Clinical Results of Cytoreduction and HIPEC for Malignant Peritoneal Mesothelioma

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Introduction

Malignant Peritoneal Mesothelioma (MPM) is rare primary neoplasm that arises from the serosal membranes of the abdominal cavity. The Surveillance, Epidemiology, and End Results (SEER) program from the U.S. National Cancer Institute maintains data from 11 cancer registries representing approximately 27% of the U.S. population; analysis of this database indicate that about 400 new cases of MPM arise annually in the U.S. [1]. This represents about 17 and 7 percent of all mesothelioma cases diagnosed in females and males, respectively.

Histologically, MPM are generally characterized as low-grade which includes adenomatoid and tubulopapillary tumours and high-grade which includes epithelioid, sarcomatoid, or biphasic tumours; biphasic mesothelioma is defined as a tumour that has both epithelial and sarcomatoid components. High-grade tumours make up between 62% - 76% of all MPM [2,3]. Nonaka and colleagues have evaluated histopathological features of MPM from patients undergoing cytoreduction and heated intraoperative intraperitoneal chemotherapy (HIPEC) and found that most tumours express calretinin and EGFR [4]. In an initial series they reported that patients with tumours that had a high nuclear grade or those with $\geq 5$ mitoses per 50 high powered field (HPF) had a significantly shorter survival than patients without those tumour features; however, nuclear grade was not a significant prognostic factor in a follow-up analysis of a larger cohort [5].

Grossly, tumours are diffusely disseminated throughout the peritoneal cavity and depending on the extent of progression can range from a few millimeters to large nodular masses which, in the late stages, will coalesce to form large nodular masses that can replace the greater and less omentum and encase viscera (Fig. 1). Ascites is a common consequence of MPM. The disease remains confined to the abdominal cavity until very late stages in the course when it can spread, usually by direct extension, through the diaphragm into the thorax; hematogenous metastases generally are rare.
MPM presents with non-specific signs and symptoms; patients present with complaints related to ascites or large tumour burden. Occasionally, patients are diagnosed incidentally. The median age of presentation is between 40 and 65 [6]. Unfortunately, due to the indolent progression of nonspecific symptoms, many patients present with advanced disease. Abdominal distension is the most frequent initial symptom and is associated with early satiety, loss of lean body mass and overall inanition. Increased abdominal girth is the presenting symptom in 56-82% of patients [7,8]. Pain is the second most common symptom, found in 27-58% of presenting patients [7-10]. Up to a third of patients present with a palpable abdominal mass [9,11].

The vast majority of patients die from complications of intraperitoneal tumour progression and based on this consistent natural history and the lack of effective systemic therapies, regional therapies designed to control disease progression with the peritoneal cavity have been actively developed over the past 20 years [12]. Reports of patients with MPM treated primarily with chemotherapy or biological agents have resulted in median survivals of less than one year [13,14]. Antman and colleagues were the first to note over 20 years ago that surgical resection (or cytoreduction) combined with intraperitoneal chemotherapy was associated with prolonged survival in some patients with MPM [15]. A number of medical centers throughout the world are now reporting long-term overall survival and median survival between 30 and 90 months for patients with MPM following cytoreduction and HIPEC; this approach has now emerged as the standard of care for selected patients with MPM (Table 1).