The indications and contraindications for the use of halothane are discussed, and it is concluded that the drug can be successfully and safely used in a standard closed-circuit apparatus.

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SARCOSPORIDIOSIS IN MAN WITH PERIARTERITIS NODOSA*

BY

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Sarcosporidiosis is a very common protozoal parasitic infestation of muscle fibres in animals in this and many other countries; it has rarely been observed in man. Since its discovery first in mice by Meischer, in 1843, it has been extensively studied in animals.

The life-cycle remains unknown, but the spores are probably ingested in food and eventually gain entry to the striated musculature. There they form large cysts within individual muscle fibres and may attain 5 mm. in length. Each cyst when fully developed shows characteristic division by septa into chambers containing myriads of sickle-shaped spores, which appear to degenerate towards the centre. Infestation has often appeared to be harmless in animals, but when heavy it has produced serious pathological effects and death. Transmission to other animals is probably due to rupture of cysts into the alimentary canal and faecal contamination of food thereby (Scott, 1943). We suggest that the disease is conveyed from animals to man by means of contamination of uncooked food by animal faeces.

We have reviewed the human cases reported, and we accept the eight cited by Feng (1932), who added a case of his own, two reported by Vuillemin (1902), and one each by Lorenz (1904), Hewitt (1933), Gilmore *et al.* (1942), Kean and Grocott (1945), Pugh (1950), and Mackinnon and Abbott (1955).

An eighteenth case is here reported because of the apparent rarity of the condition in man and also because the parasitic infestation was associated with various pathological lesions, including periarteritis nodosa, which have not been described before. In addition, no previous case has come to full necropsy examination. A complement-fixation test devised by Awad and Lainson (1954) has been used in the present case for the first time in establishing the diagnosis during life.

Case Report

A European official aged 60, retired from India before 1939, was well until April, 1953. Suddenly he collapsed,

*Based on papers read before the Wessex Physicians Club and the Association of Clinical Pathologists.

almost losing consciousness, with, however, no specific weakness, and next morning he had recovered fully. Eight months later he suddenly lost the use of his right arm, and examination revealed diminished power there with increased tendon reflexes but no sensory changes. Complete recovery gradually took place during the next two weeks. One month later a similar sudden weakness of the left arm occurred and again recovery was rapid. Complete physical examination then proved normal, and the B.P. was 140/80. During the next five months exertional dyspnoea began and rapidly increased. Chest radiographs revealed scattered ill-defined but discrete opacities in both lung fields, suggestive of disseminated vascular lesions; biopsy of a pectoral muscle was therefore performed. Subsequently a right homonymous hemianopia developed with right hemiparesis, headache, and mental deterioration. The signs of congestive cardiac failure progressed, and he died on June 21, 1954.

Laboratory Investigations.—No abnormality was found in the blood count and differential count on any occasion. The urine was repeatedly normal. The C.S.F. was normal. E.S.R. was 30 mm. in one hour, rising later to 80 mm. in one hour; serum albumin, 3.4 g. per 100 ml.; serum globulin, 3.0 g. per 100 ml.; liver-function tests normal; W.R. negative; serum complement-fixation test for sarcosporidiosis, positive 1:32; complement-fixation test for toxoplasmosis negative.

Three series of electrocardiograms taken in the last week of his life showed combined heart strain.

Muscle Biopsy.—No evidence of periarteritis nodosa was found, but a number of cystic structures were seen within individual muscle fibres (see Fig.). Each cyst had a delicate

Left-side pectoral muscle with sarcocyst. Note very thin capsule and internal septa. A thin rim of sarcoplasm still surrounds the parasite. (H. and E. $\times 145$.)

hyaline wall and contained a large number of minute basophilic sickle-shaped spores. In longitudinal section the cysts were seen to be at least 1 mm. in length and to be divided by septa into separate chambers. The spores seemed to be produced at the periphery and to degenerate towards the centre of the cyst. No inflammatory reaction was found. These appearances are typical of sarcosporidium (*Sarcocysts*).

Necropsy Findings

Necropsy confirmed that death was due to congestive right heart failure. The heart was moderately enlarged owing to left and right ventricular dilatation. Attached to the base of the tricuspid valve and spreading on to the ventricular and auricular walls was an enormous mass of friable grape-like vegetations; smaller vegetations arose in the pulmonary conus and from the papillary muscles. No vegetation was found within the left heart, but the interventricular septum showed fibrous scarring. The lungs were bulky, and all lobes contained small, firm, often yellowish stellate scars, associated with which were multiple thrombi in the branches

of the pulmonary arteries. The left kidney contained a recent infarct at one pole; small infarcts were present in the spleen. The liver showed severe chronic venous congestion.

A number of lesions were present in the brain. The left occipital pole was infarcted, apparently owing to thrombosis of the left posterior cerebral artery, and there were several small superficial cortical infarcts—two in the left parieto-occipital cortex and one in the right frontal cortex.

Microscopical examination showed the vegetation in the right heart to be granulomatous in nature. Its delicate fronds had a structureless acellular core apparently composed of laminated fibrin clothed with a thick layer of loosely packed endothelial cells, quite frequently in mitosis. Very few leucocytes were present and no bacterial colonies. The heart muscle beneath was scarred, and several coronary arterioles showed necrotizing arteritis. No sarcosporidial cysts were recognized with certainty in the myocardium. The pulmonary lesions were also largely vascular and typical of periarteritis nodosa. Often monocytic infiltration surrounded the thrombosed arteries, whilst older lesions showed organization and fibrosis. In the kidney the wall of the thrombosed polar artery showed gross destruction and disorganization with replacement fibrosis and intimal proliferation. An occasional hepatic arteriole was occluded by a plug of monocytic cells. A subacute arteritis affected the superficial cerebral vessels related to the cortical infarcts. Surrounding such arteries there was an intense monocytic infiltration, with occasional polymorphs and plasma cells. The arterial wall was in places necrotic, but no giant cells were seen. The cortical lesions were typical of ischaemic infarction.

Discussion

The occurrence of periarteritis nodosa in the present case seems likely to be related to the parasitic infestation. Experimental pathology has incriminated bacterial hypersensitivity in the aetiology of periarteritis nodosa (Pagel, 1951), and the disease has already been described in association with another protozoal disease—namely, trichiniasis (Reimann *et al.*, 1943). The presence of antibodies to sarcosporidia was demonstrated in the present case by the new complement-fixation reaction. Absence of an inflammatory reaction around the intact cysts would perhaps suggest that in this phase the organism may not be antigenic. However, an alternative explanation is the presence of the thick hyaline capsule, which may be impervious to the passage of antigenic protein. Spores from ruptured cysts were utilized to provide antigen in the complement-fixation test, and the presence of an antibody to them was demonstrated. Thus it is possible that cysts when they do rupture produce an allergic reaction, manifest as periarteritis nodosa. It is further possible that an as yet unobserved stage in the life-cycle of sarcosporidia may have been responsible for these pathological changes.

All the cases of human sarcosporidiosis previously reported have been diagnosed by the accidental discovery of the parasite in voluntary or cardiac muscle. With two possible exceptions the condition has been asymptomatic. Lorenz (1904) notes the occurrence of associated dermatomyositis, while Pugh (1950) found sarcosporidia in a case manifesting transient recurrent subcutaneous nodules resembling urticaria with an eosinophilia. A few cases of reaction to the parasite have been reported in the veterinary literature, and include myositis, heart-block, congestive heart failure, and an eosinophilic reaction (Saloman, 1935; Clark and Jackson, 1942; Wang, 1950).

The pathogenesis of the granulomatous vegetation in the right heart is obscure. Largely composed of proliferating endothelial cells, it seems more likely to represent a local reaction to the presence of a parasite than a tissue response of an allergic nature. The vegetation contained basophilic granules, but these could not be recognized definitely as parasites. Similar endothelial proliferation was seen in the lungs, liver, and cerebral arteries, and is not typical of periarteritis nodosa.

An attempt by us to transmit the infection to mice was unsuccessful. Animals were fed with suspensions of muscle tissue and the cardiac vegetation, and a second group received intraperitoneal inoculation. After twelve weeks the mice were killed, and preparations of cardiac and voluntary muscle were examined. No evidence of infection was obtained. Many previous attempts to demonstrate the pathways of transmission of the sarcosporidium have also been made without success. Experimental infections have been difficult to establish, and the feeding of large numbers of cysts to various animal species has usually failed to transmit the disease.

In view of the very heavy infestation of domestic animals used for food in this country, the incidence of human infestation must be much higher than the small number of cases reported in the literature would lead one to expect. With others we consider that the apparent infrequency of this condition is simply due to the fact that it has not been sought for in muscle fibres.

A survey of sera from a cross-section of the population using the complement-fixation test of Awad and Lainson would provide interesting data on the frequency of human sarcosporidiosis.

Summary

Sarcosporidiosis in animals and man is briefly described.

The literature in human cases is reviewed, and the eighteenth case is recorded. This is the first human case to have the diagnosis confirmed in life by the new complement-fixation test and to come to full necropsy.

Periarteritis nodosa was also present, and its association with sarcosporidiosis is discussed.

An unusual granulomatous condition was found in the right heart.

We are indebted to Dr. C. H. Devereux for referring this case to us, and to Dr. F. I. Awad, Major E. J. Balmer, Dr. L. B. Blair, Colonel C. F. J. Cropper, Dr. E. S. Duthie, Lieutenant-Colonel A. M. Pugh, and Mr. K. G. Morgan for their assistance.

ADDENDUM.—The results of the complement-fixation tests are significant in view of the recent investigations by Dr. I. A. B. Cathie (*Lancet*, 1957, 1, 816) on the occurrence of antibodies to sarcocystis and toxoplasma.

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The Scientific Film Association has recently issued a catalogue of films on cerebral palsy. The listed films are grouped according to their bearing on the disease, the sections being physiology, aetiology, clinical (general), clinical (case records), clinical (differential diagnosis), treatment, and general. An index of film titles is included. In common with the other S.F.A. catalogues of films a description of each film is given, together with size, running time, and the name of the distributor. Intending borrowers may book films through the S.F.A., but the association itself does not distribute the films. The publication of this catalogue has been made possible by a grant from the National Spastics Society. The catalogue is obtainable from the Scientific Film Association, 164, Shaftesbury Avenue, London, W.C.2 (price 2s. 6d. net).