STAPHYLOCOCCAL PNEUMONIA IN ADULTS

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Staphylococcal pneumonia has long been known as a complication of epidemic influenza. The fulminating, prostrating type encountered during the pandemic of influenza that followed the first world war was fully described in the writings of Chickering and Park (1919). At that time mortality rates of 80–90% were reported. In 1942 Finland *et al.* recorded a reduction in the death rate to 32%, which they attributed to the use of sulphonamides.

In sporadic form, however, staphylococcal pneumonia is widely regarded as a disease occurring mainly in infants. In these the prognosis is still grave. Recently, Wallman *et al.* (1955) reported 44 cases from Perth, Western Australia, with a mortality of 23%, a figure achieved by modern treatment with antibiotic agents.

In adults, relatively few cases unassociated with major influenza were reported before 1950. Heffron (1939), analysing 3,319 cases of lobar pneumonia, found only six that were considered staphylococcal. Among 298 cases of bacterial pneumonia admitted to the Central Middlesex Hospital in 1942–4, Humphrey *et al.* (1948) described seven which were thought to be staphylococcal. Only one had a history of preceding influenza-like illness.

During the last five years, however, several groups of cases have been reported. Of 110 cases of pneumonia admitted during one year to Hammersmith Hospital and reported by Crofton *et al.* (1951), 10 were considered to be staphylococcal and only two showed serological evidence of influenza B. Neither of these two patients was very ill. Grist *et al.* (1952) saw 10 cases of staphylococcal infection among 129 cases of pneumonia admitted to one hospital in Glasgow during a period of fifteen months. Serological evidence of recent influenza A infection was present in 5 of the 10 cases. Grant and Barber (1954) reported 15 cases from Belfast, constituting 3% of all pneumonia admissions. Only four cases occurred during an influenza outbreak.

Material.—This paper is based on a series of 18 cases of staphylococcal pneumonia in adults admitted to an acute medical unit in Reading during 1952–4. Many cases of pneumonia occurring in the area receive treatment at home, and, in general, only the severely ill patients not responding to penicillin and sulphonamides are admitted. There was no local influenza epidemic during the period under review, but virus studies were not made. The group formed 15% of a total of 122 consecutive patients admitted to the unit in whom the diagnosis of primary pneumonia was radiologically confirmed. There were 11 men and 7 women. Their ages ranged from 16 to 72, with an average of 51 years.

Diagnosis

The aetiological diagnosis of staphylococcal pneumonia is a matter of some difficulty and is often derived from a combination of clinical, radiological, and bacteriological

findings. In the series now reported the criteria adopted were those used by the Medical Research Council (1951) for the investigation of bacterial pneumonias—that is, “When *Staphylococcus aureus* (coagulase-positive) . . . [was] predominant in the sputum the pneumonia was regarded as staphylococcal . . . if this was clinically consistent, even when cultures from other sources were negative.”

Sputum from every case was cultured soon after admission and before the start of treatment if possible. From a number of patients minor growths of staphylococci were reported, together with non-pathogenic organisms, but, in view of the possibility of nasopharyngeal contamination of specimens yielding a few colonies only, such cases were classified as of uncertain origin and excluded from the series.

From 12 of the 18 cases reviewed staphylococci were isolated in pure culture. In the remaining six cases predominant growths of staphylococci were found, together with a proportion of non-pathogenic organisms such as *Streptococcus viridans* and neisseriae. In two cases coagulase-positive staphylococci were grown from the pleural fluid.

The organisms were reported to be penicillin-resistant in 10 cases, while results of treatment indicated that resistant strains were probably present in three other patients. Resistance to penicillin was estimated by the disk plate method, the disks being impregnated with 1.5 units of penicillin solution.

It is necessary to add that as most patients received some treatment at home it is impossible to say whether the organisms were resistant at the onset of the illness or became so only after penicillin had been given.

Clinical Features

Six of the patients gave a history of previous chest disease, such as chronic bronchitis, asthma, or recurrent pneumonia. There were serious associated conditions in two other cases—*aortic stenosis* in one and *acute nephritis* in another. Two cases occurred following abdominal operations; both later developed lung abscesses.

The duration of symptoms prior to admission ranged from two days to two months, with an average of three weeks. Pleuritic pain was complained of by 14 of the 18 patients. Rigors were present in four cases. Herpes labialis was noted in only one case. Sticky blood-stained sputum was produced by four patients.

Leucocyte counts were not found to be of great significance. They were done in nine of the cases, and the totals exceeded 10,000 per c.mm. in three.

With regard to anatomical distribution, postero-anterior and lateral x-ray films of the chest were available for all cases. The classification adopted was similar to that of Crofton *et al.* (1951). There were nine cases of lobar involvement, seven of lobular involvement, and two were segmental. This compares with the above authors' 10 cases, in which lobar distribution was seen in seven and lobular involvement in three.

The most outstanding features, however, were the severity of the clinical course and the number of serious complications. These were reflected in the duration of hospital stay, which averaged 38 days, compared with 19 days for the remaining 104 pneumonia cases admitted during the same period.

Six of the 18 patients developed abscess or empyema. Short summaries of these cases are given below. They included five men and one woman, their ages ranging from 21 to 72, with an average of 53 years. Their hospital stay averaged 58 days, with a range of 31 to 91 days.

Of the five cases of abscess, two were single and three were multiple. The abscess cavities were thick-walled and irregular, and none had the character of a thin-walled egg-shell cavity as described by Brock (1945).

In the three cases complicated by multiple abscess formation the pneumonia was of a “wandering” type, the consolidation moving from area to area and from one lung to

the other. One of the patients was admitted in a state of collapse, resembling the fulminating type of staphylococcal pneumonia described in association with influenza.

Empyema occurred in two patients. One of these, a woman of 21, developed pyopneumothorax, a complication occurring in 50% of staphylococcal pneumonias in infants but uncommon in adults. Sterile pleural effusions of moderate severity were noted in two patients. Delay in resolution of the pneumonia occurred in 12 of the 18 cases. There was no death in this series.

Treatment

After admission most patients were given penicillin while the results of sputum cultures were awaited, but it was supplemented with streptomycin for severely ill patients. Six of the 18 cases responded to penicillin, including one whose organisms were reported to be penicillin-resistant; seven responded to the tetracyclines (oxytetracycline or chlortetracycline); two to chloramphenicol; and two others to streptomycin. In one man erythromycin effected a dramatic improvement.

Only one of the 10 patients whose organisms were reported to be penicillin-resistant did, in fact, respond to penicillin treatment. On the other hand, three patients, including the case of pyopneumothorax, whose organisms were reported to be penicillin-sensitive responded to penicillin. It will be seen that the response to penicillin closely followed the results which sensitivity tests predicted, thus underlining the importance of such investigations. Of the five cases in which no sensitivity tests were done, three failed to respond to penicillin. These findings compare with those reported by Grant and Barber (1954), of whose 15 cases only six responded to penicillin.

Case 1

This patient, a man aged 64, had no history of past chest disease. Six weeks prior to his present illness he underwent an operation for inguinal hernia. On admission he complained of severe pleuritic pain in the chest and shortness of breath; his temperature was 106° F. (41.1° C.) and he had oedema of the ankles. His leucocyte count was 10,400 per c.mm. Radiography of the chest showed a left pleural effusion with consolidation and collapse of the left lower lobe, and a large abscess cavity with a fluid level. Aspiration of the left pleural space produced 4 oz. (114 ml.) of thick yellow pus which grew penicillin-resistant coagulase-positive staphylococci in pure culture.

Penicillin was first administered, without result; this was followed by tetracycline and later by chloramphenicol with moderate improvement. It then became clear that a bronchopleural fistula was present, and rib resection with open drainage was performed (Mr. C. Grimshaw).

The patient was discharged fit after 60 days but returned a month later with recurrence of cough and purulent sputum. A small abscess was shown radiographically in the left upper lobe in a different position from the previous cavity, and staphylococci were again grown from the sputum. This time he responded well to chlortetracycline.

On the follow-up a year later there was still extensive pleural thickening over the left lung but no sputum or shortness of breath.

Case 2

In 1941 a diagnosis of ankylosing spondylitis was made in a man aged 52. Four days before admission he had a rigor with vomiting and pleuritic pain at both bases of the lung. Radiography of the chest showed partial consolidation in the right upper and left lower lobes. The right upper lobe was clear within three days, but by then there was consolidation at the base of the left upper lobe. The latter extended during the next fortnight with multiple abscess formation.

Sputum culture produced on two occasions profuse growths of staphylococci resistant to penicillin, streptomycin, and chlortetracycline. There was no therapeutic response

to penicillin combined with streptomycin or to chlortetracycline, and his condition grew steadily worse. Erythromycin was then tried with immediate and dramatic improvement, and he was discharged after 31 days.

Follow-up examination two years later showed fibrosis in the upper zone of the left lung and an obliterated left costophrenic sulcus. He was well and working, and had no sputum or dyspnoea.

Case 3

A man aged 72 had been unwell for two months; pain in the right chest and severe cough had been present for two weeks. On admission he was extremely ill with cyanosis, dyspnoea, and dry tongue. Blood pressure of 70/40 mm. Hg and a pulse rate of 130 a minute were recorded. Radiographs of the chest showed consolidation of the right lower lobe with partial consolidation of the right upper lobe. Three weeks later a single round abscess had formed in the right lower lobe, and this took a further six weeks to clear. Bronchoscopy revealed no evidence of new growth.

A profuse growth of penicillin-resistant staphylococci was obtained from the sputum. He was treated with combined penicillin and streptomycin without effect. Later he responded slowly to oxytetracycline and was finally discharged after 65 days, greatly improved in general condition, with a radiographically clear chest.

Case 4

This patient, a man aged 56, gave a month's history of cough and dyspnoea. Right-sided pleuritic pain had been present for two weeks, and frothy sputum for five days. On admission he was very ill, short of breath, and cyanotic. There were clinical signs of pneumonia at the right base, and a radiograph of the chest showed consolidation in the right lower zone. The leucocyte count was 18,000 per c.mm. Treatment was begun with penicillin, but sputum culture yielded coagulase-positive staphylococci resistant to penicillin and sensitive to streptomycin.

Six days later further radiographs showed some clearing of the right base with fresh consolidation in the left upper and lower zones. He was given streptomycin with little general improvement. After 10 days there was some clearing at the left base, but the left upper lobe had become densely opaque on radiographic examination. A week later there was extensive breakdown with multiple cavitation in the left upper lobe. Treatment was then changed to chlortetracycline, but this had to be stopped because of diarrhoea. Nevertheless, the left upper lobe gradually cleared and tomograms prior to discharge showed no cavitation.

He was further investigated; a bronchogram showed deficient filling of the left upper lobe bronchi, but bronchoscopy did not reveal any abnormality. His total stay in hospital was 91 days.

At a follow-up examination two years later he was well, but radiographs showed fibrosis in the upper zone of the left lung with ring shadows suggestive of cystic changes.

Case 5

In this case, that of a man aged 55, there was no history of chest disease. Following perforation of a sigmoid diverticulum he developed peritonitis, and at operation a left inguinal colostomy was formed, but his condition deteriorated and he was transferred to the medical ward.

On admission he was febrile and very ill. He had carious teeth and foul breath. Radiographs of the chest showed a right hilar opacity. This cleared slowly, but ten days later there was mottling at both bases. In spite of some clinical improvement the radiographic opacities extended. After another three weeks there was dense consolidation in most of the left lung, collapse of the left lower lobe, and multiple cavitations in the lingular segment of the left upper lobe. Slow resolution then began and proceeded steadily, but 60 days later cystic changes were still present at the site of the previous breakdown. Sputum examination revealed a

profuse growth of staphylococci resistant to penicillin but sensitive to chlortetracycline and chloramphenicol. He was treated with chlortetracycline and discharged after 36 days.

At a follow-up examination one year later he was well; there was no dyspnoea. A radiograph of the chest showed fibrotic changes at both bases.

Case 6

One week prior to admission a woman aged 21 developed a right lower lobe pneumonia which at first responded to sulphonamides at home, but was later complicated by pleural effusion.

On examination she was found to be very ill, short of breath, and cyanotic. A radiograph of the chest showed complete collapse of the right lung with air and fluid in the pleural space. Thick, blood-stained pus was aspirated and a profuse growth of penicillin-sensitive staphylococci was obtained on culture. She was treated with intramuscular penicillin daily, together with intrapleural injections of penicillin and streptokinase. She made an excellent recovery, and was discharged after 65 days. When seen three months later there was residual pleural thickening at the right base and in the interlobar fissures.

On a final follow-up examination two years later she was free of symptoms and radiographically the lungs were within normal limits.

Discussion

Staphylococcal infection to-day presents a major problem in the treatment of bacterial disease. The staphylococcus has shown such marked adaptability to antibiotic substances that within a few years of the introduction of penicillin it was found that a high proportion of these infections failed to respond to this drug.

In this country the majority of staphylococci are still sensitive to some of the broad-spectrum antibiotics, such as the tetracyclines, chloramphenicol, and erythromycin, but resistant strains are increasingly encountered in patients previously treated with these substances. In view of the recent tendency to treat chronic bronchitis with prolonged courses of tetracyclines many more resistant cases may be seen in future.

There is good evidence that the incidence of staphylococcal pneumonia is growing. Review of the literature in the last five years suggests that they now constitute from 3 to 10% of all cases of pneumonia admitted to hospital. This is probably an underestimate of the true situation owing to the difficulties in the way of an aetiological diagnosis already mentioned.

Most observers reporting large series of cases of pneumonia during the last ten years have noted the high proportion of patients whose sputum fails to grow pathogenic organisms. It is generally believed that this is due to chemotherapy before admission to hospital. Anderson (quoted by Grist *et al.*, 1952) studied a series of 500 patients between 1939 and 1941, and encountered only eight from whom pathogens were not isolated. Ten years later Crofton *et al.* (1951) were unable to identify an aetiological agent in 52 of the 110 cases of pneumonia studied at Hammersmith Hospital.

In our series of 122 cases of pneumonia admitted in 1952-4 an aetiological diagnosis was made in 50, of which 18 were staphylococcal. It is our belief that these 18 cases did not represent the total number of cases of staphylococcal pneumonia in the series. Staphylococci were, in fact, grown from the sputum of several other cases, but they were excluded because the evidence seemed inconclusive. Before admission to hospital most of the cases were treated with penicillin or sulphonamides, and some with oxytetracycline. Such treatment may have prevented the growth of the responsible organisms without effecting a cure. That this explanation for the failure to grow pathogenic organisms may not be the whole answer, however, is suggested by the

results of a recent investigation by Batty Shaw and Fry (1955) into 80 cases of acute chest infection in general practice. Eight general practitioners in South London, in association with the local hospitals, made every effort to obtain sputum or throat swabs from their patients before any treatment was started. In spite of this early collection of specimens pathogenic organisms were isolated only from 25 of the 80 cases.

Staphylococcal infection often directs its attack against damaged tissues and where local or general resistance is low. Such circumstances were present in 10 of the 18 cases in our series. It is significant in this respect that in fibrocystic disease of the pancreas, where recurrent chest infection is frequent, the staphylococcus is responsible for the majority of cases and accounts for a high proportion of deaths (Anspach, 1947; Shwachman *et al.*, 1949). It is also of interest that most cases of staphylococcal pneumonia in infants occur under the age of 6 months (Wallman *et al.*, 1955).

Reports already referred to and the results of our own review of 122 consecutive pneumonia admissions show that the average age of patients is over 50 years, and that a history of previous chest disease is obtained in at least 40% of the cases. It is not surprising, therefore, that the staphylococcus should play an increasing part in these infections.

Summary

Eighteen cases of staphylococcal pneumonia in adults are reported to have occurred in a series of 122 consecutive cases of pneumonia admitted to one medical unit in 1952-4. There was no epidemic influenza in the area during that period. The outstanding feature in these cases was the severity of the clinical course and the number of suppurative complications. All 18 cases recovered, but only six responded to treatment with penicillin.

There is some evidence that this form of pneumonia is becoming more frequent and that staphylococcal infections are responsible for a considerable number of cases where failure of response to penicillin is encountered. The important part played by pre-existing chest disease or reduced resistance is stressed. Tetracycline and erythromycin are suggested as the antibiotics of choice in these cases.

In future, staphylococcal infections are likely to present a major problem in the treatment of pneumonia.

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