professionals may move to the more lucrative private health sector. It is essential therefore to establish and nurture units and centres with a multidisciplinary base and reasonable tenure. To do this the United States federal government has funded through the Agency for Health Care Policy and Research 10 to 15 centres of excellence for health services research. In contrast, in Britain there is a tendency to run down and disestablish health services research units in favour of grants for individual programmes and projects.

UNITED KINGDOM

The efforts of the Medical Research Council in training have been more modest. Three special training fellowships in health services research have been awarded each year for the past two years. Among the advanced course studentships, three or four each year go to MSc programmes in medical statistics. Other young graduates who finally work in health services research may of course receive support from other parts of the council's training programme. For example, this year there will be nine MSc places on epidemiology or statistics courses, or both. The Wellcome Trust has recently begun to support training in health services research with one or two posts each year. The position in the United Kingdom is perhaps best summarised by the secretary of the council of the Medical Research Council during a visit to the United States at the end of 1991, who reported that "it seems the USA is taking training and manpower very seriously; the UK would do well to follow suit."

If an infrastructure in health services research is to develop, additional resources for multidisciplinary research will be needed. Additionally, the whole process of medical education needs to be infused with the behavioural and social sciences disciplines not only for the research and development strategy but also for the changes in medical education proposed by the General Medical Council (consultation document, 1991).

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Hammersmith Staff Rounds

Postinfectious myocarditis

Still a largely clinical diagnosis

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Patients with post-infectious myocarditis may present with unexplained heart failure or arrhythmia and fever. There is no universally accepted definition of this condition, although the Dallas classification has helped to establish firm histopathological criteria for diagnosis.[1] We present a case of probable coxsackie B myocarditis which illustrates some of the controversies surrounding this disease.

Case history

A 30 year old man developed shoulder pain, sharp retrosternal chest pain, a dry cough, and a sore throat seven weeks before admission to hospital. He subsequently noticed progressive breathlessness on exertion; by the day of admission he could walk no more than 18 m on the flat. He had no history of orthopnoea and ankle swelling or palpitations. Four days before admission a painful swelling had developed on the left side of his neck. His medical history was unremarkable. He smoked 20 cigarettes a day, took no prescribed drugs, and had not been abroad recently.

On examination he was unwell, dyspnoeic at rest, and flushed but afebrile. No signs of endocarditis or vasculitis and no superficial lymphadenopathy were evident but he had fullness of the left supraclavicular fossa. He had a high arched palate but no other features of Marfan syndrome. He had a sinus tachycardia of 100 beats per minute and a blood pressure of 100/70 mm Hg. His venous pressure was raised at 8 cm above the manubriosternal angle and the apex beat was laterally displaced and diffuse. Auscultation showed third and fourth heart sounds but no murmur and no rub. All pulses were palpable, and he had no peripheral oedema. Respiratory examination showed bilateral basal inspiratory crackles. Abdominal and neurological examination gave normal results.

On the night of admission he developed swelling of the whole of the left arm and distension of the superficial veins. The main clinical diagnosis was myocarditis, but in view of the probable left subclavian vein thrombosis we considered other causes.

Investigations showed he had normochromic normocytic anaemia with a haemoglobin concentration of 101 g/l. Peripheral blood leucocyte count was normal at $10{\cdot}8\times10^9$/l. His platelet count was raised at 708×10^{12}/l. A blood film showed thrombocytosis, anisocytosis, and some rouleaux but no nucleated red cells. The erythrocyte sedimentation rate was 102 mm in the first hour, and C reactive protein concentration was 195 mg/l (normal 0-10 mg/l). His biochemical profile, including creatinine kinase concentration and thyroid function tests, was normal. Repeated blood cultures were sterile. A Paul-Bunnel test for infectious mononucleosis and latex and dye tests for toxoplasmosis gave negative results. The electrocardiogram showed extensive T wave inversion over the inferior and precordial leads. Chest radiography showed cardiomegaly, blunting of both costophrenic angles due to small pleural effusions, and septal lines in both lower zones (fig 1).

He was treated with bed rest, intravenous heparin to produce full anticoagulation, oral diuretics, and a single daily dose of 75 mg oral aspirin. During admission further investigations were done as follows.

Cardiac structure and function—An echocardiogram showed normal valves. The right and left ventricles showed hypokinesis of the free wall and the right ventricle was dilated. Invasive study of the heart was deferred for four weeks, and by then his clinical state

was much improved. At this time his right ventricular pressure was 20/4 mm Hg; pulmonary arterial pressure 13/2 mm Hg with mean pulmonary capillary wedge pressure 6 mm Hg; and left ventricular pressure 96/7 mm Hg with normal to low left ventricular end diastolic pressure of 6 mm Hg. A left ventriculogram and coronary arteriogram appeared normal. An endomyocardial biopsy showed no evidence of active inflammation.

Evaluation of possible enteroviral infection—No organisms were isolated from the throat or stools. Serum taken at admission contained IgM antibodies against coxsackie B virus, which was consistent with recent infection. In addition, the titre of antibody against *Mycoplasma pneumoniae* rose from 1 in 8 to 1 in 128 during his hospital stay, suggesting exposure to this organism at around the time of admission. Antibodies to coxiella phase II antigens were also found, indicating previous but not recent infection. Tests for coxiella phase 1, HIV-1, HIV-2, and mumps serology gave negative results. The results of serological testing were deemed consistent with coxsackie B myocarditis.

Cause of subclavian venous thrombosis—Intravenous digital subtraction angiography confirmed occlusion of the left subclavian and axillary veins with filling of the innominate veins through extensive collaterals (fig 2). Thrombosis, vasculitis, or local extrinsic compression by lymphadenopathy were possible causes of this unusual picture. Extensive haematological investigations showed no evidence for an underlying cause for thrombosis. Ultrasonography of the neck showed no evidence of extrinsic venous compression or lymphadenopathy but extensive luminal clotting in the left internal jugular vein was found. Computed tomography of the chest showed several small, discrete, but enlarged mediastinal lymph nodes. However, histological examination of these nodes (after mediastinoscopy and biopsy) showed only reactive changes.

He responded well to treatment, with a return to his usual exercise tolerance. His condition was subsequently maintained with warfarin and diuretic treatment. Follow up electrocardiography showed resolution of the repolarisation abnormalities in the inferior and precordial leads. Repeat echocardiography showed no new changes.

Comment

This case shows some of the problems in establishing a diagnosis of myocarditis. Estimates of the incidence

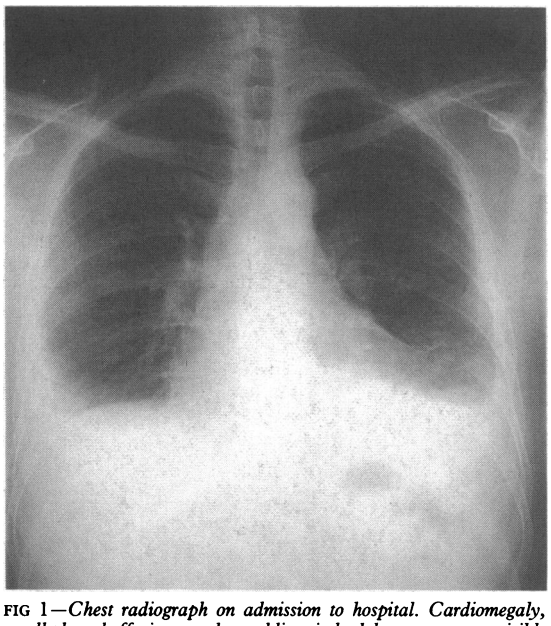

FIG 1—*Chest radiograph on admission to hospital. Cardiomegaly, small pleural effusions, and septal lines in both lower zones are visible*

FIG 2—*Venous digital subtraction angiogram of left arm showing occlusion of subclavian and axillary veins with filling of innominate veins through collaterals*

of this condition have varied. At routine postmortem examination myocarditis has been reported in up to 10% of myocardial specimens.[2] Numerous agents can produce myocardial inflammation, including viruses; protozoa and metazoa; rickettsias; chlamydias; and mycoplasmas, mycobacteria, and other bacteria. Non-infective agents include drugs (doxorubicin, cocaine) and chemicals (lead, carbon monoxide).[3,4] Enteroviruses are the most commonly implicated pathogens, and most cases in which viral infection is confirmed serologically or by isolation of the virus have been shown to be due to coxsackie B virus infection.[5]

Direct virally mediated myofibril damage has been proposed as a possible mechanism for myocardial dysfunction. However, as damage can continue after apparent clearance of the virus from the myocardium others have proposed an autoimmune process.

Clinical features are non-specific and include fever, fatigue, dyspnoea, palpitation, myalgia, and precordial discomfort. The physical signs are of moderate to severe congestive heart failure together with disturbances in cardiac rhythm. A pericardial rub may be present. Electrocardiography shows conduction defects and repolarisation changes, although repolarisation may be obscured if there is associated pericarditis.[3]

The diagnosis is usually based on objective evidence of myocardial dysfunction without any other obvious cause and with evidence of recent viral infection. The virus is rarely isolated from the stools or throat, and a rise in antiviral antibody titres is most commonly cited as supportive evidence. However, this has to be set against the high prevalence of antibodies for enteroviruses in the asymptomatic population. Raised IgM titres are thought to correlate with recent infection, possibly persisting for six to eight weeks after onset of symptoms.[6]

Endomyocardial biopsy is regarded as the most reliable method of diagnosis, but the correlation between clinical myocarditis and changes in myocardial tissue on biopsy is poor. Biopsy confirmation of the diagnosis varies from 2·5% to 67% of cases.[7-13] This variation may be due to sampling errors, with biopsies being taken from unaffected areas of myocardium, or to biopsies having been performed during the healing phase of the condition. The interval between the onset of symptoms and time of biopsy ranged between two weeks and 12 months.[7-13] Interobserver differences in the interpretation of biopsy specimens may also account for some of the variation.[14] The polymerase chain reaction has been used to amplify and identify

virus specific nucleotide sequences in biopsy specimens from patients with idiopathic dilated cardiomyopathy.[15]

Discussion

CMO: Despite the large number of patients seen with dilated cardiomyopathy acute viral myocarditis is very difficult to prove. The Dallas criteria have gone some way towards improving diagnosis. An American trial of the effects of immunosuppression in treating myocarditis is still recruiting after three years because of the difficulty in obtaining patients who fulfil all clinical and histopathological criteria. I do not believe that most cases of dilated cardiomyopathy follow viral infection. The Finnish 20 year follow up study of epidemic myopericarditis found no cases of dilated cardiomyopathy.[16] Our own preliminary efforts to detect viral residues in biopsy specimens using virus specific DNA probes have been disappointing.

CTD: This patient was a young man with severe heart failure, yet biopsy showed no evidence of cellular infiltrate. What could have caused that degree of impairment of ventricular function?

CMO: Sampling error is always cited as a reason for negative biopsy results, and we know myocarditic changes are fairly focal.

CTD: The biopsy was taken from the right ventricle, which on echocardiography was the more severely affected chamber.

CMO: That is usually so in experimental and clinical myocarditis. Of course, we did not perform the biopsy until much clinical improvement had occurred. I expect him to have a good long term prognosis with every chance of a full recovery.

CTD: Do we know the C reactive protein concentration at the time of the biopsy?

ADH: It was about 150 mg/l.

CTD: So it was still greatly raised.

CMO: The patient presented an acute picture with impairment of ventricular function and an undilated heart—this is all highly suggestive of acute viral myocarditis.

CTD: Dr Cohen, do you think this patient had acute coxsackie B virus and do you think this was related to his heart failure?

JC: The association between dilated cardiomyopathy and viral infection is difficult to establish. In this patient it does seem likely that acute heart failure was related to infection. There is, however, as much evidence for mycoplasma infection as coxsackie B virus infection. *Mycoplasma pneumoniae* is a well documented but less common cause of a myocarditis type picture. The absence of biopsy evidence of inflammation despite ventricular impairment may be consistent with the presence of circulating myocardial depressant substances akin to those found in shock states.

CTD: Which cells produce these substances?

JC: They are thought to be substances produced by macrophages.

CTD: Was the biopsy specimen tested by the polymerase chain reaction for mycoplasma or coxsackie B virus?

ADH: We did not look for mycoplasma, but studies looking for enteroviral nucleotide sequences are underway.

CTD: Does the finding of subclavian vein thrombosis suggest another cause?

CMO: We agonised over this. Occasionally jugular or innominate vein thrombosis is seen in severe heart failure, usually in elderly people. We searched hard for another cause but in this case, we could not find one.

CTD: In summary, a previously fit 30 year old man presented with a short history suggestive of progressive heart failure after an antecedent 'flu-like illness. Myocarditis was diagnosed clinically and it seems likely that this was caused by a viral infection, probably with cocksackie B virus. However, myocardial biopsy four weeks after presentation was not diagnostic.

We thank Dr J S Haldane, department of histology, for expert advice.

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Correction

The irritable bowel syndrome

An author's error occurred in this article in the ABC of Colorectal Diseases by K J Moriarty (2 May, pp 1166-9). The fourth paragraph of the section on management, subtitled "Drug therapy," states incorrectly that mebeverine is an anticholinergic drug.