

Fatal Lyme carditis and endodermal heterotopia of the atrioventricular node

N.R.B. Cary, B.Fox, D.J.M. Wright¹, S.J. Cutler¹, L.M. Shapiro² and A.A. Grace²

Departments of Histopathology and ¹Medical Microbiology, Charing Cross and Westminster School, London W6 8RF, and ²Cardiac Department, Papworth Hospital, Papworth Everard, Cambridge CB3 8RE, UK

Summary: A fatal case of Lyme carditis occurring in a Suffolk farmworker is reported. Post-mortem examination of the heart showed pericarditis, focal myocarditis and prominent endocardial and interstitial fibrosis. The additional finding of endodermal heterotopia ('mesothelioma') of the atrioventricular node raises the possibility that this could also be related to Lyme infection and account for the relatively frequent occurrence of atrioventricular block in this condition. Lyme disease should always be considered in a case of atrioventricular block, particularly in a young patient from a rural area. The heart block tends to improve and therefore only temporary pacing may be required.

Introduction

Lyme disease is caused by the spirochaete *Borrelia burgdorferi* and may affect the heart. Clinically, Lyme carditis is commonly associated with atrioventricular block.^{1–3} There are few reports of histopathological changes in the heart, these being from the United States.^{1,4} Fatal Lyme carditis has only rarely been reported and not previously in Great Britain.

Case report

A 31 year old male farmworker from Suffolk was found following an interval appendicectomy to have a bradycardia due to narrow complex complete heart block. Three months previously an appendix abscess had been drained. At that time he had mild hypertension 180/110 mmHg, left ventricular hypertrophy and a small left kidney. There was no previous history of systemic upset or skin rash to suggest a diagnosis of Lyme disease. The Lyme ELISA⁵ was strongly positive > 100 units and the immunofluorescent antibody titre⁵ was positive at 1/512. IgM direct immunofluorescence, which would be expected to be positive from about the 2nd to the 6th week in a case of Lyme disease, was negative. There are no data available on the prevalence of Lyme

antibodies in Suffolk. However, examination of 643 ante-natal sera from a rural high incidence area (Salisbury – D.J.M. Wright, personal communication) gave the following results: 601 (93.5%) were negative, 35 (5.4%) were weakly positive and 7 (1.1%) gave positive results. Of these 7 positive sera all but one were of less than 40 ELISA units and the remaining specimen was positive at 48 units. In the context of these results the serological findings in this case are strongly suggestive of Lyme infection. The negative IgM direct immunofluorescence would suggest that the infection was beyond the initial acute phase. ASO titres, serology for syphilis, viral and autoimmune screen were negative except for the finding of thyroid microsomal antibody.

At autopsy there was an enlarged heart (530 grams) with biventricular hypertrophy and an organizing fibrinous pericarditis mainly over the right atrial appendage. There was some thickening of the mitral valve cusps with increased amounts of cellular connective tissue. Other valves were normal. The endocardial surface of both ventricles showed white patches and histology confirmed prominent endocardial fibrosis (Figure 1) with focal loss of myocytes and areas of mononuclear inflammatory cell infiltration. There were occasional small aggregates of lymphocytes and macrophages within the myocardium (Figure 2) and multiple small foci of myocardial fibrosis. A Warthin-Starry stain for spirochaetes was negative. The coronary arteries showed minimal atherosclerosis. Examination of the conducting system revealed endodermal

Correspondence: N.R.B. Cary, M.A., M.B., B.S., M.R.C.Path., Papworth Hospital, Papworth Everard, Cambridge CB3 8RE, UK.

Accepted: 26 July 1989

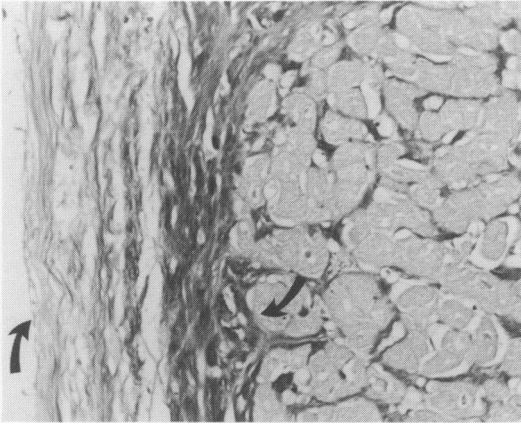


Figure 1 Band of endocardial fibrous thickening (between arrows), van Gieson's method for collagen $\times 150$.

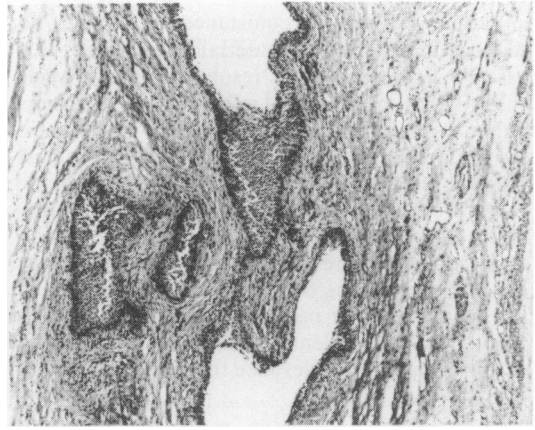


Figure 3 Endodermal heterotopia of atrioventricular node, haematoxylin and eosin $\times 24$.

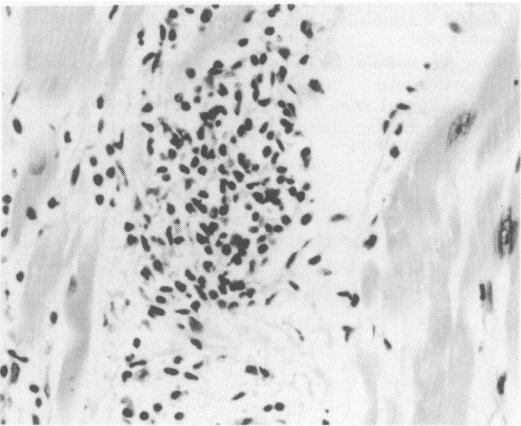


Figure 2 Myocarditis, haematoxylin and eosin $\times 240$.

heterotopia of the atrioventricular node (Figure 3) characterized by small spaces lined by epithelioid cells with some surrounding lymphocytic infiltrate. Immunoperoxidase staining of the epithelioid cells using antibodies to the epithelial markers CAM 5.2 and CEA was positive and to Factor VIII-related antigen, vimentin and desmin was negative. These results are in keeping with others⁶ who have suggested that this proliferation is of endodermal rather than mesodermal origin and therefore the more widely used term 'mesothelioma' is best avoided. Other significant findings at autopsy were a large spleen (500 g) which showed prominent autolysis with expansion of the red pulp and a small coarsely scarred left kidney (30 g) which histologically showed a chronic interstitial nephritis. There was a conspicuous diffuse lymphocytic infiltrate with germinal centres in the thyroid gland. Sections from liver, lung, right kidney, lymph node, synovia and brain were within normal limits.

Discussion

A recent report³ has reviewed the manifestations of Lyme carditis and emphasized its increasing importance as a reversible cause of atrioventricular block. The failure to consider the diagnosis may prompt the unnecessary implantation of a permanent pacemaker with all the long term implications of this decision. Despite the low incidence of Lyme disease in the United Kingdom we would recommend the clinician to be especially vigilant in young patients from rural areas presenting with heart block and to thoroughly review any antecedent history suggesting exposure to insect bites or systemic upset. If any such history is obtained then temporary pacing should be considered and an attempt be made to establish the diagnosis of Lyme disease serologically. The heart block associated with Lyme disease tends to improve over a short period and an expectant approach has been recommended as the long term prognosis is excellent.

As well as conduction disorders there may be clinical evidence of myocarditis and pericarditis in Lyme disease.¹⁻³ Endomyocardial biopsy in one case¹ showed a lymphocytic infiltrate and myocyte necrosis. In another autopsy case⁴ with co-existent babesiosis the myocardial and sub-endocardial inflammatory cell infiltrate included plasma cells. The carditis in this case of Lyme disease affected all parts of the heart: there was pericarditis, prominent endocardial fibrosis and focal myocarditis. Applying the Dallas criteria for the diagnosis of myocarditis⁷ this case would be classified as showing mild predominantly lymphocytic inflammation and moderate endocardial and interstitial fibrosis. However, it should be remembered that the Dallas criteria were devised for the interpretation of sequential endomyocardial biopsies and clearly a single examination of the whole heart in this case is

a rather different circumstance. Although no sequential histological material is available, this case may represent a later 'resolving' stage of Lyme carditis than previously described cases, with less inflammation and prominent areas of fibrosis, particularly in the endocardium. It is of interest that the histological features in this case resemble those seen in idiopathic dilated cardiomyopathy and it is possible that some cases of this condition may actually represent an end stage of Lyme carditis. The finding of endodermal heterotopia of the atrioventricular node in this case, itself a rare lesion, may be incidental to the presence of Lyme carditis, though of relevance to the sudden death.

However, given that Lyme carditis is commonly associated with complete heart block we feel that it is important to draw attention to this association as well as describing the carditis of Lyme disease. Could Lyme infection have induced proliferation of endodermal cell rests in the region of the atrioventricular node either directly or by induction of inflammation in this area?

Acknowledgement

We are very grateful to colleagues at Ipswich Hospital for their help in this case and to Mr R. Barnett for photography.

References

1. Steere, A.C., Batsford, W.P., Weinberg, M. *et al.* Lyme carditis: cardiac abnormalities of Lyme disease. *Ann Intern Med* 1980, **93**, 8-16.
2. Veyssier, P., Davous, N., Kaloustian, E., Maitre, B., Lallemand, P.Y. & Serret, A. Atteintes cardiaques au cours de la maladie de Lyme, deux observations. *Rev Med Interne* 1987, **8**: 357-360.
3. McAlister, H.F., Klementowicz, P.T., Andrews, C., Fisher, J.D., Feld, M. & Furman, F. Lyme carditis: an important cause of reversible heart block. *Ann Intern Med* 1989, **110**: 339-345.
4. Duray, P.H. & Steere, A.C. Clinical pathologic correlations of Lyme disease and related disorders. *Ann NY Acad Sci* 1988, **539**: 65-79.
5. Cutler, S.J. & Wright, D.J.M. Comparison of immunofluorescent and enzyme-linked immunosorbent assays for the diagnosis of Lyme disease. *J Clin Pathol* 1989, **42**: 869-871.
6. Fine, G. & Raju, U. Congenital polycystic tumour of the atrioventricular node (endodermal heterotopia, mesothelioma). *Hum Pathol* 1987, **18**: 791-795.
7. Aretz, H.T. Myocarditis: the Dallas Criteria. *Hum Pathol* 1987, **18**: 619-624.