Case Report

Accepted: January 22, 1996

Nephron 1996;74:611-612

Combined Chemotherapy and Radiotherapy for Esophageal Carcinoma in a Hemodialyzed Patient

Long-Term Survival

J.M.		Rebibou
B.		Chauffert
M.		Dumas
C.		Mousson
M.C.		Bone
Y.		Tanter
G.		Rifle

Service de Néphrologie-Réanimation, Service de Médecine Interne, Laboratoire de Pharmacologie, Centre Hospitalier Universitaire, and Centre Georges-François-Leclerc, Dijon, France

Key Words

Esophageal carcinoma
Maintenance hemodialysis
Chemotherapy
Radiotherapy

Abstract

The use of antimitotic chemotherapy in hemodialysis patients is not yet well codified, and each individual decision remains difficult. We report the case of a 68-year-old hemodialyzed man who developed a squamous cell carcinoma of the upper third of the esophagus. Necessarily disabling surgery was rejected, and three courses of combined radio- and chemotherapy with 5-fluorouracil and cis-platinum were performed without decreasing standard doses. The percentage of drugs removed during hemodialysis sessions was low; peak and residual platinum plasma concentrations were only slightly above those observed in normal renal function patients. The treatment was perfectly well tolerated, and tumor response was satisfactory without any relapse for 3 years. This observation suggests that hemodialysis patients could benefit from such 'full therapies', if necessary, without major adverse effects.

G. Rifle, Service de Néphrologie – Réanimation, Hôpital du Bocage, 2, Boulevard Maréchal-de-Lattre-de-Tassigny, BP 1542, F-21034 Dijon Cedex (France)

Introduction

Esophageal carcinomas have a poor prognosis, especially in debilitated patients, such as those on maintenance hemodialysis [1,2]. We report successful treatment of an esophageal carcinoma with a chemotherapy-radiotherapy combination.

Case Report

An anuric 68-year-old man on maintenance hemodialysis for 3 years for alcoholic liver cirrhosis-associated IgA nephropathy complained of dysphagia in April 1989. Endoscopy revealed an upper thoracic esophageal squamous-cell carcinoma. There was no evidence of metastatic spread. Surgery was rejected because of necessarily disabling laryngectomy, whereas the prognosis was considered poor. Despite a rather poor nutritional status (plasma albumin level 32 g/l), a combination of chemo- and radiotherapy was then

initiated. Chemotherapy consisted of 5-fluorouracil (5-FU), 800 mg/m²/day by continuous infusion from days 1 to 5, and short-lasting infusion of cisplatin, 20 mg/m²/day from days 1 to 5. Simultaneously, from days 1 to 5, 3 Gy daily fractions of megavoltage radiotherapy were delivered to the esophageal lesion. Three cycles of this combined therapy were performed on days 1, 28 and 56. During the last cycle, radiotherapy reached 30 Gy, giving a total cumulative dose of 60 Gy. During the whole treatment period, hemodialysis sessions were maintained at 3 times a week, without any technical modification; the continuous 5-FU infusions were simply stopped during the dialysis procedure. Only a transient hematologic toxicity was observed after the first cycle (minimum white blood cell count: 1,600/mm³). No other side effects occurred, in particular no clinical hyp-

acusia. Dysphagia disappeared after the first cycle, and did not reappear. Esophagoscopy was performed after the third cycle and showed a complete disappearance of the esophageal lesions. It was therefore decided to abandon the idea of radical surgery. The patient did well for the next 3 years on maintenance home hemodialysis. Biannual esophagoscopy and abdominal echography failed to detect any local or metastatic relapses. In November 1992, 3.5 years after the first carcinologic event, a mouth hemorrhage revealed a second carcinoma of the vallecula. A 70-Gy local irradiation within 7 weeks resulted in a fleeting improvement, but death occurred in July 1993.

Platinum concentrations were measured by atomic absorption spectroscopy in plasma and effluent dialysate (40 liters closed recirculating circuit with cuprophane membrane). Plasma concentrations never exceeded 3.05 µg/ml (1.56×10^{-5} M) at the end of an infusion. During the 5-day series of daily infusions, the residual platinum concentration before each infusion remained less than 1.76 µg/ml (9.02×10^{-6} M). Just before the second and third cycles, residual plasma platinum concentrations were 1.32 (6.77×10^{-6} M) and 1.03 µg/ml (5.28×10^{-6} M) respectively. The platinum extraction per dialysis session ranged from 0.4 to 1.2 mg, i.e. less than 5% of the infused doses. In a population of 25 patients with normal renal function receiving the same therapeutic regimen for various malignancies, and tested in our laboratory, the residual platinum concentration was 2.18 ± 0.38 µg/ml (1.12×10^{-5} M) before the fifth infusion of the first cycle, and reached 0.59 ± 0.12 (3.03×10^{-6} M) and 0.77 ± 0.18 µg/ml (3.95×10^{-6} M) just before the second and third cycles, respectively.

Discussion

Several reports suggest that new therapeutic protocols, such as combined chemo- and radiotherapy with or without subsequent surgery, could improve survival rates of patients with squamous-cell cancers or adenocarcinomas of the esophagus [2]. Currently, such therapeutic protocols are not used in patients with chronic renal insufficiency, or on maintenance hemodialysis, because of the theoretically increased risk of drug accumulation and toxicity, and/or of postoperative bleeding. However, radical esophagectomy is possible, when using frequent and short hemodialysis sessions with low doses of heparin [1]. Concerning chemotherapy, the clearance of 5-FU is essentially hepatic and tissular fixation is very fast, therefore neither renal failure nor dialysis modifies usual doses. On the other hand, the kinetics of cisplatin is modified in renal insufficiency. Cisplatin elimination is compatible with a double mammillary compartment, as for patients with normal renal function; only the first period of elimination depends on renal function [3]. Few studies have investigated the kinetics of cis-platinum in dialyzed patients [4]. The percentage

of drug removed seems low: 3-8% with polyacrylonitrile hemofiltration [5], 0.5-5% with cuprophane hemodialysis in our case, probably because of high protein binding [6]. Dialysability also depends on the timing of hemodialysis sessions: it is effective only within a short time after drug administration, due to the rapid and stable binding of cis-platinum to proteins in the peripheral tissues [7]. In addition, peak and residual platinum plasma concentrations observed with usual doses seem only slightly above those observed in normal renal function patients [4, 5, this case], which suggests that the total dose needs only to be slightly reduced, if at all.

Finally, the excellent tolerance of the cisplatin-5-FU association observed in the few anuric patients suggests that, from now on, dialyzed patients with malignancies of poor prognosis need not be deprived of the benefits of such full therapeutic protocols. The respective place of surgery and combined chemo- and radiotherapy requires further studies.

References

- Kitamura M, Hiraga S, Takamiya T, Lida T, Hida M, Sato T, Hara S, Hara K: Radical esophagectomy on a maintenance hemodialysis patient. *Nephron* 1990;56:103-104.
- Herskovic A, Martz K, Al-Sarraf M, Leichman L, Brindle J, Vaitkevicius V, Cooper J, Byhardt R, Davis L, Emami B: Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. *NEngl J Med* 1992;326:1593-1598.
- Giudicelli CP, Ricordel I, Josipovici JJ, Falcot J, Renaudeau G, Bassoulet J, Meunier J: Etude de la cinétique d'élimination plasmatique du cis-diamminedichloroplatine dans un cas de cystadénocarcinome ovarien compliqué d'insuffisance rénale. *Thérapie* 1981;36:653-658.
- Gorodetsky R, Vexler A, Bar-Khayim Y, Biran H: Plasma platinum elimination in a hemodialysis patient treated with cisplatin. *Ther Drug Monit* 1995;17:203-206.
- Gouyette A, Lemoine R, Adhemar JP, Klein-knecht D, Man NK, Droz JP, Macquet JP: Kinetics of cisplatin in an anuric patient undergoing hemofiltration dialysis. *Cancer Treat Rep* 1981;65:665-668.
- De Gislain C, Tanter Y, Dumas M, Chadoint-Nouveau V, Fargeot P, Mayer F, Riflé G, Guerrin J: Intérêt de la plasmaphérèse dans la prévention de la néphrotoxicité du cisdiamminedichloroplatinum. A propos d'un cas clinique. *Cancer Commun* 1988;2:337-340.
- Sauer H, Fuger K, Blumenstein M: Modulation of cytotoxicity of cytostatic drugs in hemodialysis in vitro and in vivo. *Cancer Treat Rev* 1990;17:293-300.

612

Nephron 1996;74:611-612

Rebibou/Chauffert/Dumas/Mousson/Bone/ Tanter/Riflé