L. ROSSI: CASE OF CARDIAC LYMPHANGITIS WITH ATRIOVENTRICULAR BLOCK

FIG. 1

FIG. 2

FIG. 3

FIG. 4

FIG. 5

FIG. 1.—Area of sclerosis above the central fibrous body, involving the atrioventricular node (bottom right)—the abnormal lymphatic vessels are barely visible. (H. and E. $\times 11$.)

FIG. 2.—Dilated lymphatic vessels with endothelial cells protruding into the lumen. (H. and E. $\times 435$.)

FIGS. 3, 4, and 5.—Perilymphatic infiltration with round cells. (H. and E. Fig. 3, $\times 445$; Figs. 4 and 5, $\times 110$.)

Occurrence of Tetany in Litters of New Zealand White Rabbits Associated with Spontaneous Vertebral Fractures and Limb Malformations

[WITH SPECIAL PLATE]

Brit. med. J., 1965, 2, 32

The New Zealand white rabbit is widely used in research institutions, particularly in the testing of drugs for teratogenicity. This preliminary communication describes the occurrence of spontaneous tetany in a breeding colony producing animals for this purpose. The colony consists of some 80 breeding does. They and their progeny are fed entirely on diet 18 (Bruce and Parkes, 1947). To date, eight affected litters have been recorded with 25–50% of the young in a litter exhibiting the condition.

The first signs appeared in the young about the fourteenth day after birth, when weakness and dragging of the hind limbs became apparent. Attacks of tetany supervened, the animal showing a complete board-like rigidity before slowly toppling on to its side, where it remained with spasm of the musculature of the whole body (see Special Plate, left below). At this stage, during the periods between the attacks of spasmodic contraction, the muscles remained easily excitable, and the slightest touch would evoke a burst of contractions. Trismus made it difficult or impossible for the young to feed naturally, or for them to be fed even with the aid of a fountain-pen filler; after

a period of hours to days they died after severe tetanic convulsions. Animals less severely affected recovered. After a period of months some of the recovered animals were indistinguishable from normal; others showed weakness of the spine and splay deformity of the feet.

X-ray examination of the severely affected young revealed the presence of fractures and fracture-dislocation of the thoracic vertebrae, generally at the level T7-T8 (Special Plate, left above). Irregular calcification of the teeth was noticed. Gross examination of the nervous system revealed no detectable abnormality. The parathyroid glands were enlarged, and in one case cystic. The blood calcium level was around 15 mg./100 ml. by Nuclear Fast Red method (Kingsley and Robnett, 1961).

Breeding experiments revealed that in one group of affected animals the parentage of the syndrome could be traced back to a single male with inheritance through some of his sons and daughters. The incidence appears to be equal in the two sexes. Treatment of the severely affected young with massive doses of calcium gluconate, and vitamins A, D, and E, were all equally fruitless. Further investigations are in progress.

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Medical Memoranda

Case of Cardiac Lymphangitis with Atrioventricular Block

[WITH SPECIAL PLATE]

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Interest has recently been shown in the pathology of the cardiac lymphatic system, and there is both experimental (Kline *et al.*, 1963; Miller *et al.*, 1963) and clinicopathological evidence (Kline *et al.*, 1964) to suggest that an impairment of lymph flow can cause myocardial damage and endocardial fibroelastosis. It has been pointed out that in the heart as elsewhere in the body disordered lymph drainage predisposes to inflammation and to infection (Miller *et al.*, 1964a), and this has in fact been demonstrated in experimental bacterial endocarditis (Miller *et al.*, 1964b).

Cases of heart-block associated with an abnormality of the cardiac lymphatic vasculature have been the subject of previous papers, but they have been rare. The present apparently unique case has already been briefly reported (Rossi, 1964) and is now described in greater detail.

CASE REPORT

A woman aged 78 was admitted to the Fatebenefratelli Hospital, Milan, in June 1963 with a left hemiplegia of a few days' duration and suspected myocardial infarction. No past history of severe

infectious disease was obtained. Since 1960 she had been moderately hypertensive with average blood-pressure readings of 180/100 to 200/110 mm. Hg, rising to 210/120 at the onset of her hemiplegia. From 1960 till May 1963 electrocardiograms had shown complete heart-block, with a ventricular rate between 40 and 50 a minute.

On admission the patient was mentally confused, and complained vaguely of chest pain and headache. She was found to have a severe left hemiplegia with marked facial involvement, a pulse rate ranging between 54 and 70, and a blood-pressure of 140/90 mm. Hg. The white-cell count was 10,000/c.mm., and the haemoglobin, red cells, blood sugar, and blood urea were normal.

Two electrocardiograms (see accompanying tracings) were recorded at three days' interval, with similar findings. The second tracing showed complete A-V dissociation, with an atrial rate of 84 and a

E.C.G. showing heart-block.

ventricular rate of 68. The P wave was of normal shape; the QRS complex was of normal duration (0.08 second); the S-T segment was slightly depressed in leads I, aVL, and V₆; and the T waves were flattened or inverted in I and aVL. The pattern indicated heart-block and suggested anterolateral ischaemia and left ventricular strain. The patient died within six days of admission from cerebral haemorrhage and heart failure.

Post-mortem Findings.—**Brain:** There was a recent haemorrhage into the white matter in the right parieto-occipital region, while an old apoplectic cyst was found in the left putamen. The larger arteries were atherosclerotic. **Heart:** This weighed 360 g. The left ventricle was moderately dilated and hypertrophied, the parietal and valvular endocardium was smooth, and the myocardium was brownish yellow. No macroscopical changes were found around the outlet of the coronary sinus or around the pars membranacea septi. The coronary arteries were moderately atherosclerotic. **Aorta:** This was atheromatous, with some ulcerated plaques in the abdominal part. The remaining viscera were congested and the lungs were oedematous.

Microscopical Findings.—A single block comprising the base of the interatrial septum and the upper three-quarters of the inter-ventricular septum was fixed in formalin and embedded in paraffin. Serial sections were cut 50 μ apart and stained with haematoxylin and eosin, azan, or orcein. The region adjacent to the central fibrous body, which is normally rich in fatty and soft connective tissue, was found to be diffusely and coarsely fibrotic (Special Plate, Fig. 1). The atrioventricular node and its connexions with the right atrium showed sclerosis and severe atrophy. Within the predominant fibrous strands and interlaced with elastic fibrils there were several channels, scattered or in groups, lined by thick layers of swollen endothelial cells often occluding the lumen. A few channels were slightly dilated and lined by a single layer of endothelial cells which sometimes protruded into the lumen (Special Plate, Fig. 2), and some of these were empty while others contained acidophilic debris. The sections, however, did not have a cystic pattern. Perilymphatic infiltration with round cells was often seen (Special Plate, Figs. 3, 4, and 5). A small amount of calcium was deposited among the fibrous strands. The area of abnormal histology involved a few square millimetres on each of the sections from the base of the inter-atrial septum to the upper border of the bundle of His, but it was never very well demarcated. Distally the right bundle branch was normal but the roots of the left were partially damaged. Sections from the walls of both ventricles showed no areas of myocarditis.

DISCUSSION

Five cases of heart-block ascribed to lymphangio-endothelioma of the heart have been reported (Armstrong and Mönckeberg, 1911; Lloyd, 1929; Perry and Rogers, 1934; Rezek, 1938; Mahaim, 1945). The diagnosis in these cases was made on the necropsy findings of whitish nodules and of cysts, and confirmed by the histological demonstration of cells

aggregated in columns or clusters and of numerous cysts in a "honeycomb" pattern (Perry and Rogers, 1934), with little or no evidence of an inflammatory process (Rezek, 1938). The diagnosis of lymphangio-endothelioma was challenged, however, by Rezek (1938), who suggested that the "tumour" in these cases had arisen in ectopic endodermal, probably foregut, epithelium. This hypothesis has been put forward, too, in other cases where the cystic element was prominent but the conducting system not involved. It has also been suggested by Mahaim (1945) that the "tumours" may have a mesothelial (coelomatic) origin.

In the present case, however, the affected area was not visible to the naked eye, and histological examination showed it to be poorly demarcated and to consist mainly of coarse fibroelastic tissue and inflamed, proliferating lymph vessels. Dilatation and new formation of vessels and epithelial-like proliferation of endothelium are to some extent common features of both lymphangio-endothelioma and chronic proliferative lymphangitis. However, the predominance of the fibrous over the angioblastic component in this case, and in particular the presence of perilymphangitis, are suggestive of an inflammatory process.

It is easy to conceive a sequence of events leading from long-standing lymphangitis with impairment of lymphatic drainage to sclerosis and atrophy following the pattern outlined by Drinker and Yoffey (1941) and described in human endomyocardial fibroelastosis by Kline *et al.* (1964). It is possible that congenital dysplasia of lymphatic vessels predisposes to lymphangitis; but this is unlikely to have been the case here, since lymphangiectatic malformations usually present at a much earlier age (Kline *et al.*, 1964). It is therefore postulated that the cause of the damage to the conducting system and of the heart-block in this case was a chronic proliferative lymphangitis.

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Imipramine in Treatment of Parkinsonism : a Double-blind Placebo Study

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A review of the literature discloses such fundamental differences of opinion regarding the efficacy and mode of action of imipramine that further clinical studies are more than justified.

Though a number of reports confirm the specific anti-depressive effect first described by Kuhn in 1957, a recent comprehensive survey of American and British journals revealed ten placebo-controlled trials in which the effect of imipramine on depression was better than that produced by the placebo in four, no better in five, and equivocal in one (Hare *et al.*, 1964). The slight improvement obtained by these authors was ascribed entirely to sedative effects. Rees *et al.* (1961) stated that imipramine influenced anxiety more favourably than depression.

Sigwald *et al.* (1959), who first used the drug in Parkinsonism, were particularly impressed with the improvement of akinesia. In spite of the chemical similarity of imipramine to the phenothiazines, subsequent reports tended to confirm its value in Parkinsonism, though its mode of action was disputed. Strauss (1959) and Blomberg and Eriksson (1961) stated that the neurological effects were entirely secondary, while, on the other hand, Di Cristo and Di Cristo-Tedeschi (1961), Denmark *et al.* (1961), Mandell *et al.* (1961), and Gillhespy and Mustard (1963) claimed that the neurological improvement resulted from the specific action of the drug.

In view of its anticholinergic, antihistaminic, and anti-serotonin properties (Domenjoz and Theobald, 1959) it would be surprising indeed if imipramine did not possess a measurable specific action in ameliorating the symptoms of Parkinsonism.

CLINICAL MATERIAL AND METHODS

Seventy unselected patients were given, alternatively, either imipramine or placebo tablets, the exact sequence differing with