluid	1
Tachypnea	14
Cyanosis	12

These physical signs were present for an average of 12.8 days, but ranged from no signs at all to signs for 41 days.

The maximum recorded temperature averaged 103.5° F. with a range of 99° F. to 106° F. The charted temperature curves of individual patients also showed great variations. The commonest type of curve was moderately remittent, and rarely was either high persistent fever or markedly intermittent fever seen. Defervescence was usually by lysis over a period of more than one day.

Karpel and his workers found that the fever was of the septic type, with an afternoon and night rise that ranged between 102° F. and 106° F., and a fall to normal, or nearly so, by morning. The period of fever in the majority of the patients ranged from four to nine days. McDonald and Ehrenpries report a fever that usually subsided by lysis in two to five days.

Mild hyperemia of the pharynx is common and was found in most patients studied by Adams and his workers. He also found that glands were often found to be enlarged on admission, but they subsided early in convalescence. The posterior cervical group were those most often affected. The glands were small, firm, discrete and not tender.

Pulmonary Signs: Owen reports the most consistant finding in the chest was moist rales. However, other changes, alone or in combination, were often present. In almost half of the cases the chest revealed nothing unusual on admission examination, but in the greater majority it did subsequently disclose physical findings.

Rales usually heard early in atypical pneumonia were fine, "sticky" crepitations, occurring in showers at the end of fairly deep inspirations, and accentuated by coughing. As the disease progressed, the rales became louder and coarser, and were heard during a greater portion of the inspiratory phase and later during the complete respiratory cycle. (Most writers agree in essence with the description by Owen.) At times the coarse rales faded promptly, but often they persisted after the roentgenographic changes had disappeared, and the patient was well along in his convalescence.

Owen found one of the most atypical features of this pneumonia to be the complete dissociation between the findings in the chest and the extent of the patient's symptoms. Disability, fever, and other complaints are between either of these factors and the roentgenographic appearance of pulmonary cloudiness.

A significant factor is the slow pulse. The temperature may reach 104° F. while the pulse has stayed around 90 to 100

per minute (Curtzwiler and Moore). MacDonald and Ehrenpries report that the pulse rate usually corresponds to the temperature level. Most writers report a relative bradycardia in a large percentage of cases (Bahlke).

Course: The course of the disease is variable, depending on the severity. The moderately sick patients have a fever varying from four to twelve days with defervescence by lysis. The more severly ill may be febrile for over twelve days. The dry cough, usually one of the first symptoms, in most cases becomes productive as resolution takes place. A moderately productive cough may persist for several weeks in spite of a clearing of the lung field on x-ray examination.

The first x-ray signs usually appear by the third to fifth day. At this time the physical signs are minimal. As the disease progresses the number of coarse rales increase over the involved area.

The leukocyte count, which is usually normal or near normal, begins to increase, in many cases, late in the course of the disease.

Convalescence is prolonged. Weakness and malaise may persist for three to six weeks following clinical recovery (Yoskalka, Seeds and Mazer).

RADIOGRAPHIC PICTURE

Bowen, in 1935, presented what is probably the first radiographic picture of primary atypical pneumonia as we know it today. He described the shadow as extending outward from the hilus well into the periphery. The appearance is that of a confluent mottled, or rounded, area usually of homogeneous, moderate density in the central portion, with the borders fading into the normal lung. It is similar in roentgenographic appearance to the exudative inflammation around the lung abscess, to the perifocal reaction in nodose tuberculosis, and to the exudative lesions of childhood tuberculosis.

Since this description, many writers have added their observations of the radiographic patterns and classified them.

Films taken within thirty six hours of onset usually show no definite pathology; however, films taken from thirty six to seventy two hours generally reveal pathologic changes. X-rays taken after a week or ten days of illness generally show pathology to be at its maximum or receding (Showacre, Wightman and Moore).

In order to better understand the various roentgenographic findings a brief review of the pathological process seems in order.

The pathology is that of an interstitial pneumonitis (Lewis and Lusk), and has been described by Longcope and Lewis).

Grossly, the hilar lymph nodes are hyperplastic and edematous. The large bronchi are inflamed. (These pathological changes may explain the increased size and density of the hilar shadows seen in the roentgenograms.) The walls of the smaller bronchi are thick and rigid, and project above the lung surface when seen on cut sections.

This thickening and rigidity is represented on the roentgenograms by increased pulmonary markings. Although the lung, for the most part, is air containing, focal areas of atelectasis or alveolar exudation are seen. These may explain the mottled density demonstrable roentgenographically in the lung parenchyma.

Microscopically there is a profound infiltration of mononuclear cells, affecting chiefly the bronchial walls, peribronchial structures, and intra-alveolar septa.

X-RAY DESCRIPTION

From our physical and x-ray examinations we find that the manifestations in the lung fall naturally into four phases (Lewis and Lusk).

They are: Bronchitic, peribronchitic, alveolar, and broncho-alveolar, depending on what part of the pulmonary tract is involved.

Bronchitic phase: The bronchitic phase is characterized by increased size and density of one or both hilar shadows (Kornblum and Riemann). The markings of the smaller bronchi, likewise, may be demonstrated in the peripheral zone of the lung. The findings might be explained by congestion of the hilar lymph nodes and by infiltration and congestion in the bronchial and peribronchial tissues.

Certain lesions of the various types of bronchitis cannot be differentiated by x-ray studies alone; dependence must be placed also on the history and laboratory findings.

Peribronchitic phase: The peribronchitic phase is characterized by an increase in prominence of the truncal markings as they extend from the hila downward into the cardiophrenic sinuses and lower lobes and outward into the lung parenchyma. Intimately associated with the increased density of the bronchial and peribronchial shadows, irregular areas of varying opacity and soft mottling are seen (Lewis and Lusk).

Alveolar phase: In the alveolar phase, the lesion is variable with respect to location, size, shape, and density (Smitey, Showacre, Lee, and Ferris). It may occur anywhere

in the lung margin; it may occur along the bronchus dorsalis as seen when roentgenograms are made in the lateral position (Curtzwiler and Moore).

In about twenty percent of the cases, it is bilateral (Dingle and Finland).

Characteristically, all lesions are of a soft density. The shadows take on a cloud-like, hazy, downy, ground glass appearance, fading toward the periphery.

Broncho-alveolar phase: The broncho-alveolar phase is characterized by irregular, soft, patchy, mottled areas of increased density in the lung parenchyma. These parenchymal densities may exist as small patches, or occasionally, as coarse mottling in the direction of the pulmonary markings. The roentgen manifestations of the broncho-alveolar phase could be explained pathogenically by the small areas of atelectasis and alveolar exudation intermingled with emphysematous areas (Lewis and Lusk).

WHITE BLOOD COUNT

Owen, in his series of cases, found that a relative leukopenia with respect to fever and severity of illness was characteristic. The average leukocyte count on admission was 9,860; although the mean count, 9,080, was more represent-

ative. The lowest count was 2,600; the highest, 30,000. The summer counts averaged distincly lower (9,200) than the winter ones (10,250).

Cass stated in his series that most leukocyte counts ranged from 2,500 to 4,500 (80-90% polys.), with the lower counts representing the more seriously ill patients.

Going back to Owen's work, we find among patients who were critically ill, counts of 15,000 to 18,000 were common, uninfluenced by treatment with sulfanilamides. With convalescence the leukocytosis usually dropped parallel with clinical improvement, while low counts tended to rise to normal or slightly higher. It has also been observed that cases with an increased white blood count were more apt to respond to the sulfanilamides.

Curtzwiler and Moore report that during the height of the temperature, and at the time of the early x-ray findings, the count is not above normal (8,000 to 10,000). Later in the disease, and at the height of physical findings, the counts may rise to 14,000 to 15,000. No leukopenia has been observed.

Hubbard and Applebaum report leukocyte counts as normal, or showing a tendency to leukopenia.

According to Meyer and Thewlis, at the onset of the disease, and even after the disease is well established, the leukocyte count is normal.

There is an increase in neutrophils (Rieman, Kneeland and Smetna) and monocytes (Middleton).

HEMAGGLUTINATION

It has been known that cells of an individual are occasionally agglutinated by his own serum. This fact has been known for many years. It has also been known that clumping of cells was decidedly more marked when the serum was chilled, and that this seldom occurred at body temperature (Humphery, Horstman, and Curnen et al).

It has been noted that in sera obtained from patients with primary atypical pneumonia and stored for long periods of time, the capacity for cold hemagglutinins appeared to be less than in sera recently obtained from similar patients (Peterson et al and Horstmann and Tatlock).

The cold agglutinins develop during the second week of the disease, reach their highest titre between the tenth and twentieth day, slowly diminish and disappear after several weeks or months (Horstmann and Tatlock).

Autohemagglutins in significant titres seem to follow the course of primary atypical pneumonia, rising as the fever abates, reaching a peak as chest signs and symptoms are most acute, and receding as the lung clears and temperature returns to normal. This is the usual course of events.

Since the cold agglutinins appear eight to twelve days after the onset of the disease and disappear upon recovery, it suggests an antigen antibody reaction. Most antibodies are found in the globulin fraction of the serum protein; therefore, it seems probable that this agglutinin would be found there (McNeil).

McNeil extracted the globulin fraction, set it up in serial dilutions with washed type O cells. The globulin portion was found to be not quite as strong in the low dilutions, but was of equal titre as the serum.

SEDIMENTATION RATE

The sedimentation rate usually ranges from 20 to 40 mm./hr. in the acute stage. With clinical improvement the rate gradually goes down. This can be correlated with clinical and x-ray findings (Von Ravenswaay et al). Owen and his group made estimations on admission and thereafter at weekly intervals. The highest value obtained was 45 mm./hr. on the twelfth day of hospitalization. This was exceptional. The sedimentation rate in the early stages averaged 19 mm./hr. Curnen found the sedimentation rate was almost always increased during the acute phase of illness and this finding persisted for some weeks during convalescence. In a few instances the sedimentation rate remained or became normal while the patient was still acutely ill.

ELECTROCARDIOGRAM

Curnen took serial electrocardiograms on 50 patients with primary atypical pneumonia, none of whom gave a history of previous cardiovascular disease. No significant deviations from normal were detected during any stage of the illness from the third through the thirtieth day after onset. Specifically, there was no increase in the P-R interval, no elevations or depression of the S-T segment, and no T wave change.

Because of the presence of gallop rhythm in six cases in a series reported by Goodrich and Bradford, electrocardiograms were obtained. Three patients, all severly ill, showed abnormalities. In two instances, T wave abnormalities occurred in leads II and III. These changes were interpreted as possibly reflecting increased cardiac strain.

SPUTUM EXAMINATION

Sputum examinations and throat cultures usually show no significant organisms. Such commensals as nonhemolitic streptococci, streptococci veridans, catarrhalis rarely pneumococci, diphtheroid bacilli, and occasionally staphylococci were cultured. Since no specific agent has thus far been

isolated, it would seem that little information of diagnostic value is obtained from sputum examination. A negative sputum is of value in differentiating atypical pneumonia from those of bacterial origin (Curnen, Holmes and Goodrich, and Bradford).

DIAGNOSIS

The patient presents himself with rather vague symptoms. He usually has felt badly for several days and may feel that he has a fever. In many cases, this may be the only history obtainable, or he may have a cough with or without a moderate headache. He may also complain of various body aches and pains.

Examination is quite unsatisfactory. A temperature of 103° F. or 104° F. is usually present, and the patient appears definitely uncomfortable. Physical examination of the chest most frequently gives entirely negative results, and the patient is tagged with a working diagnosis of upper respiratory infection, even though upper respiratory symptoms are vague and mild. The usual routine laboratory examinations on blood and urine are reported negative. For a period of forty eight hours the patient is watched carefully and treated symptomatically. The temperature usually does not

drop, and an x-ray examination of the chest is ordered. The information gained from the x-ray film is usually the deciding factor in making a diagnosis of primary atypical pneumonia (McNeil and Showacre, Wightman and Moore).

Since most of the patients are tagged with a diagnosis of nasopharyngitis or bronchitis, the predominating problem is to distinguish pneumonia from these infections of the upper respiratory tract. With positive findings in the chest the problem is usually not difficult. In the remainder, unusual malaise, persistent nonproductive cough, or protracted illness without obvious cause makes one suspect primary atypical pneumonia.

Difficulty should ordinarily not be experienced in differentiating primary atypical pneumonia from acute influenza due to influenzal virus A and B. In influenza, the onset is acute with generalized aching and hyperesthesia, usually severe headache, and marked prostration. Catarrhal symptoms are not pronounced; however, there is marked injection of the conjunctiva and nasopharynx. In addition, leukopenia is characteristically present.

Patients with bronchitis, which is not on an allergic basis or has not been preceded by the influenza common cold, should be examined carefully for evidence of primary atypical pneumonia, and in such cases it is advisable to x-ray the

chest. It seems likely that a certain proportion of cases diagnosed as bronchitis are actually suffering from primary atypical pneumonia. Furthermore, it is by no means clear that the latter infectious process invariably proceeds to involve the parenchyma of the lungs, and certain patients may suffer from bronchitis without pulmonary involvement (War Medicine).

The differential diagnosis from psittacosis cannot be made on clinical grounds alone. In this specific disease process, the diagnosis may be established by isolation of the infectious agent, or else by the demonstration that specific immunity to the virus has developed upon recovery from the disease (Parker).

A fever likewise cannot be differentiated on purely clinical grounds. The diagnosis in this case may be established by isolating the richettsia responsible for the infection or by immunilogical studies.

Differentiation from pulmonary coccidiomycosis can be made by specific clinical and laboratory reactions, if the test material is available.

The differentiation from bacterial pneumonia, whether of bronchial or lobar distribution, should cause no difficulty. For example, in primary atypical pneumonia, the leukocyte count is normal or near so, the pulse and respir-

atory rates are only slightly elevated, the physical signs over the lungs and x-rays of the chest do not coincide, and the atypical pneumonia doesn't respond to the sulfonamide drugs (War Medicine).

Tuberculosis may be suggested by the hazy mottled roentgen appearance, especially when the disease occurs in the upper lobes, and by the occasional occurrence of blood stained sputum. The clinical illness, the sputum negative for acid fast organisms, and the rapidly clearing roentgenogram tend to rule out tuberculosis (Owen).

SUMMARY AND CONCLUSIONS

The disease process has been described and has become fairly uniform since it was first brought to attention by Bowen in 1935. Briefly the clinical picture is as follows:

1. There is an insidious febrile onset, accompanied by headache and chest pain. On the third or fourth day there is development of a cough, usually nonproductive. The physical signs are minimal early, and if present consist of fine rales over the involved area, gradually progressing to coarse rales later in the course of the disease. X-ray evidence is usually present from the third or fourth day on.

The clinical course usually lasts from twelve days to two weeks, and fever falls by lysis.

2. The leukocyte count is usually near normal early in the disease with a mild rise late in the course.

3. Hemagglutinins are apparently of some value in following the course of the disease process.

4. The sedimentation rate is increased during the acute stage of the disease.

Diagnosis: The following tests are suggested as the course to follow in making the diagnosis of primary atypical pneumonia:

1. Symptoms of sore throat, headache, fever, dry cough, malaise, and substernal pain.

2. Negative lung signs early in the disease, changing to rales, without consolidation.

3. Chest roentgen ray evidence of pneumonia.

4. Negative sputum examination for pathogenic organisms.

5. Normal white blood count and differential, or slight leukocytosis.

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