NEUROLOGICAL COMPLICATIONS IN ATYPICAL PNEUMONIA

BY

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During the past few years there have been many accounts of the acute pulmonary infection which is usually called "primary atypical pneumonia." It is now generally accepted that this condition is due to infection by a virus, but attempts to identify a single aetiological agent have so far been unsuccessful. It is probable that many viruses are capable of producing the pulmonary lesions of atypical pneumonia: they have been noticed in influenza, psittacosis, rickettsial infections, and lymphocytic choriomeningitis. The present state of knowledge of the disease has been reviewed by Middleton (1945). Reports in the literature indicate that the mortality rate is low and that the disease usually runs a benign course without serious complications or sequelae. Rarely, however, serious neurological symptoms occur during the course of the disease. The purpose of this article is to describe six cases with such symptoms.

Physical signs of pulmonary disease are usually minimal, and the clinical diagnosis of atypical pneumonia depends almost entirely upon the radiological appearances in films of the chest, which reveal patchy opacities in one or both lungs. These opacities show a streaky increase in density radiating from the lung root and conforming to the general distribution of the bronchi. Superimposed upon this appearance is a mottled type of shadowing which is usually in the lower lobes. Unless serial films are taken during the course of the disease there may sometimes be difficulty in distinguishing the appearances from those of pulmonary tuberculosis. The areas of increased density are as a rule much larger than would be inferred from physical examination of the chest. On rare occasions pleural effusions and multiple fractures of ribs from severe coughing may be seen.

It is probable that much of the increase in recognition of atypical pneumonia in recent years is due to more frequent routine radiological examination of the chest in respiratory infections, particularly in the more benign cases. Little information of diagnostic value is obtained from laboratory investigations. There may be a leucopenia, and many workers have found "cold agglutinins" in the serum, but these features are inconstant and have no specific diagnostic value. The red cell sedimentation rate is usually much increased in the acute stage of the disease, and gradually returns to normal during recovery.

Case Reports

The cases here described include two cases of "acute infective polyneuritis," two cases of lymphocytic meningitis, one of "serous meningitis," and one of encephalitis. In each case the diagnosis of atypical pneumonia was based upon the radiological appearances.

"Acute Infective Polyneuritis"

Case 1.—A poultry-breeder aged 65 was seen in consultation with Dr. R. D. Neville on Nov. 8, 1944. For a week he had had upper respiratory infection with severe cough, dyspnoea, malaise, and pyrexia of 100–101° F. (37.8–38.3° C.); there was no response to sulphapyridine. On Nov. 7 the patient became confused and irrational and complained of increasing weakness of both legs and inability to pass urine. On examina-

tion signs in the chest were minimal—a few basal rales—although respiratory distress was evident. There was severe flaccid paresis of both legs, and only slight toe movements could be performed. Knee- and ankle-jerks and abdominal reflexes were absent; the plantar responses were indefinite. Neurological signs were not seen in the cranial nerves, arms, or trunk. Sensory disturbance in the legs was minimal—impaired vibration sense in lower legs and slight loss of position sense in toes. The bladder was distended, and catheterization yielded 25 oz. (0.7 l.) of urine. The patient was transferred to hospital. Lumbar puncture showed: clear cerebrospinal fluid under a pressure of 100 mm.; cells, 19 lymphocytes per c.mm.; protein, 120 mg. per 100 ml.; chlorides, 710 mg. per 100 ml.; Lange's test, no change; Wassermann reaction negative. On Nov. 9 the patient became more confused and irrational, pyrexia 100–101° F. There were still only scanty signs in the chest, and some reddening of the pharynx. A skiagram of the chest revealed characteristic bilateral basal mottling of atypical pneumonia, which disappeared later. Leucocytes numbered 13,000 per c.mm. (polymorphs 81%). Frequent catheterization was necessary. The mental confusion persisted for a further two days, then subsided, leg movements began to return, and complete recovery from the flaccid paresis occurred in eight days. The patient was then able to stand, but he still had difficulty in starting micturition. He had full sphincter control three days later. Convalescence was uneventful. He returned home after fourteen days, and has remained well up to the time of writing.

Case 2.—A market gardener aged 53 was seen in consultation with Dr. F. W. Harrowell on March 1, 1945. He had been ill for about ten days with malaise, high pyrexia, severe cough, and respiratory distress. During the previous three days a progressive weakness of the legs and arms had appeared. More recently he had developed difficulty in swallowing, his voice had become hoarse, and he had great difficulty in raising himself from the bed. There was no sphincter disturbance. On examination the temperature was 103° F. (39.4° C.), respirations 36, and pulse 140. Rales and rhonchi were heard at both lung bases, and there was some injection of the pharynx; the blood pressure was 120/80. There was flaccid paresis of arms and legs. The legs were almost completely paralysed except for slight toe movements. All tendon-jerks and abdominal reflexes were absent, and plantar responses were flexor. There was doubtful loss of position sense in the legs, but no other sensory disturbance. Weakness of the erector spinae, recti abdominis, and intercostal muscles was noted. Respiration was almost entirely maintained by the diaphragm and accessory muscles in the neck. As respiratory paralysis appeared imminent the patient was removed to hospital so that a Drinker respirator could be used, but this was not necessary. Examination of the cerebrospinal fluid showed: pressure 130 mm.; no cells seen; protein, 80 mg. per 100 ml.; Lange's test, no change; Wassermann reaction negative. On March 2 the leucocytes numbered 13,200 per c.mm. (polymorphs 71%), the pyrexia was subsiding, and there was no increase in paralysis. The temperature became normal in three days. A skiagram of the chest showed basal mottling of atypical pneumonia. The paralysis cleared up very rapidly. On March 10 the patient was able to stand without aid, and thereafter his recovery was uneventful. His hoarseness and dysphagia were cured before the limbs. The tendon-jerks had not returned six weeks after his discharge from hospital on March 10, but he has remained well since.

Lymphocytic Meningitis

Case 3.—An airman aged 26 was admitted to hospital on April 23, 1943. He had been ill for one day with severe frontal headache, sore throat and dysphagia, pain in the back, and general malaise. There was slight vomiting, and his voice was hoarse. The temperature was 101.4° F. (38.55° C.), respirations 24, and pulse 72. The tongue was dry and coated; the fauces and tonsils were reddened, with greyish pseudo-membrane between the right tonsil and uvula. Klebs-Loeffler bacilli and haemolytic streptococci were not grown from a swab. He was given 16,000 units of diphtheria antitoxin. Next day he was slightly confused and delirious; temperature 102° F. (38.9° C.). He vomited during the night. The tonsils were still congested, and there was profuse nasal discharge. On the 25th the temperature was 102.5° F. (39.15° C.), and he still had headache and

backache. He resented flexion of the neck, but no definite meningism was present, and no evidence of otitis. Neck rigidity was more definite on the 26th. Cerebrospinal fluid showed: pressure, 130 mm.; fluid clear; cells, 64 lymphocytes per c.mm.; protein, 90 mg. per 100 ml.; chlorides, 690 mg. per 100 ml.; culture sterile; Wassermann reaction negative. Next day the readings were: pressure, 150 mm.; cells, 122 lymphocytes per c.mm.; protein, 100 mg. per 100 ml.; chlorides, 640 mg. per 100 ml.; culture sterile. The general condition was improved and the headache less, but neck rigidity was still present. On May 3 there was no headache or pyrexia, but he still had sore throat and some cough. The cerebrospinal fluid readings were: pressure, 100 mm.; cells, 380 per c.mm. (98% lymphocytes); chlorides, 730 mg. per 100 ml.; protein, 120 mg. per 100 ml. A skiagram of the chest on May 5 showed moderate bronchial striation and bilateral basal mottling, characteristic of atypical pneumonia. There were no definite physical signs in the chest. The patient was free from symptoms on the 7th, and the cell count had fallen to 12 lymphocytes per c.mm. He was discharged to a convalescent unit on May 10.

Case 4.—A schoolboy aged 13 was admitted to Wrexham E.M.S. Hospital on March 3, 1945. He became ill on Feb. 9 with what was called "influenza." Two days later he developed acute pain and tenderness in the left frontal region. After this he developed pain and stiffness in the neck, with Kernig's sign and bilateral extensor plantar responses, but no other neurological signs. The cerebrospinal fluid was said to have been normal on Feb. 15. On admission cerebation was slow, and he had difficulty in answering questions. Slight neck rigidity and Kernig's sign were present. There were no other neurological signs, no signs in the chest, and no papilloedema. Tachycardia 100 per minute. The cerebrospinal fluid showed: pressure, 300 mm.; cells, 100 per c.mm. (50% lymphocytes); protein, 30 mg. per 100 ml.; chlorides, 680 mg. per 100 ml.; culture sterile. Leucocytes numbered 9,000 per c.mm. (84% polymorphs). A skiagram of the chest showed slight thickening of the horizontal interlobe and pleural thickening in the lower part of the left lateral chest wall, with patchy shadowing over the left lower lobe. On March 9 the cerebrospinal fluid readings were: pressure, 160 mm.; cells, 60 per c.mm. (50% lymphocytes); protein, 60 mg. per 100 ml. Further progress was uneventful. A skiagram of the chest on March 26 showed no abnormal shadows in the lung fields apart from pleural thickening at the left base. The patient was discharged on April 23.

Serous Meningitis

Case 5.—A man aged 37 was admitted to hospital on Feb. 25, 1939. He had had pyrexia of 102–103° F. (38.9–39.4° C.) for three days, with severe cough and malaise, followed by intense frontal headache that was much aggravated by coughing. Only scanty moist sounds were heard in the chest. There was no papilloedema, meningism, or other neurological sign. The nasal sinuses transilluminated well. The cerebrospinal fluid showed: pressure, 300 mm.; no increase in cells; protein, 80 mg. per 100 ml.; Wassermann reaction negative. He was given 40 ml. of 50% dextrose intravenously, with some relief of headache. On Feb. 26 the headache was again severe, but it was relieved by further lumbar puncture and intravenous dextrose. The cerebrospinal fluid pressure was still 300 mm. Next day the headache was less severe, but there were still no neurological signs. The cerebrospinal fluid showed: pressure 250 mm.; no increase in cells. A skiagram of the chest revealed characteristic basal mottling of atypical pneumonia. Recovery was rapid and uneventful.

Encephalitis

Case 6.—A housewife aged 29 was first seen on Sept. 2, 1945, in consultation with Dr. O. W. R. Tomkinson. She had been admitted to an isolation hospital on Aug. 28 with severe pharyngitis which clinically resembled diphtheria, but no Klebs-Loeffler bacilli were found. Pyrexia of 102–103° F. (38.9–39.4° C.) continued, and there was respiratory distress, but only scanty rales and rhonchi were heard in the chest. An initial dose of 32,000 units of diphtheria antitoxin had been given, and, subsequently, full doses of sulphathiazole, but without satisfactory response. On Sept. 1 the patient became confused and delirious, and slight neck rigidity was noticed. Next day the cerebral symptoms were more prominent. The patient

was in a state of irritable stupor, neck rigidity and bilateral extensor plantar responses were present, and the pyrexia was still 102–103° F., but there were no other neurological signs. She was transferred to the Staffordshire General Infirmary, and a lumbar puncture revealed a clear cerebrospinal fluid under a pressure of 160 mm.; no cells; protein, 30 mg. per 100 ml.; culture sterile; Wassermann reaction negative. The pyrexia subsided gradually during the second week of the illness, but widespread rales and rhonchi appeared in the chest and a skiagram showed the characteristic woolly mottling of atypical pneumonia. The meningeal irritation, confusion, and extensor plantar responses disappeared at the end of the second week of the illness. Further skiagrams of the chest showed the gradual disappearance of the opacities. The patient made a complete recovery and was discharged from hospital on Sept. 30.

Discussion

Neurological complications in primary atypical pneumonia are undoubtedly rare, but it is probable that in many cases, such as those described here, the severe neurological symptoms may distract attention from the associated pulmonary infection, which may be unrecognized unless skiagrams of the chest are taken. Turner (1945) mentions one case of transverse myelitis in 286 cases of atypical pneumonia. Sheppe *et al.* (1943) describe one case of meningo-myelitis in 150 cases. Gundersen (1944) noted one fatal case of haemorrhagic encephalitis in 122 cases, and mentions another fatal case, with cerebral symptoms, which did not come to necropsy. Campbell *et al.* (1943) describe one fatal case of encephalitis in 200 cases. Ravenswaay *et al.* (1944) noted meningeal symptoms in 0.4% of 1,862 cases, and Glendy *et al.* (1945) noted three cases of "meningism" in 180 cases. Scadding (1937) and Perrone and Wright (1943) each reported a fatal case of encephalitis. Many other reports of large series of cases contain no reference to any neurological complications. Reimann (1938) and Hein (1943) report cases of meningo-encephalitis in which complete recovery took place.

The first two cases described above as "acute infective polyneuritis" closely resemble those described by Gordon Holmes (1917), Rose Bradford *et al.* (1918–19), and Guilain, Barré, and Strohl (1916). All these authors mention the association of the neurological picture with a respiratory infection, the nature of which at that time was unrecognized. The case of meningo-myelitis described by Sheppe *et al.* (1943) was very similar in its clinical manifestations to my two cases of infective polyneuritis, but there was a high cell count in the cerebrospinal fluid, predominantly of lymphocytes. The sensory system was unaffected in their case and was only very slightly affected in my two cases. Another similarity, also mentioned in the earlier accounts, was the very rapid recovery from a severe flaccid paraplegia.

While it is realized that there is no evidence on which to attribute the above cases to the same infective agent, the presence of similar pulmonary lesions in all of them justifies, at any rate, a clinical correlation. The diagnosis of atypical pneumonia in such cases by radiological examination of the chest may have little value from the therapeutic point of view, but it may be of help in giving a hopeful prognosis. It seems probable from the very infrequent incidence of neurological complications that the virus of atypical pneumonia is primarily viscerotropic, and that when nervous involvement does occur the results are not as severe as in infection with primarily neurotropic viruses.

The clinical symptoms of these cases are comparable to those found in other virus infections of the nervous system, but residual damage has been absent. Although fatal cases of myelitis and encephalitis have been reported they appear to be rare.

Summary

Six cases are described in which symptoms of severe spinal and cerebral lesions occurred in association with pulmonary lesions presenting the radiological appearances of "atypical pneumonia." Recovery was rapid and complete. Although the clinical picture was variable it was in each case suggestive of a virus infection of the nervous system.

A review of the literature suggests that the nervous system is rarely involved in atypical pneumonia, but that when this does occur the tendency is towards complete recovery without sequelae.

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DEFICIENCY DISEASES IN REOCCUPIED HONG KONG

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In a paper entitled "Nutritional Diseases in Hong Kong before the Japanese Invasion" (Fehily, 1945) I described the widespread occurrence of B avitaminosis among the Chinese population in Hong Kong which was undoubtedly due to the high consumption of imported highly milled, and, latterly, long-stored rice. This vitamin B deficiency manifested itself mainly in beriberi, which was the second highest cause of death in Hong Kong in 1940; while maternal B avitaminosis (either latent or manifest) was the cause of infantile beriberi, a disease which often appeared in such an acute and lethal form that the term "human milk intoxication" was suggested for it. Practically no other deficiency diseases were observed before the occupation; isolated cases of vitamin A and C deficiencies, mainly secondary, were encountered in unwanted female infants who were fed only on rice paste.

Absence of Gross Deficiency Diseases

On the reoccupation of Hong Kong the medical officers of the British Military Administration were surprised at the absence of widespread beriberi and pellagra; owing to fishing restrictions gross vitamin A and protein deficiencies were also expected, but these did not materialize; neither was real starvation evident, although the population of Hong Kong was obviously in a state of subnutrition. However, on close inspection the signs of chronic and mild vitamin B deficiency, mainly that of aneurine and riboflavin, were detected.

It seems that during the Japanese occupation of Hong Kong rice was severely rationed, and as soon as old long-stored stocks had been exhausted relatively fresh rice was issued to the population. In addition people ate whatever was available, and centuries-old food fads and prejudices

were thrown overboard. Wherever possible, people grew their own vegetables and kept hens and rabbits, even in flats and cubicles. These practices undoubtedly saved the population of Hong Kong from severe deficiency diseases as well as from starvation.

Extensive Relief Work by the Military Administration

After the reoccupation of Hong Kong the Relief Section of the British Military Administration opened free-food kitchens and unstintingly supplied free rations to charitable institutions and to all under-privileged persons, while the British and Australian Red Cross Societies assisted by issuing Red Cross parcels not only to civilian internees and to prisoners of war and their dependants but also to the sick and needy and to orphans.

Unfortunately, since the liberation of the Colony virtually all the rice available has been highly milled, but it has been rationed and supplemented by fresh Australian wheat-flour, which, although highly milled, is richer in vitamin B than highly milled rice, and by blue peas, which are rich in vitamin B. In addition the Military Administration distributed vitamins on a large scale; indeed, the population of Hong Kong became vitamin-conscious for the first time in its history. The popularity of vitamins may be judged from the fact that on occasion only vitamins were pilfered when warehouses were broken into.

When I arrived in the Colony six months after the liberation undernourishment had almost disappeared and the population was apparently in good health. Admittedly B avitaminosis was still encountered, but with the return of prosperity some people were able to get expensive highly milled rice on the black market and thus defy the rationing system. In addition the return of Hong Kong residents and the large influx of immigrants (many of these returning residents as well as immigrants were already B avitaminotic) made control of nutrition more difficult. Indeed, during the first nine months of liberation the population of Hong Kong tripled and almost reached its pre-war level, so that eventually the issue of rations had to be restricted to returning residents, and immigrants had to patronize the black market, where they purchased highly milled rice as their staple food. In spite of this the incidence of B avitaminosis in Hong Kong was very low compared with that of the years 1938-41, and undoubtedly its complete eradication could be effected if lightly milled rice (or other high-extraction cereals) became the staple food of the population. It is gratifying to know that the Killearn Nutrition Conference in Singapore last year passed the following resolution; "There should be laws or regulations to prevent the high milling of cereals to a degree dangerous to the health of the public, because high milling not only removes valuable nutrients from the food but also reduces the quantity of food available for consumption." However, owing to present world conditions any rice available for importation into the Colony during the last year was only too welcome.

Vitamin B Deficiency in Infants

Special attention was paid to orphanages, infant welfare centres, and milk-distribution centres in order to detect any signs of deficiency diseases. In one foundling home with 75 orphans up to the age of 5 years I observed signs of vitamin B deficiency in 27 children. The ocular signs of ariboflavinosis were especially prevalent; 12 children had conjunctivitis of the type described as being common in Chinese in Shanghai (Hou, 1940, 1941), and 10 other children had photophobia alone. On entering the infants' ward one was surprised to see so many infants with their heads buried in their pillows, while others were doubled