Oddi sphincter fibrosis due to chemotherapy agents in small cell lung cancer: case report

Canan EREN DAĞLI[1], Ali ÇETİNKAYA[2], Mehmet Emin GELEN[1], Nurhan ATİLLA[1], Bülent KANTARÇEKEN[2], Nurhan KÖKSAL[1], Çetin TANRIKULU[1]

[1] Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı,
[2] Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Gastroenteroloji Bilim Dalı, Kahramanmaraş.

ÖZET

Küçük hücreli akciğer kanseri olgusunda kemoterapiye bağlı gelişen oddi sfinkter fibrozis

Altmış iki yaşında erkek hastaya küçük hücreli akciğer kanser tanısı koyuldu. Sisplatin (80 mg/m^2) birinci gün ve etoposid (100 mg/m^2) ikinci ve üçüncü gün olmak üzere kemoterapi protokolü (21 günde bir) başlandı. Hasta 3. kürünü aldıktan sonra, sarılık ve hiperbilirubinemi saptandı. Hepatik ultrasonografide koledok ve intrahepatik biliyer kanalda dilatasyon izlendi. Viral hepatit açısından serolojik ve biyokimyasal testler normal bulundu. Endoskopik retrograd kolanjiyopankreatografi (ERCP) yapıldı. İlk ERCP'de endoskopik sfinkterotomi yapıldı, iki gün sonra ikinci ERCP'de oddi sfinkteri fibrotik ve stenotik izlendi ve stent yerleştirildi. Stent takıldıktan bir gün sonra direkt bilirubin 6.2 mg/dL saptandı ve 10 gün sonra laboratuvar parametreleri normal izlendi. Akciğer kanserinde sisplatin ve etoposid kemoterapisi esnasında gelişen oddi sfinkter fibrozis olgusu bildirilmediği için ilginç bir olgu olarak sunulmuştur.

Anahtar Kelimeler: *Oddi sfinkteri, fibrozis, kemoterapi.*

SUMMARY

Oddi sphincter fibrosis due to chemotherapy agents in small cell lung cancer: case report

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Yazışma Adresi (Address for Correspondence):
Dr. Canan EREN DAĞLI, Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, 46050 KAHRAMANMARAŞ - TURKEY
e-mail: cananerdagli@yahoo.com

[1] Department of Chest Diseases, Faculty of Medicine, Kahramanmaras Sutcu Imam University, Kahramanmaras, Turkey,
[2] Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Kahramanmaras Sutcu Imam University, Kahramanmaras, Turkey.

A 62-year-old, man patient was diagnosed as small cell lung cancer. Cisplatin (80 mg/m^2, first day) and etoposide (100 mg/m^2, three days) chemotherapy was started for once 21 days. As the patient received third course of chemotherapy, jaundice and hyperbilirubinemia were detected. Hepatic ultrasonography showed dilated choledochus and intrahepatic biliary tract. Hepatic markers and serologic tests for viral hepatitis were found as normal. Finally endoscopic retrograde cholangiopancreatography (ERCP) was performed. Endoscopic sphincterotomy was performed in the first ERCP and two days later, second ERCP was performed and oddi sphincter was seen as fibrotic and stenotic and stent was placed. One day after the stent placement, direct bilirubin was found as 6.2 mg/dL and 10 days later laboratory parameters were detected as normal. Oddi sphincter fibrosis occurred due to lung cancer chemotherapy treatment is an interesting case for fibrosis not having been reported due to cisplatin or etoposide before.

Key Words: *Oddi sphincter, fibrosis, chemotherapy.*

Small cell lung cancer (SCLC) accounts for about 20% of all lung cancers and is a more type. Lung cancer is usually treated with a combination of modalities (i.e., surgery and chemotherapy and radiation). Without treatment, SCLC has the most aggressive clinical course of any type of pulmonary tumour, with median survival from diagnosis of only two to four months. The overall survival at five years is 5% to 10% (1,2). Combination chemotherapy produces results that are clearly superior to single-agent treatment but organ toxicities due to chemotherapy are significant side effects (3,4).

Other organ fibrosis due to cisplatin chemotherapy are reported in the literature (1-5). We present Oddi sphincter fibrosis occurred due to SCLC chemotherapy treatment, an interesting case for not having been reported due to cisplatin or etoposide before.

CASE REPORT

A 62-year-old, man patient was diagnosed as SCLC in August 2006 (Figure 1). Cisplatin (80 mg/m^2, first day) and etoposide (100 mg/m^2, three days) chemotherapy was started for once 21 days. As the patient received third course of chemotherapy, jaundice and hyperbilirubinemia (direct bilirubin level: 17.76 mg/dL, total bilirubin level: 21.52 mg/dL) were detected. Hepatic ultrasonography showed dilated choledochus and intrahepatic biliary tract. Hepatic markers and serologic tests for viral hepatitis were found as normal. Finally endoscopic retrograde cholangiopancreatography (ERCP) was performed. Endoscopic sphincterotomy was performed in the first ERCP and two days later, second ERCP was performed and Oddi sphincter was seen as fibrotic and stenotic and stent was placed (Figure 2). One day after the stent placement, direct bilirubin was found as 6.2 mg/dL and 10 days later laboratory parameters were detected as normal.

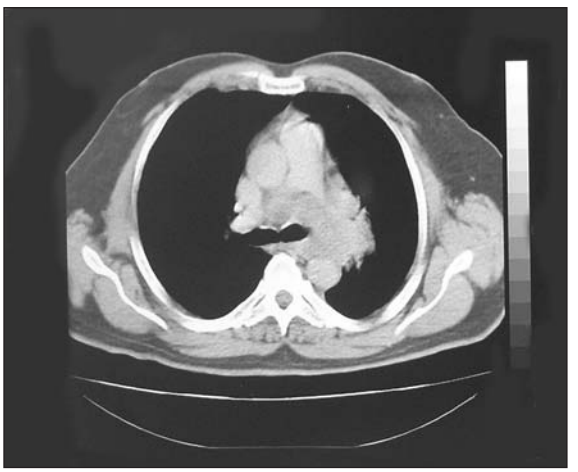

Figure 1. Pulmonary mass lesion.

We think that Oddi sphincter fibrosis occurred due to lung cancer chemotherapy treatment and it is an interesting case for fibrosis not having been reported due to cisplatin or etoposide before.

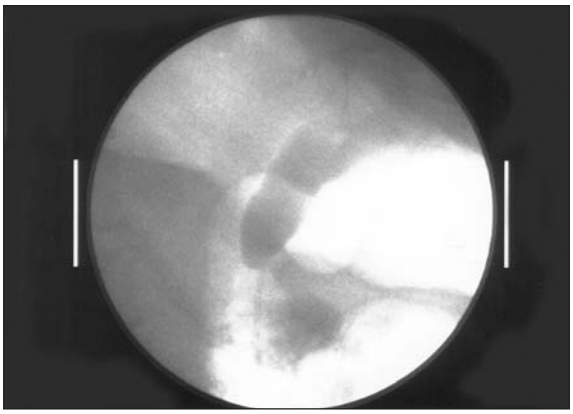

Figure 2. Stenotic and fibrotic Oddi sphincter.

DISCUSSION

Platinum-based combination chemotherapy represents the first-line treatment for patients with SCLC. The most widely used chemotherapeutic regimen is cisplatin and etoposide. Patients with limited-stage SCLC usually receive four to six cycles of platinum-based combination chemotherapy with cisplatin plus etoposide (3,4).

Cisplatin has a number of side-effects such as nephrotoxicity, neurotoxicity, nausea, vomiting, ototoxicity, alopecia, hypomagnesaemia, hypokalaemia and hypocalcaemia. Local soft tissue toxicity has been reported rarely following extravasation of cisplatin. Infiltration of solutions of cisplatin may result in tissue cellulitis, fibrosis and necrosis. Etoposide common side effects are low blood pressure, hair loss, pain, constipation or diarrhea, metallic food taste, bone marrow suppression, nausea, vomiting, allergic type reactions, rash, fever, mouth sores. Etopside may cause pulmonary fibrosis (1-4).

Our case was diagnosed as SCLC and cisplatin (80 mg/m^2, first day) and etoposide (100 mg/m^2, three days) chemotherapy was started for once 21 days. As the patient received third course of chemotherapy, jaundice and hyperbilirubinemia (direct bilirubin level: 17.76 mg/dL, total bilirubin level: 21.52 mg/dL) were detected. Hepatic markers and serologic tests for viral hepatitis were found as normal. Finally ERCP was performed. Endoscopic sphincterotomy was performed in the first ERCP and two days later, second ERCP was performed and Oddi sphincter was seen as fibrotic and stenotic and stent was placed (Figure 2). One day after the stent placement, direct bilirubin was found as 6.2 mg/dL and 10 days later laboratory parameters were detected as normal.

Other organ fibrosis due to cisplatin chemotherapy are reported in the literature. Fassia A et al. reported a non-Hodgkin lymphoma case, who after a standard chemotherapy protocol, developed retroperitoneal fibrosis in the absence of radiotherapy or other known causes (5). Turk et al. reported a case of a 51-year old man with SCLC who developed superior vena cava syndrome due to obstruction of the superior vena cava at the junction of the brachiocephalic vein by a fibrotic band, two months after completing six cycles of chemotherapy with cisplatin and etoposid (6). Progressive renal fibrosis and cisplatin-induced renal interstitial fibrosis in neonatal rats have been reported (7,8). In these studies, alpha-SMA-positive myofibroblastic cells were seen exclusively in the fibrotic lesions. Additionally, the numbers of macrophages reacting with ED1 (specific for exudate macrophages), ED2 (for resident macrophages), and OX6 (recognizing MHC class II antigens expressed in antigen-presenting macrophages/dendritic cells) were significantly increased around the affected renal tubules. A greater immunoreaction for transforming growth factor-beta1 (TGF-β1) was seen mostly in the renal epithelial cells of CDDP-treated neonates. These findings indicated that macrophage populations and myofibrolastic cells as well as TGF-β1 could be responsible for the production of renal interstitial fibrosis.

Sphincter of Oddi fibrosis has not been reported due to chemotherapy with cisplatin and etoposide. Possible mechanisms of fibrosis are reported as activated macrophages producing TGF-β1 and tumor necrosis factor-alpha, fibrogenic factors mediate induction of myofibroblastic cells (8,9). Chemotherapy may increase the local synthesis of proinflammatory cytokines and these cytokines may induce fibrotic changes. Yara et al. reported that the reduced synthesis of several fibrosis related cytokines was well correlated with the inhibition of pulmonary fibrosis (10). In our case we did not detect metastasis to

the sphincter of Oddi, just stenotic fibrotic sphincter after third course of chemotherapy with cisplatin and etoposide.

Oddi sphincter fibrosis in lung cancer due to cisplatin-etoposide combination treatment should be kept in mind.

REFERENCES

1. *Johnson BE, Grayson J, Makuch RW, et al. Ten-year survival of patients with small-cell lung cancer treated with combination chemotherapy with or without irradiation. J Clin Oncol 1990; 8: 396-401.*
2. *Lassen U, Osterlind K, Hansen M, et al. Long-term survival in small-cell lung cancer: Posttreatment characteristics in patients surviving 5 to 18+ years-an analysis of 1,714 consecutive patients. J Clin Oncol 1995; 13: 1215-20.*
3. *Takada M, Fukuoka M, Kawahara M, et al. Phase III study of concurrent versus sequential thoracic radiotherapy in combination with cisplatin and etoposide for limited-stage small-cell lung cancer: Results of the Japan Clinical Oncology Group Study 9104. J Clin Oncol 2002; 20: 3054-60.*
4. *Johnson BE, Bridges JD, Sobczeck M, et al. Patients with limited-stage small-cell lung cancer treated with concurrent twice-daily chest radiotherapy and etoposide/cisplatin followed by cyclophosphamide, doxorubicin, and vincristine. J Clin Oncol 1996; 14: 806-13.*
5. *Fassina A, Boscolo Berto R, El Mazloum R, et al. Retroperitoneal fibrosis after chemotherapy. Eur Urol 2007; 51: 270-1.*
6. *Turk HM, Camci C, Buyukberber S, et al. Superior vena cava syndrome caused by chemotherapy-induced fibrosis. J Chemother 2002; 14: 417-9.*
7. *Yang T, Vesey DA, Johnson DW, et al. Apoptosis of tubulointerstitial chronic inflammatory cells in progressive renal fibrosis after cancer therapies. Transl Res 2007; 150: 40-50.*
8. *Yamate J, Machida Y, Ide M, et al. Cisplatin-induced renal interstitial fibrosis in neonatal rats, developing as solitary nephron unit lesions. Toxicol Pathol 2005; 33: 207-17.*
9. *Yamate J, Machida Y, Ide M, et al. Effects of lipopolysaccharide on the appearance of macrophage populations and fibrogenesis in cisplatin-induced rat renal injury. Exp Toxicol Pathol 2004; 56: 13-24.*
10. *Yara S, Kawakami K, Kudeken N, et al. FTS reduces bleomycin-induced cytokine and chemokine production and inhibits pulmonary fibrosis in mice. Clin Exp Immunol 2001; 124: 77-85.*