特別講演

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At early or metastatic stage, pathological analysis gives important clinical informations in colorectal cancer

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Colorectal carcinomas (CRC) may be diagnosed at any stage from malignant polyp detected during a regular screening to metastatic disease. At all stages, pathological analysis of tumor gives key information notably for the prognosis but also for the therapeutic strategy. This presentation will discuss the role of pathologist at this 2 different stages.

Malignant polyps constitute a form of early carcinoma (pT1) that may often be cured by endoscopic polypectomy alone. However, the incidence of an unfavorable outcome for malignant polyps treated by polypectomy alone varies from about 10% to 20%. Different histopathological parameters are associated with a significantly increased risk of adverse outcome such as high tumor grade, angiolymphatic invasion and tumoral cells present in the diathermy effect of endoscopic resection. More recently, new criteria have been validated in Japanese studies underlining the prognosis importance of tumoral budding and measurement of depth and width of submucosal invasion. Despite the fact that such pathological criteria have a central role in the decision-making process for patients who had endoscopically resected polyps, few data on inter- and intra-observer variability in histologic diagnoses of these early colorectal endoscopical resection were available. Therefore, we undertook a multi-institutional study to assess reproducibility of 100 malignant polyps by 13 gastrointestinal pathologists using κ statistic. Agreement between pathologists was i) poor for differentiation, angiolymphatic invasion and Kudo's or Haggitt's classifications, ii) moderate with regard to T stage, budding, resection margin and quantitative measurements of depth and width of submucosal invasion. A better reproducibility was observed for specimens showing a good orientation and among pathologists working in most active interventional endoscopic centers.

More than 50% of patients with CRC will develop liver metastases. Over the last decade, combined chemotherapy regimens including irinotecan, oxaliplatin and bevacizumab have markedly improved the response rate and the survival. This response to chemotherapy has been mainly reported as a variation in the radiological size of the tumor, which evaluates mostly tumor shrinkage and little is known on the underlying histological changes. By analyzing the histopathological characteristics of 525 liver metastases, we have demonstrated that tumor regression was most common among oxaliplatin-treated patients and associated with better clinical outcome. As a side-effect, chemotherapeutic damage to the non-neoplastic liver is increasingly observed, particularly in association with oxaliplatin. We have shown that oxaliplatin may induced different vascular hepatic lesions such as sinusoidal obstruction syndrome or nodular regenerative

hyperplasia. Interestingly, these oxaliplatin-related lesions appear less frequent in patients treated with bevacizumab, suggesting that this drug has a preventive effect. Our molecular study provides new insights into mechanisms underlying chemotherapy-related hepatotoxicity in humans and potential targets relating to its diagnosis and prevention.

（文責　Benoit Terris）