Case Reports

CEREBRAL NOCARDIOSIS

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NOCARDIOSIS is an uncommon disease. It has been seldom reported in the British Isles and a brief account of this case therefore seems to be justified.

Case Report

In mid-November, a 40-year old boilerman had a febrile illness lasting only one day, with headache and myalgia. Two weeks later he developed dull aching pain in the left chest with pyrexia and a cough productive of scanty brownish sputum. There was a pleural rub and the chest radiograph showed an area of consolidation in the left upper zone. Despite treatment with penicillin for a week, the area of consolidation extended (Fig. 1) and he was admitted to hospital on 20th December. On sputum culture a pneumococcus and a micrococcus were isolated but repeated examinations failed to reveal either *myco. tuberculosis* or mycelial filaments. From 21st December until 9th January he was treated with chlortetracycline and he had become afebrile by 30th December. From 10th to 29th January he had penicillin and streptomycin in combination. His clinical progress was initially satisfactory, the sputum became mucoid, and partial resolution of the pneumonia occurred (Fig. 2).

On 19th January he began to suffer from intermittent headache of increasing severity at first frontal and later occipital. On 27th January lumbar puncture produced clear CSF under normal pressure; the protein content was 40 mg./100 ml. and there were 70 leucocytes/cu. mm. On 29th January the CSF was slightly turbid, the protein content was 60 mg./100 ml. and leucocyte count 1020/cu. mm. (75% polys). No organisms were cultured from either specimen. Intellectual impairment with variable confusion became apparent and he complained of intermittent diplopia. Bilateral papilloedema developed with neck-stiffness, inco-ordination of both arms, and a left homonymous visual field defect. He remained afebrile. Bronchoscopy on 28th January showed no abnormality.

On 31st January ventriculography was attempted, but due to raised intracranial pressure and the small size of the ventricles, very little air could be introduced. Bilateral carotid angiography showed a slight shift of the anterior cerebral arteries to the right, with some upward displacement of the left middle cerebral and downward displacement of the left posterior cerebral artery. The appearances were thought to indicate a deep-seated lesion in the left temporo-parietal area. He remained alert, though rather facile and with episodes of confusion. A right abducent paralysis appeared on 2nd February, and next day he became suddenly unconscious and died within half an hour.

Necropsy. The upper lobe of the left lung contained an area of unresolved pneumonia measuring 10 x 6

FIG. 1.—Chest radiograph on 20 December.

FIG. 2.—Chest radiograph on 30 January.

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cm.; this showed a moderate degree of fibrosis and a small cavity 1.5 cm. in diameter containing brownish pus was noted near the pleural surface. The overlying pleura was thickened. The brain showed general swelling, with a cerebellar pressure cone and slight bilateral herniation of the uncus at the tentorial aperture. On section multiple abscesses, varying from 0.5 to 1.5 cm. in diameter, were found in the following situations: on the right side in the caudate nucleus, lentiform nucleus, insular cortex, frontal operculum, thalamus, and the white matter of the inferior temporal gyrus and the occipital lobe; on the left side in the precentral gyrus, cingulate gyrus and occipital white matter. Cerebellar abscesses were present bilaterally in the cortex and in the white matter on the left side. There was no evidence of meningitis. No lesions were found elsewhere. Culture of the pus from both the pulmonary and the brain lesions yielded a pure growth of *Nocardia asteroides*.

Discussion

In a review of 95 reported cases of nocardiosis, most of them in the United States, Ballenger and Goldring (1957) found 29 examples of involvement of the nervous system. Since then there have been several further reports; however, nocardiosis of the nervous system remains an uncommon disorder and no description has appeared in the British literature since that by McDonald (1904).

Organisms of the genus *Nocardia* are aerobic members of the family Actinomycetaceae. While the most common cause of human Nocardiosis is *N. asteroides*, at least nine other pathogenic species have been identified. Their natural habitat is the soil.

The high incidence of primary pulmonary lesions indicates that the respiratory tract is the organism's most common site of entry, but infection occurs through the alimentary tract in some cases (Hickey and Berglund, 1953; Cupp, Edwards and Cleve, 1960). The organism may infect cutaneous abrasions but apparently cannot penetrate the intact skin. As in the present case the pulmonary disease often begins as an acute pneumonitis; this may become chronic, when its course may closely resemble that of tuberculosis, both clinically and radiographically, the principal symptoms being fever, cough with mucoid or purulent sputum, anorexia, weight loss, dyspnoea and chest pain. Haemoptysis may occur but is not usual.

Haematogenous spread may occur to the central nervous system alone, or this may be part of a general dissemination (Larsen, Diamond and Collins, 1959; Carlile, Holley and Logan, 1963). It may give rise to purulent meningitis (Gilligan, Williams and Perceval, 1962), meningo-encephalitis (Cupp and others, 1960), cerebral

abscess (Cupp and others, 1960; Pizzolato, Ziskind and Derman, 1961), cerebellar abscess (Larsen and others, 1959; Hathaway and Mason, 1962), or paraplegia due to infection of the spinal cord (Welsh and Rhoadesher, 1961).

Nocardiosis must be carefully distinguished from actinomycosis since the drug of choice in treatment differs (McQuown, 1955). Nocardia appears in stained smears of pus, fresh sputum or centrifuged CSF as gram-positive, variable acid fast, single or branching filamentous rods. It grows well on ordinary media under aerobic conditions, but while mycelial colonies usually appear in twenty-four to seventy-two hours, four to six weeks may be required for recognisable growth. Failure of diagnosis in the present case may have been due to the cultures being discarded too early. Nocardia species are usually destroyed by techniques for concentrating tubercle bacilli and cultures should be made before concentration.

If the diagnosis is made early the prognosis is more favourable than was formerly thought. The drug of choice is undoubtedly sulphadiazine to which the organisms are usually highly sensitive, and dosages sufficient to maintain a serum concentration of 8-12 mg./100 ml. are recommended (Murray, Finegold, Froman and Wilp, 1961). A reasonable daily dose for an adult is 4 to 6 g., increased to 8 or 9 g. in severely ill patients (Peabody and Seabury, 1960). Sensitivity of individual strains to penicillin, erythromycin, tetracyclines, streptomycin and chloramphenicol has been reported and sensitivity studies should be carried out in all cases; an appropriate antibiotic may then be added to the sulphonamide if necessary. Treatment should be continued for several months after apparent clinical cure has been achieved. Initial intrathecal therapy, e.g. with streptomycin, may be indicated in cases with meningitis. An indispensable part of the treatment is adequate surgical drainage of purulent collections, and most cases of cerebral nocardiosis who have survived have had either ventricular drainage (Jacobson and Cloward, 1948), or excision of a brain abscess (Krueger, Norsa, Kenney and Price, 1954; List, Williams, Beeman and Payne, 1954; Munslow, 1954; Hathaway and Mason, 1962). When there are multiple cerebral abscesses, as in the present case, the outlook is probably hopeless.

The incidence of nocardiosis appears to be increasing (Murray and others, 1961), and should be considered in cases of chronic infection, especially when both pulmonary and cerebral lesions are present.

Summary

A fatal case of pleuro-pulmonary nocardiosis with multiple cerebral and cerebellar abscesses is reported. The features of the disease and the characteristics of the organism are briefly described.

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NONMETASTATIC NEPHROGENIC HEPATOSPLENOMEGALY AND EPILEPSY

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IN RECENT years a variety of general systemic manifestations and unusual syndromes have come to be recognised as presenting features of an otherwise occult neoplasm. Their diversity has included the purely dermatological manifestations, including acanthosis nigricans, dermatomyositis and erythema gyratum repens; a variety of neuromuscular syndromes; skeletal disturbances including clubbing, pulmonary hypertrophic osteoarthropathy and pachydermoperiostosis; thrombophlebitis migrans and phlebothrombosis; erythrocytosis and red cell aplasia; and various hormonal and metabolic disturbances (Greenberg, Divertie and Woolner, 1964). Familiarity with such manifestations are of dual importance; firstly, as diagnostic pointers and secondly, in the frequent observation that successful removal of the primary lesion may lead to complete regression of these features.

Creevy (1935) recorded three patients with hypernephroma presenting with clinical features suggesting cirrhosis of the liver. Stauffer, at the

1961 annual meeting of the American Gastroenterological Association drew attention to non-metastatic hepatosplenomegaly from renal carcinoma. The published abstract (Stauffer, 1961) mentions five cases, but Greenberg and others (1964) ascribe 10 such cases to the author; four with splenic enlargement and all with grossly abnormal results of liver function tests. The abnormal findings returned to normal after nephrectomy. Such a favourable response is well recognised for renal polycythemia and is at times noted with proven pulmonary metastasis. That this should obtain on occasion with hepatosplenomegaly is of considerable interest as wider appreciation of this phenomenon would lead to more of these cases being offered operative treatment despite markedly deranged liver function, with a prospect of effecting complete cure. The frequency with which such an outcome may be expected is unknown and accordingly a case of renal carcinoma recently encountered by us and diagnosed only at necropsy but who showed