The palliation of malignant pleural effusions

Malignant pleural effusions are a common complication of many cancers, usually representing metastatic disease. Over 50% of cases are the result of primary lung or pleural malignancy (Janssen et al, 2007), but they may also be caused by other malignancies including lymphoma, breast or ovarian carcinoma. An effusion can be the result of direct tumour involvement, or result from indirect effects such as lymphatic obstruction, sometimes referred to as a paramalignant effusion.

The majority of patients will be symptomatic at presentation, with breathlessness the most common symptom. Mechanisms of dyspnoea are diverse and include reduction in chest wall or pleural compliance, diaphragmatic impairment, and lung volume reduction. Patients may present with chest pain as a result of local tumour invasion, or more generalized symptoms such as weight loss and malaise (Roberts et al, 2010).

General palliative care

There is a high degree of overlap between treatment and diagnosis of malignant pleural effusions – diagnosis and therapy can often be achieved with a single procedure.

In conjunction with pleural procedures, the other symptoms associated with effusions should also be addressed, especially if pleural intervention is delayed or unsafe. Nasal oxygen to improve hypoxaemia or air blown onto the face can improve the sensation of dyspnoea. Low dose opiates can be effective at managing breathlessness and pain, although benzodiazepines can have similar effects and may also reduce any agitation (Navigante et al, 2010). One must also remember to address the fears and expectations of patients and families as anxiety will heighten symptoms.

Acute management of pleural effusions

If invasive treatment is appropriate then immediate management of dyspnoea should be guided by the level of distress. Acutely, large volume effusions causing compromise should be managed with thoracocentesis or intercostal drain insertion. However, the physiology of dyspnoea is complex and often multifactorial. Interplay exists between the stimulation of peripheral and central chemoreceptors, mechanoreceptors to flow, volume, pressure and temperature, as well as vagally-mediated 'rapid' and 'slow' receptors in the lung. The sensation of dyspnoea can also relate to the rapidity of onset of fluid, or the 'sense of effort' a patient may feel in relation to his/her ability to deal with a particular muscular load, sometimes referred to as neuromechanical dissociation (Schwartzstein, 2011).

This means that in those with even large effusions, removing as little as 200 ml can relieve symptoms immediately. In practice, a larger volume is removed to maintain the symptom-free period and allow discharge home. Such patients can then be referred to the respiratory outpatient clinics for planning of further more permanent treatments. Patients with symptomatic malignant pleural effusions should not therefore be treated with intercostal drainage and admission unless the diagnosis is known and definitive management is planned during this admission, or unless pleural infection is suspected.

Pleural specific interventions

The treatment of 'sub-acute' malignant pleural effusions can be approached in one of two ways. The first is instillation of sclerosant into the pleural space in an attempt to encourage pleural inflammation and adhesion, and thus the obliteration of the pleural space. This can be achieved with a bedside chest drain and 'slurry', or via medical thoracoscopy or video-assisted thoracoscopic surgery, which has the added benefit of simultaneous diagnostic capability. The second method is insertion of an indwelling pleural catheter – a 'long-term' tunnelled chest drain – and subsequent patient-driven drainage over time.

Talc and indwelling pleural catheters

Talc has been the pleural sclerosing agent of choice for many years. Talc slurry instillation has a typical success rate of around 75% (Stefani et al, 2006), although this figure can be difficult to replicate in real world practice because of variations in practice between centres and between individual clinicians. It has traditionally been used in those with an existing chest drain but can alternatively be sprayed thoracoscopically under direct vision (poudrage). Insertion of talc via a drain can be burdensome to patients: pain can be significant despite analgesia and the typical requirement is for a 5–7-day inpatient stay, at least 24 hours of which is spent with pleural suction in place.

More recently, indwelling pleural catheters have become more widely available and can be safely inserted as a day-case procedure. Once at home, fluid is drained off as it re-accumulates by carers or patients. Indwelling drains have been proven to improve quality of life indices and patients' symptoms, and can be cheaper for health-care providers if used for less than 6 weeks, despite the need for proprietary drainage kits (Olden and Holloway, 2010). Additionally, pleurodesis can be achieved in up to 73% of patients, although this is significantly lower with primary pleural or lung malignancies (Warren et al, 2008). Indwelling catheters can usually be removed within 2 months of insertion once there is no further evidence of fluid accumulation. However, their use is heavily dependent upon the skills of local clinicians and the availability of community services.

Despite significant advantages, indwelling drains can also cause significant pain, and occasionally pleural infection; one series described empyema formation in just over 3% of cases. In addition, despite proficient personnel, the failure rate for insertion was still 4% (Tremblay and Michaud, 2006). The use of indwelling

drains must also be weighed against the possibility of malignant seeding along the insertion tract, a problem which is much less likely with a simple drain.

The question of which method of drainage is better overall remains unanswered, in no small part because of the variety of situations which may arise when managing malignant pleural effusions. If there is evidence of a trapped lung (i.e. inability of the lung to re-expand) then indwelling pleural catheters are considered more appropriate. If there has been a failed talc pleurodesis but no trapped lung then there is little evidence to guide the next step in management – patients could be offered an indwelling pleural catheter but must be made aware of the potential complications as well as the benefits. The more common situation, however, is that of the patient who has an effusion but no drain as yet – would an indwelling pleural catheter be a more appropriate first-line intervention? The answer will hopefully be clarified by the TIME 2 trial (ISRCTN87514420), which looks to address this question directly and is due to report in early 2012.

Conclusions and future directions

The palliation of malignant pleural effusions should always begin with simple measures, especially in those in whom invasive pleural procedures are not warranted. Significant acute breathlessness should be managed with intercostal drainage, but most patients will present more insidiously or even incidentally. Malignant pleural effusions characteristically recur and so early definitive treatment with pleurodesis is preferable. This has traditionally been attempted by talc slurry instillation but indwelling pleural catheters may provide a viable alternative. While both of these methods can be effective, alternative agents for pleurodesis are always being sought. Bacterial proteins, pro-fibrotic compounds such as transforming growth factor-β, and anti-angiogenic molecules are among the alternatives being researched currently.

Studies in this area may lead to a cultural shift in the future management of malignant pleural effusions, but for the time being any physician faced with such patients should remember that symptomatic control for the individual is the highest priority, regardless of the method used. **BJHM**

KEY POINTS

- Malignant pleural effusions are a common complication of many cancers, and are usually indicative of metastatic disease and poorer prognosis.
- Diagnosis and therapy of malignant pleural effusions can often be achieved with a single procedure, such as simple aspiration or thoracoscopy.
- Removal of only a few hundred millilitres of fluid can result in substantial symptomatic benefit, and does not always need to involve a chest drain.
- The most effective method for pleurodesis remains talc instillation via a chest drain, but indwelling pleural catheters are often a viable outpatient alternative.
- When faced with a pleural effusion, addressing patients' symptoms quickly and effectively should remain the highest priority.

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