Disproportionate elevation of jugular venous pressure in pleural effusion

Constrictive pericarditis is characterized by elevation in jugular venous pressure disproportionate to the severity of concurrent breathlessness. As pleural effusion may be an associated feature it is recommended that jugular venous pressure should be documented in all patients who present with pleural effusion.

Since the publication, 22 years ago, of a series of 30 cases characterized by a diagnosis of constrictive pericarditis having been missed in patients presenting with pleural effusion (Tomaselli et al, 1989), missed diagnosis of constrictive pericarditis has been a recurring theme in patients presenting with pleural effusion of unknown cause (Sadikot et al, 2000; Yamamoto et al, 2002; Crandall and Mulvagh, 2010; Farkas et al, 2011).

In the NHS, one of the most striking examples of missed diagnosis of constrictive pericarditis was the report, compiled over a period of 5 years in a single health region, of 25 patients (including 24 with pleural effusion) in whom raised jugular venous pressure was an associated feature which, in some cases, had been missed on initial examination (Marshall et al, 2006). Accordingly, this review heightens awareness of constrictive pericarditis when patients with pleural effusion present with elevation in jugular venous pressure which seems disproportionate to the severity of breathlessness.

Pleural effusion is characterized by an extensive differential diagnosis (Rahman and Munavvar, 2009; Hooper et al, 2010) requiring, in its own right, rigorous investigation of underlying causes. Over and above this, clinical teaching should also recognize that the association of pleural effusion and an elevation in jugular venous pressure which seems disproportionate to symptoms and signs of pulmonary congestion should raise the index of suspicion for constrictive pericarditis as the underlying cause.

Haemodynamic factors

This discrepancy between systemic congestion, exemplified by elevation in jugular venous pressure, and pulmonary congestion, exemplified by effort dyspnoea, is believed to be attributable to the fact that pulmonary congestion resulting from constrictive pericarditis-related left ventricular diastolic dysfunction (with consequent reduction in cardiac output) is ameliorated by concurrent reduction in output from the right ventricle (Sawyer et al, 1952).

According to Paul Wood (1961), concurrent reduction in output from the right ventricle is a consequence of the right ventricle being 'hampered' as much as the left in constrictive pericarditis. In his study, a manifestation of impairment of right ventricular function was the observation that, in constrictive pericarditis, pulmonary artery systolic pressure was not as high as in a comparable group of patients with restrictive cardiomyopathy. Pulmonary artery systolic pressure exceeded 40 mmHg in only 5% of 21 patients with constrictive pericarditis, whereas it exceeded 40 mmHg in as many as eight of ten patients with restrictive cardiomyopathy, all of whom had a clinical presentation simulating constrictive pericarditis (Wood, 1961).

However, where pericardial constriction predominantly involves the 'left heart chambers' a different picture emerges, as reported by White and colleagues (1948). In this patient, pulmonary artery systolic pressure reached 72 mmHg, with the consequence that the patient experienced shortness of breath 'even when … lying in a semi-erect position in bed' (White et al, 1948).

The documentation of severe breathlessness in the patient with predominant constriction of the left heart chambers (White et al, 1948) contrasts with the observation by Wood (1961) that swelling of the abdomen was the initial symptom, antedating effort dyspnoea, in 30 patients with constrictive pericarditis who presented in an already chronic state. In those patients, all of whom had raised jugular venous pressure, hepatomegaly appeared to be proportional to the height of the venous pressure.

As in Wood's study, another series of 30 patients with constrictive pericarditis observed that shortness of breath was not a prominent presenting feature, despite universal elevation of jugular venous pressure, characterized by elevation to the angle of the jaw in 17 instances (Lewis and Gotsman, 1973). Pulmonary arterial pressure was only modestly elevated, to a mean pressure of 28 mmHg, and the investigators felt that the absence of so-called 'important' pulmonary hypertension was attributable to the inability of the right ventricle to increase its output on exercise (Lewis and Gotsman, 1973). As the vascular segments which comprise the pulmonary circulation are arranged in series (Gao and Raj, 2005), when the right ventricle increases its output, it exerts its effect on pulmonary artery systolic pressure by increasing right ventricular systolic pressure. However, right ventricular

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systolic pressure seldom exceeds 52 mmHg in patients with constrictive pericarditis (Vaitkus and Kussmaul, 1991).

In addition to its dependence on output from the right ventricle, pulmonary artery systolic pressure also depends on pulmonary vascular resistance and left ventricular end-diastolic pressure (Lam et al, 2009). Pulmonary vascular resistance was elevated in as many as 82% of 39 patients with constrictive pericarditis (Dubiel and Kolasińska-Kloch, 1990a). Additionally, average values of left ventricular end-diastolic pressure were higher (21 mmHg *vs* 15.2 mmHg) in patients with pulmonary hypertension than in counterparts with normal pressure in the pulmonary circulation.

In a separate study, the same investigators noted that patients with New York Heart Association class II constrictive pericarditis had lower mean values for left ventricular end-diastolic pressure and pulmonary artery systolic pressure than their more breathless counterparts in New York Heart Association class III. Left ventricular end-diastolic pressure averaged 11.4 mmHg in patients with New York Heart Association class II – significantly lower (P=0.01) than the mean value of 19.4 mmHg in patients in class III. Correspondingly, patients in New York Heart Association class II had a mean pulmonary artery systolic pressure of 24.5 mmHg, significantly (P=0.005) lower than the mean value of 39.5 mmHg in New York Heart Association class III patients (Dubiel and Kolasińska-Kloch, 1990b).

It is conceivable that absence of 'important' pulmonary hypertension might account for breathlessness not being a prominent symptom in the patients reported by Lewis and Gotsman (1973).

Pulmonary artery wedge pressure, which reflects left atrial pressure (Connolly et al, 1954), also needs to be taken into account in the evaluation of functional status in patients with constrictive pericarditis. In the study by Lewis and Gotsman (1973), characterized by patients who were not particularly breathless, pulmonary artery wedge pressure averaged only 20 mmHg, only marginally higher than the level of 18 mmHg which predisposes to pulmonary oedema (Ware and Matthay, 2005). Even lower pulmonary artery wedge pressures were documented in two other studies, one consisting of 15 patients which found mean levels of 16 mmHg (Khullar and Lewis, 1976), and the other of 16 patients with constrictive pericarditis which had mean levels of 14 mmHg (Dayem et al, 1967). Unfortunately, neither study documented the prevalence of breathlessness in patients in whom haemodynamic studies were performed. Nevertheless, given the relationship between pulmonary wedge pressure and pulmonary oedema (Ware and Matthay, 2005) it is likely that patients with mean pulmonary wedge pressure <18 mmHg might, even in the context of constrictive pericarditis, be less liable to pulmonary oedema than those with pulmonary artery wedge pressure >18 mmHg.

Hormonal factors

Blunted secretion of atrial natriuretic peptide has been proposed as an alternative explanation for infrequent occurrence of pulmonary oedema in constrictive pericarditis (Spodick, 1992), as this peptide alters vascular permeability and increases transcapillary water shifts (Huxley et al, 1987; Curry, 2005). Compared with counterparts who have congestive heart failure attributable to left ventricular systolic failure, patients with constrictive pericarditis have significantly (P<0.0001) lower blood levels of atrial natriuretic peptide (Ferrari et al, 1996), and this has been proposed as the underlying reason for the more marked retention of sodium and water in constrictive pericarditis than in patients with myocardial disease (Anand et al, 1991).

In a study by Ferrari et al (1996) clinical, haemodynamic and hormonal parameters were compared in 12 patients with constrictive pericarditis and in 19 patients with congestive heart failure attributable to left ventricular systolic dysfunction. Despite raised jugular venous pressure, hepatomegaly and ankle oedema being documented in all patients in both groups, ascites was seen in 11 of the 12 patients with constrictive pericarditis but only five of the nine patients with left ventricular systolic failure. Furthermore, despite mean extracellular volume and mean total exchangeable sodium being 414 ml/kg and 72 nmol/kg respectively in patients with constrictive pericarditis, as opposed to 296 ml/kg and 60 nmol/kg in patients with left ventricular systolic failure, mean New York Heart Association functional class was 2.9 in patients with constrictive pericarditis and 3.5 in patients with left ventricular systolic failure. The corresponding levels of mean pulmonary wedge pressure were 23 mmHg in constrictive pericarditis and 28 mmHg in left ventricular systolic failure.

Ferrari et al (1996) also found atrial natriuretic peptide levels to be significantly (P<0.0001) lower in patients with constrictive pericarditis than in those with left ventricular systolic failure. One interpretation is that haemodynamic factors, exemplified by attenuation of the rise in mean pulmonary wedge pressure, and neuroendocrine factors, exemplified by blunting of atrial natriuretic peptide secretion, both have a role in mitigating the severity of breathlessness in constrictive pericarditis, even in the face of severe fluid retention.

In constrictive pericarditis onset of effort dyspnoea might be delayed, either as a result of impairment of right ventricular function (Sawyer et al, 1952; Wood, 1961; Lewis and Gotsman, 1973) or as a result of blunting of atrial natriuretic peptide secretion (Anand et al, 1991; Ferrari et al, 1996)(even in the face of severe fluid retention). Despite this, as many as 29% of patients with this disorder might eventually deteriorate to New York Heart Association class II, 63% to class III and 6% to class IV, with concurrent elevation in jugular venous pressure in 99% of cases (McCaughan et al, 1985).

Even though the 231 patients in that study (McCaughan et al, 1985) might have been representative of most patients with constrictive pericarditis, it is reasonable to recommend, on the basis of other observations (Wood, 1961; Lewis and Gotsman, 1973; Ferrari et al, 1996), that there should be a high index of suspicion for constrictive pericarditis in a patient with signs and symptoms of right-sided failure (including raised jugular venous pressure and fluid retention) that are disproportionate to symptoms of pulmonary or left-sided heart disease (Nishimura, 2001).

Elevated jugular venous pressure is, arguably, the most specific sign of right-sided failure, and was present in 100% of 30 patients in one series (Lewis and Gotsman, 1973), 100% of 16 cases in another series (Anand et al, 1991), and in 100% of 62 patients in yet another series (Gimlette, 1959), being so pronounced in some cases that the veins filled to the angle of the jaw even in the upright position. A similar observation was made in 25 patients with constrictive pericarditis (including 24 in whom pleural effusion was a manifestation of fluid retention) where a raised jugular venous pressure was documented in each instance but, in some cases, had been missed on initial examination (Marshall et al, 2006). Likewise, in a study of 30 patients in whom pleural effusion of unknown origin was a presenting feature of constrictive pericarditis, jugular venous distension was noted in 23 (85%) of 27 patients in whom the venous pulse was documented (Tomaselli et al, 1989).

Despite this, distinguishing between constrictive pericarditis and its close mimic, restrictive cardiomyopathy can be extremely difficult, because raised jugular venous pressure is an almost invariable feature in both disorders. In one study, raised jugular venous pressure was documented 'in all but mild cases of RCM [restrictive cardiomyopathy]' (Ammash et al, 2000). In that series of 94 patients with restrictive cardiomyopathy, the clinical similarity between constrictive pericarditis and restrictive cardiomyopathy was so close that constrictive pericarditis was clinically suspected in as many as 40 cases, necessitating additional tests such as computed tomography (in 19 cases), cardiac catheterization (in 18) and, in three cases, even thoracotomy, for its exclusion (Ammash et al, 2000).

As constrictive pericarditis is a potentially reversible disorder, jugular venous pressure should be documented in all patients with pleural effusion to increase the index of suspicion for its diagnosis, despite this not being recommended either in an authoritative module of continuing medical education (Rahman and Munavvar, 2009) or in guidelines (Hooper et al, 2010).

Pathophysiological basis of constrictive pericarditis-related pleural effusion

During their review of laboratory parameters in patients with constrictive pericarditis who had presented as pleural effusion of unknown cause, Tomaselli et al (1989) proposed that pleural effusion in their patients might be attributable to impaired venous drainage from the pleura, as a result of the association of raised left atrial pressure, pulmonary venous hypertension and capillary hypertension (Tomaselli et al, 1989). More recently it has become apparent how incomplete our understanding is of the complexity of the regulation of pulmonary venous tone and hence fluid filtration (Gao and Raj, 2005). It is also possible that an associated increase in right atrial pressure could augment the tendency to pleural fluid formation by interfering with pleural and lymphatic drainage (Tomaselli et al, 1989).

Nevertheless, even as recently as June 2011 it was acknowledged that the precise pathophysiology is unknown (Farkas et al, 2011), and that some reported cases yielded transudative effusions (Tomaselli et al, 1989; Yamamoto et al, 2002; Akhter et al, 2006; Crandall and Mulvagh, 2010), and others had exudative effusions (Tomaselli et al, 1989; Sadikot et al, 2000; Farkas et al, 2011) in patients who did not even have underlying pleural disease.

Chronic inflammatory pleural disease may have the same aetiology as constrictive pericarditis-related pericardial disease and, in that context, may give rise to the association of exudative pleural effusion and constrictive pericarditis. This is strikingly the case in tuberculosis where, according to one study, tuberculous pleurisy was a feature in as many as 12 out of 16 cases of tuberculous constrictive pericarditis (Andrews et al, 1948). In another study among 49 patients with constrictive pericarditis-related pleural effusion, there was one with typical caseating necrosis in the pleural biopsy specimen (Yang et al, 2001). Despite this, constrictive pericarditis-related pleural effusion is not necessarily attributable to tuberculous inflammation of the pleural cavity, even among patients with proven tuberculous constrictive pericarditis. Accordingly, in one study, among 16 patients with tuberculous constrictive pericarditis in whom pleural effusion was an associated feature, there were four patients in whom pleural effusion appeared to be: 'a result of mechanical factors only…with no evidence in life or after death of [pleuritic] tuberculous infection' (Andrews et al, 1948).

Conclusions

Regardless of whether a pleural effusion is an exudate or a transudate, and also notwithstanding underrecognition of constrictive pericarditis as an underlying cause in the differential diagnosis of pleural exudates (Hooper et al, 2010), jugular venous pressure should be routinely recorded in all patients being investigated for the underlying cause of pleural effusion. Furthermore, as shown by the example of a patient with coexisting constrictive pericarditis and pleural effusion in whom a pleural biopsy specimen was characterized by 'typical caseating necrosis' (Yang et al, 2001), the same rule should apply regardless of whether or not tuberculosis has been validated as the underlying cause of pleural effusion. In

other words, even when a tuberculous aetiology has been established for pleural effusion, the jugular venous pressure should be documented to mitigate the risk of overlooking the co-existence of tuberculous constrictive pericarditis, the latter requiring a different and specific management strategy.

Evaluation of jugular venous pressure should preferably be made with the patient sitting up, as: 'a deep venous column visibly distended above the right clavicle in the sitting position has a sensitivity of 65% and a specificity of 85% to identify truly elevated venous pressure' (Sinisalo et al, 2007), and also because the peak level of the jugular venous pressure may sometimes be evident only when the patient is sitting up (Gimlette, 1959; Lewis and Gotsman, 1973; Anand et al, 1991).

Both constrictive pericarditis and restrictive cardiomyopathy are much less prevalent than cardiac failure attributable to other aetiologies. It is good practice to document jugular venous pressure in all cases of pleural effusion, to heighten the index of suspicion both for congestive cardiac failure of whatever aetiology and for constrictive pericarditis itself, especially as the latter is a potentially reversible disorder. **BJHM**

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KEY POINTS

- In constrictive pericarditis systemic congestion, exemplified by elevation in jugular venous pressure, is disproportionate to stigmata of pulmonary congestion such as effort dyspnoea and seems to have a typical haemodynamic and hormonal profile.
- Extreme elevation in jugular venous pressure and pleural effusion should heighten the index of suspicion for constrictive pericarditis, irrespective of whether the pleural effusion is a transudate or an exudate.
- Even when pleural effusion is the sole presenting feature, jugular venous pressure should be recorded to mitigate the risk of overlooking co-existing constrictive pericarditis, as the latter might be the cause of pleural effusion.
- This precaution should be taken even in patients with confirmed tuberculous pleural effusion, as this effusion may co-exist with tuberculous constrictive pericarditis.