Regional Therapy of Pancreatic Cancer

Hiroshi Yoshida, MD, Yasuhiro Mamada, MD, Nobuhiko Taniai, MD, Yoshiaki Mizuguchi, MD, Tetsuya Shimizu, MD, Yoshiharu Nakamura, MD, Takayuki Aimoto, MD, Eiji Uchida, MD, and Takashi Tajiri, MD

Contents

Introduction
Techniques of Regional Chemotherapy
Hyperthermia
Radiation
Gene Therapy
Results
References

Summary

Pancreatic cancer is a major cause of cancer death. Despite impressive advances in early hospital mortality and morbidity rates, overall, the chance of long-term survival is extremely low. Surgical treatment is currently the only potentially curative strategy for pancreatic cancer, but surgery alone cannot guarantee a cure. Regional therapy, such as regional chemotherapy or radiation, has been widely used in patients with advanced pancreatic cancer, with some success in controlling the cancer locally. The rationale for regional chemotherapy of pancreatic cancer is to enhance cellular drug uptake. There are various techniques of regional therapy, such as chemoembolization, arterial or portal venous infusion, hyperthermia, radiation, and gene therapy. This article reviews English reports of regional therapy for pancreatic cancer cited in the Medline database of Pubmed up to July 2005.

Key Words: Regional therapy; pancreatic cancer; celiac trunk infusion; hypoxic abdominal perfusion; radiation; hyperthermia.
1. INTRODUCTION

Pancreatic cancer is a major cause of cancer death. Despite impressive advances in early hospital mortality and morbidity rates, overall, the chance of long-term survival is extremely low. Surgical treatment is currently the only potentially curative strategy for pancreatic cancer, but surgery alone cannot guarantee a cure. Regional therapy, such as regional chemotherapy or radiation, has been widely used in patients with advanced pancreatic cancer, with some success in controlling the cancer locally. The rationale for regional chemotherapy of pancreatic cancer is to enhance cellular drug uptake. It is of key importance in chemotherapy to apply a high enough concentration of the drug to the tumor locally to overcome drug resistance, without increasing systemic toxicity at the same time. Studies suggest that intraarterial infusion (regional chemotherapy) will avoid the first-pass effect of chemotherapy and direct a higher concentration of the drug locally to the tumor cell membrane.

This article reviews English reports of regional therapy for pancreatic cancer cited in the Medline database of Pubmed up to July 2005.

2. TECHNIQUES OF REGIONAL CHEMOTHERAPY

2.1. Antitumor Agents

Chemotherapy is a therapeutic modality for the neoadjuvant or adjuvant treatment of operable pancreatic cancer or the treatment of inoperable pancreatic cancer. Various antitumor agents have been used in chemotherapy for the treatment of pancreatic cancer—examples are 5-fluorouracil (5-FU), mitomycin C (MMC), cisplatin, Adriamycin, epirubicin, mitoxantrone, folinic acid, methotrexate, paclitaxel, cytarabin, bromodeoxyuridine, melphalan, streptozotocin, and gemcitabine. Gemcitabine is the most active single agent for pancreatic cancer and is also a potent radiation sensitizer (1).

Lygidakis et al. (2) performed adjuvant regional immunotherapy, with interleukin-2, in patients with pancreatic cancer who had undergone pancreatic resection.

2.1.1. CHEMOEMBOLIZATION

Reducing or completely blocking blood flow can increase drug exposure at the tumor site, and thus drug uptake. The regional concentration of the cytostatic drug is inversely related to the regional arterial blood flow, i.e., the lower the blood flow, the higher the regional drug concentration and vice versa (3). In addition, the systemic drug concentration is decreased because of a reduced drug washout from the tumor.

Numerous trials have been performed in an attempt to achieve this, by injecting embolizing agents such as gelatin sponge particles (Gelfoam, Upjohn, Kalamazoo, MI), Lipiodol (Lipiodol Ultrafluide, Laboratoire Guerbet, Aulnay-sous-Bois, France), or degradable starch microspheres (Spherex, Pharmacia, Sweden).

Embolization with Gelfoam results in tumor necrosis and possible increased cytotoxicity of the infused antitumor agent. However, long-lasting or permanent vascular occlusion leads to unacceptable morbidity, jeopardizing repeated applications, especially when this procedure is used for the treatment of pancreatic cancer.

Therefore, a requirement of chemoembolization is that the particles of the embolizing agent should be small enough to lodge in precapillary vessels. This will allow a more homogenous distribution throughout the entire organ. It will also permit repeated appli-