



Primary aortoduodenal fistula in testicular cancer: A fatal complication associated with retroperitoneal lymph node metastasis

Hiromichi Sakurai^a, Koji Kawai^a, Mizuki Onozawa^a, Masaaki Akahane^b, Reo Takizawa^c, Jun Miyazaki^{a,*}

^a Department of Urology, International University of Health and Welfare Narita Hospital, Narita, Japan

^b Department of Radiology, International University of Health and Welfare Narita Hospital, Narita, Japan

^c Department of Vascular Surgery, International University of Health and Welfare Narita Hospital, Narita, Japan

ARTICLE INFO

Keywords:

Testicular cancer
Aortoduodenal fistula
Retroperitoneal lymph node metastasis

ABSTRACT

A primary aortoduodenal fistula (PADF) has rarely been reported as a complication of testicular cancer. A 48-year-old Japanese male with relapsed retroperitoneal lymph node metastases received four courses of paclitaxel, ifosfamide, and cisplatin (TIP). On day 19 of the fourth cycle of TIP, he developed hematochezia and hypovolemic shock. Angiography confirmed the presence of a PADF, and we then deployed an endovascular stent graft in the aorta. Although the bleeding improved, the patient died of re-bleeding that developed 18 days later. It is important to recognize this severe complication in order to achieve its early diagnosis and optimal surgical intervention.

Introduction

A primary aortoenteric fistula is a rare and potentially fatal clinical disorder caused by the spontaneous erosion of the aorta into the gastrointestinal tract. Over half of the fistulas occurred between the aorta and the duodenum (usually its third portion), followed by cases between the aorta and the esophagus.¹ Although duodenal involvement by retroperitoneal lymph node (RPLN) metastasis is frequently seen in testicular cancer, primary aortoduodenal fistula (PADF) is extremely rare. We describe PADF affecting a patient after chemotherapy for relapsed RPLN metastasis.

Case presentation

A 48-year-old Japanese male with testicular cancer was referred to our hospital. At the previous hospital, he received the diagnosis of right testicular seminoma with pT4. Computed tomography (CT) revealed multiple liver metastases and showed that bulky RPLN metastasis invaded the third portion of the duodenum (Fig. 1A). Laboratory tests showed a human chorionic gonadotropin (hCG) level of 24 IU/L, LDH at 1060 IU/L, and normal alpha-fetoprotein. Four cycles of bleomycin, etoposide, and cisplatin (BEP) had been administered at the previous hospital. In the BEP regimen, the cisplatin dose was reduced to 90%, and the

start of the fourth cycle of BEP was delayed by 1 week.

After the completion of the BEP regimen, the patient's hCG and LDH values were normalized, and contrast-enhanced CT (Fig. 1B) and positron emission tomography (PET)-CT at 1 month after the completion of the BEP revealed the disappearance of liver metastases; however, a 4-cm RPLN mass remained with positive 18-fluorodeoxyglucose (18F-FDG) uptake. Six weeks later, the patient was referred to our hospital for further management.

Because the tumor markers were in the normal range at the time of referral, we considered that retroperitoneal lymph node dissection (RPLND) was reasonable treatment option. But, repeat PET-CT performed at our hospital showed increasing 18F-FDG uptake in RPLN metastases (Fig. 1C), and new uptake was observed in the right iliac lymph node metastases. Since those findings indicated disease progression, we decided to perform salvage chemotherapy with paclitaxel, ifosfamide, and cisplatin (TIP) rather than RPLND. No severe adverse effects were observed during the TIP treatment, but CT after two courses of TIP demonstrated that the RPLN metastasis did not respond to chemotherapy.

The adverse effect of two additional courses of TIP was also acceptable, but the patient developed sudden-onset hematochezia and hypovolemic shock on day 19 of the fourth cycle of TIP. Blood tests showed hemoglobin 4.7 g/dL, neutrophil count $4.8 \times 10^9/L$, and

* Corresponding author. Department of Urology, International University of Health and Welfare Narita Hospital, 852 Hatakeda Narita, Chiba, 286-0124, Japan.
E-mail address: jmiyazaki@iuhw.ac.jp (J. Miyazaki).

<https://doi.org/10.1016/j.eucr.2021.101746>

Received 23 May 2021; Received in revised form 5 June 2021; Accepted 6 June 2021

Available online 8 June 2021

2214-4420/© 2021 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

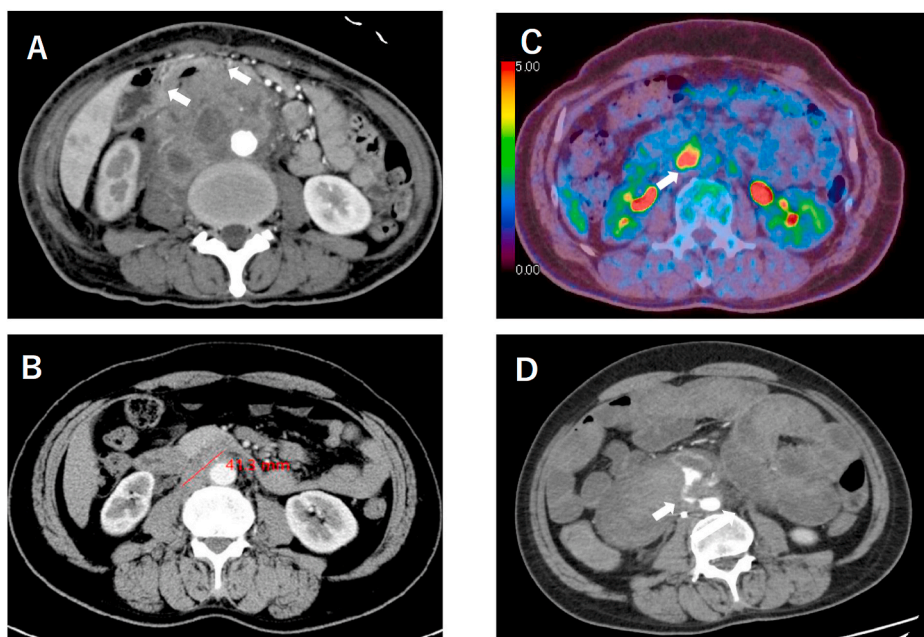


Fig. 1. CT/PET-CT images at different time points over the patient's course. **A:** Pretreatment CT showing bulky retroperitoneal lymph node (RPLN) metastasis invading the third portion of the duodenum (arrow). **B:** CT at 1 month after the completion of the BEP revealed the residual RPLN mass. **C:** PET-CT before the start of the salvage chemotherapy, showing strong 18F-FDG uptake (arrow) in the RPLN metastases. **D:** CT showing a dilated bowel loop fulfilled with a massive clot and direct extravasation of contrast from the aorta into the third portion of the duodenum (arrow).

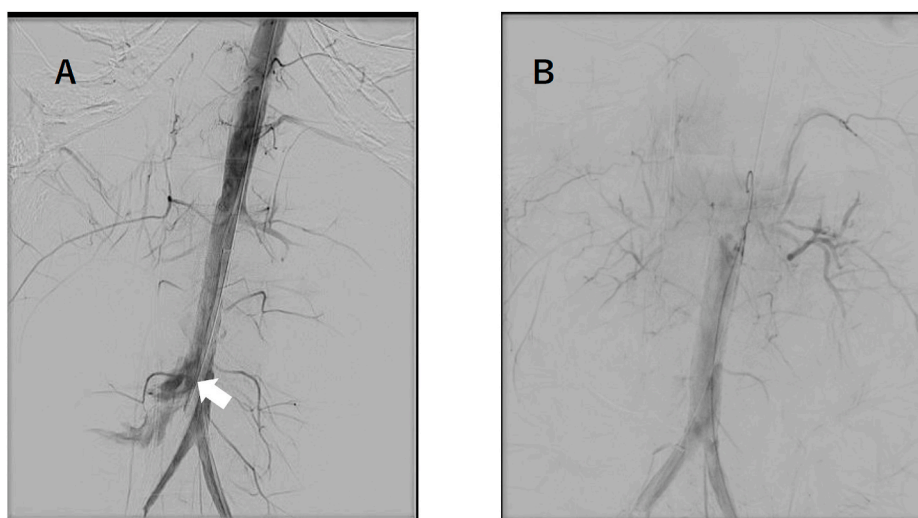


Fig. 2. Abdominal angiogram. **A:** Emergent angiography confirming the presence of a PADF (arrow). **B:** Control angiography showing minimal residual hemorrhage after the placement of an endovascular stent graft.

platelet count $4.9 \times 10^9/L$. CT depicted a dilated bowel loop fulfilled with a massive clot and a direct extravasation of contrast from the aorta into the third portion of the duodenum (Fig. 1D). The RPLN mass remained without a decrease in size. Endoscopic therapy was considered to be impossible because of the massive bowel clot. Since a patient was hemodynamically unstable, a decision was made to attempt angioembolization rather than surgical repair. Emergent angiography confirmed the presence of a PADF (Fig. 2A), and we then deployed an endovascular stent graft in the aorta. Control angiography showed minimal residual hemorrhage (Fig. 2B). Extensive fluid infusion and blood transfusion were needed to maintain the patient's blood pressure.

Despite intensive care, the patient developed sepsis, disseminated intravascular coagulation (DIC), and multiple organ failure (MOF). Definitive surgical repair awaited the patient's recovery from MOF and DIC, but massive bleeding recurred 18 days after the first hemorrhage, and the patient died. Both septic shock due to graft infection and uncontrolled bleeding were considered to be cause of death. Permission for

autopsy was refused.

Discussion

Over 80% of primary aortoenteric fistulas are associated with an aneurysmal aorta which is followed by a foreign body, tuberculosis infection, and tumor. Saers and Scheltinga identified eight cases (10%) of cancer-associated primary aortoenteric fistulas among 81 reported cases.¹ RPLN is the most common metastatic site of testicular cancer, and even though RPLN metastases with duodenum involvement are frequently seen, PADF is extremely rare as a complication of testicular cancer. To our knowledge, only four such cases of PADF are reported in the literature.²⁻⁵ Two of those four patients had undergone RPLN dissection and radiation 13 years and 20 years before the development of the PADF.^{2,3} One of the patients suffered from a PADF 4 weeks after receiving BEP for RPLN metastases, and an autopsy confirmed a PADF secondary to extensive metastatic choriocarcinoma.⁵ A PADF is thus not

necessary directly caused by chemotherapy. In our patient's case, although an autopsy was not performed, the lack of a response to chemotherapy suggested residual cancer cells in his RPLN metastases. The reduced intensity of the initial BEP might have been responsible for the patient's refractory disease.

The classic triad of PADF is upper gastrointestinal hemorrhage, abdominal pain, and a pulsating abdominal mass, but this triad was present in only 11% of the reported cases.¹ The most frequently used diagnostic modalities were endoscopy and CT followed by angiography. However, the endoscopic diagnosis of the lower third of the duodenum is complicated, especially when the presence of a massive clot is involved as in the present case. In contrast, CT is less invasive and easier to perform. The confirmation of a PADF is based on the extravasation of contrast agent into the bowel, but this is observed in only approx. 25% of the cases. The presence of air within the aortic wall, focal bowel wall thickening, and the disruption of the aortic fat cover are CT findings suggesting a PADF.¹

PADF has been recognized as a highly fatal entity, but the proportion of patients who undergo surgery has increased over time, and the overall mortality rate has diminished. Investigations of cases reported between 1994 and 2003 showed that 84% of 81 patients with a PADF underwent surgery, and the mortality rate was 34%.¹ It is important to recognize this severe disease in order to achieve an early diagnosis and provide the optimal surgical intervention.

Conclusions

PADF is a rare but severe complication that can occur in testicular

cancer with RPLN metastases. Bleeding can be fatal, an early diagnosis and prompt treatment are mandatory.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors have no conflict of interest to disclose.

Acknowledgements

We thank our colleagues for their support. This work was supported by JSPS KAKENHI Grant Number JP19K09705 and JP21K09410.

References

1. Saers SJ, Scheltinga MR. Primary aortoenteric fistula. *Br J Surg.* 2005;92:143–152.
2. Kalman DR, Barnard GF, Massimi GJ, Swanson RS. Primary aortoduodenal fistula after radiotherapy. *Am J Gastroenterol.* 1995;90:1148–1150.
3. Jayarajan S, Napolitano LM, Rectenwald JE, Upchurch Jr GR. Primary aortoenteric fistula and endovascular repair. *Vasc Endovasc Surg.* 2009;43:592–596.
4. Nord C, Fosså SD, Giercksky KE. Gastrointestinal presentation of germ cell malignancy. *Eur Urol.* 2000;38:721–724.
5. Hansen KS, Sheley RC. Aortoenteric fistula in advanced germ cell tumor: a rare lethal complication. *J Urol.* 2002;167:2131.