REVIEW

Biology of Colorectal Liver Metastases: A Review

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Metastatic growth is a selective, non-random process, which in the case of colorectal cancer, frequently occurs in the liver and is the major cause of cancer related death in these patients. This review summarises attempts to find biological and molecular markers of metastasis and their role in establishment of secondary tumours. Recent evidence suggests that liver metastases are phenotypically different to the primary from which they were derived and thus represent a separate disease entity.


KEY WORDS: colorectal cancer; liver metastasis; molecular markers

INTRODUCTION

Colorectal cancer is the second most common cancer in the United Kingdom, with a steady reported annual incidence rate of around 57 per 100,000 population [1–4]. Prevalence is greater in males (approx. 60% of cases) and these tumours become more prevalent with increasing age, with almost 50% of cases occurring in those over 60 years of age [4]. Metastatic disease of the liver is a frequent event for patients with colorectal cancer and remains a major cause of cancer-related death [4]. Approximately 25% of patients have detectable liver metastases at the time of presentation (synchronous metastases) and a further 25% of patients will develop metastases during the course of their disease (metachronous metastases), usually within a 2-year period following initial surgical treatment of their primary tumour [5]. Overall survival is closely related to tumour burden. Patients with single or multiple metastases restricted to one lobe of the liver (unilobar disease) have an expected median survival of less than 24 months [6]. Patients with bilobar disease have even poorer outcomes, with median survival of less than 18 months [7]. If left untreated, the majority of patients would not be expected to survive much beyond 9–12 months [8]. Thus, with improvements in surgical technique, sub-total hepatectomy has become the treatment of choice with 5 year survival figures in the order of 35%–40% [9]. Concerns over the possible effects of the subsequent regenerative process on remaining occult tumour are unresolved [10].

Whilst most patients die from metastatic disease, the majority of the literature is concerned with the biology of primary colorectal cancer. Paradoxically, the biological properties of metastases can be quite different from those of the primary tumour; these may be defined partly by host-tumour interactions and partly by the genetic and phenotypic alterations that allowed detachment and survival from the primary tumour in the first place. Once established at their secondary site, the tumour cells can undergo further phenotypic changes, depending on their location within the growing metastasis. This review attempts to summarise the current knowledge of colorectal liver metastasis in terms of the molecular events responsible for the arrest, growth and subsequent proliferation of tumour cells in the liver. Much published material on liver metastasis relates to prediction of the chances of developing metastases in the liver and has focused on findings in the primary tumours of patients who subsequently developed metastases in the liver. It is important to separate these findings from those obtained by direct examination of liver metastases. This review will concentrate primarily on the latter.

METASTATIC CASCADE

Growth of metastases in distant organs is a highly selective, non-random process first described by Paget in his ‘seed and soil’ hypothesis [11]. In this, the metastatic...