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Late relapsing testicular cancer detected with 18F-FDG PET preceded by long-term alpha-fetoprotein elevation

Hiromichi Sakurai [a], Akinobu Katami [a], Hiroshi Yuki [a], Ryosuke Matsuoka [b], Koji Kawai [a], Takayuki Shiomi [b], Jun Miyazaki [a,*]

[a] Department of Urology, International University of Health and Welfare Narita Hospital, Narita, Japan
[b] Department of Pathology, International University of Health and Welfare Narita Hospital, Narita, Japan

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ABSTRACT

Late relapse (LR) of testicular cancer is often associated with chemoresistance, and thus the first choice of therapy is surgery if complete resection is possible. In some LR cases (including our patient, a 31-year-old Japanese man), elevation of alpha-fetoprotein (AFP) may precede the radiologic detection of LR. Approximately 500 days after the start of our patient's AFP elevation, 18F-fluordeoxyglucose positron emission tomography (FDG-PET) revealed strong FDG uptake in an equivocally enlarged external iliac lymph node. The lymphadenectomy as salvage surgery resulted in long-term complete remission without further treatment. Using FDG-PET made it possible to perform effective salvage surgery.

1. Introduction

A late relapse (LR) of testicular cancer is relatively rare and often associated with chemoresistance. The dominant marker at an LR is alpha-fetoprotein (AFP) followed by human chorionic gonadotropin (hCG). In some cases, an elevation of AFP may precede the radiologic detection of LR beyond 1 year, reflecting the slow progression of occult disease.[1] We present a case of LR detected with 18F-fluordeoxyglucose positron emission tomography (FDG-PET) preceded by long-term AFP elevation. FDG-PET made it possible to perform effective salvage surgery in his case.

2. Case presentation

A 31-year-old Japanese man visited a different hospital with the complaint of a right testicular mass. The orchiectomy specimens revealed embryonal carcinoma, yolk sac tumor, and immature teratoma. At that hospital, the patient's levels of lactate dehydrogenase (LDH), AFP, and hCG were slightly elevated. Radiographically, retroperitoneal lymph node (RPLN) and multiple lung metastases were detected. He received four courses of bleomycin, etoposide and cisplatin (BEP).

Since the lung metastases completely responded to the chemotherapy, the patient was referred to our hospital for a post-chemotherapy retroperitoneal lymph node dissection (RPLND). The RPLND was performed successfully, and the removed specimen revealed only mature teratoma. After 3.5 years of complete remission (CR), only the patient's AFP re-increased. Systemic radiological examinations did not detect any metastases, and the left testis had remained normal. When the patient's AFP level rose to 200 ng/mL, treatment with paclitaxel, ifosfamide, and cisplatin (TIP) was started. Four courses of TIP achieved AFP normalization.

However, about 18 months later, again, the AFP level began to increase and reached 11 ng/mL (day 0 of Fig. 1). FDG-PET at this point (Fig. 2) showed an equivocally enlarged right external iliac lymph node (12 mm dia.), but the lesion revealed no FDG uptake, and the lesion had been already revealed by computed tomography (CT) before the AFP elevation.

As shown in Fig. 1, the patient's AFP continued to rise, but repeated FDG-PET (on days 320 and 440) showed an FDG-negative lymph node with a slightly increased size (Fig. 2). Around day 500, the AFP started to rise sharply, and it reached 1334 ng/mL on day 520. FDG-PET at this point showed strong FDG uptake (maximum standard uptake value [SUVmax], 24.7) in the right external iliac lymph node. Since there were no other abnormal findings, we elected to perform lymphadenectomy as salvage surgery.

After the salvage surgery, the patient's serum AFP level declined in accord with its biological half-life and normalized. The histological examination of the surgical specimens revealed an AFP-positive germ cell

* 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).

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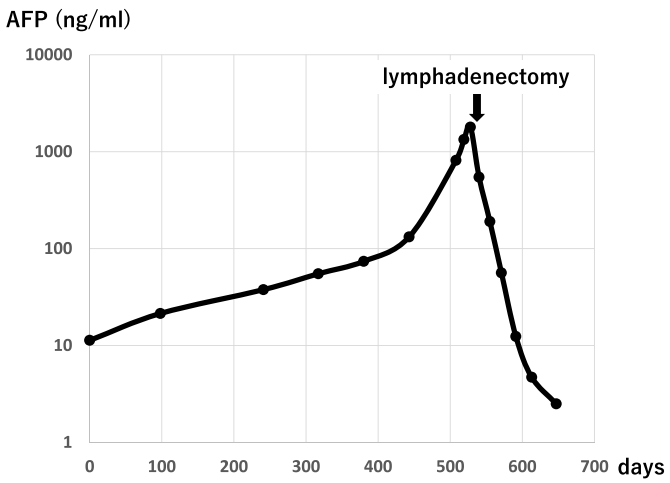

Fig. 1. The patient's clinical course after the re-elevation of AFP. The patient's AFP level started to re-increase at ~18 months after remission induced by TIP. Since the FDG-PET examination conducted 540 days after the start of the AFP re-elevation showed strong FDG uptake in in the right external iliac lymph node, a lymphadenectomy was performed. The AFP normalized soon after the surgery.

tumor (Fig. 3). Immunohistochemically, tumor cells were also positive for glypican-3 and SALL4 and negative for c-kit and CD30. Based on these findings, the diagnosis of yolk sac tumor (YST) was made. The patient has been free from disease progression for 1.5 years from the salvage surgery, with no additional treatment.

3. Discussion

We have described a case of late relapsed testicular cancer detected with FDG-PET and preceded by long-term AFP elevation. FDG-PET was useful to identify the target lesion for salvage surgery. Approximately 2%–4% of patients with testicular cancer experience LR, and the time to LR has ranged from 2 to 43 years with a median of 7–10 years.[1] AFP is the predominant marker of LR (52%–76%).[1] In some cases, an elevation of AFP may precede the radiologic detection of LR. Gerl et al. reported that AFP elevation was documented 6–44 months (median 27 months) prior to the radiological detection of relapse.[2] The initial doubling time of AFP has been 56–600 days (median 155 days).[2] Several other investigators reported a preceding AFP elevation in LR cases, reflecting the slow-growing nature of the tumors.[1]

Since an LR is usually chemoresistant, the first choice of therapy in patients with localized disease is considered surgery rather than chemotherapy. Therefore, if an AFP elevation has preceded the LR, treatment should be started after a radiological confirmation of the target lesion. In our patient's case, an equivocally enlarged right external iliac lymph node was identified, but the lesion was noted before the patient's AFP elevation. The repeated FDG-PET examinations showed no uptake in the lesion, but ~500 days after the start of the AFP elevation, FDG-PET revealed strong FDG uptake in the lymph node. The lymphadenectomy as salvage surgery resulted in a long-term CR without further treatment.

In seminomas, FDG-PET is commonly used to evaluate the viability of any residual mass after chemotherapy. FDG-PET has a high negative predictive value in seminoma patients with residual masses that are >3 cm in largest diameter. However, the usefulness of FDG-PET in the diagnosis of non-seminomas is not yet clear. Soydal et at. described the utility of FDG-PET in staging and restaging for both seminoma and non-seminoma.[3] In seminoma, the sensitivity and specificity of FDG-PET for lymph nodes were 67% and 100% and the corresponding values for non-seminoma was rather high at 84% and 100%.[3] Alongi et al. also evaluated the diagnostic value of FDG-PET in the cases of 114 patients with testicular cancer with suspected recurrent disease, of which 40% was non-seminoma; the sensitivity and specificity of FDG-PET were 87% and 90%, respectively.[4] Alongi et al. pointed out that FDG-PET findings changed the therapeutic management in 23% of their patient series.[4]

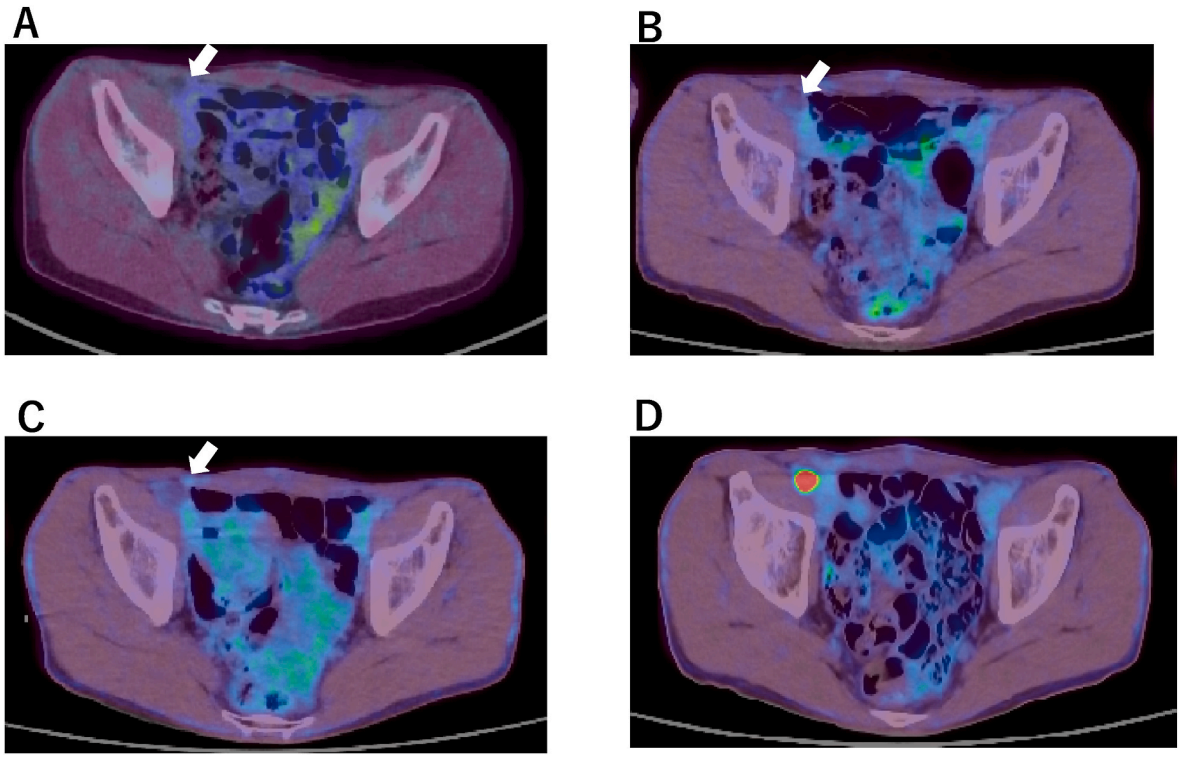

Fig. 2. FDG-PET images after the re-elevation of AFP. **A:** Day 0, AFP 11 ng/mL. **B:** Day 320, AFP 55 ng/mL. **C:** Day 440, AFP 132 ng/mL. **D.** Day 520, AFP 1334 ng/mL. FDG-PET on day 520 revealed strong FDG uptake in the equivocally enlarged right external iliac lymph node.

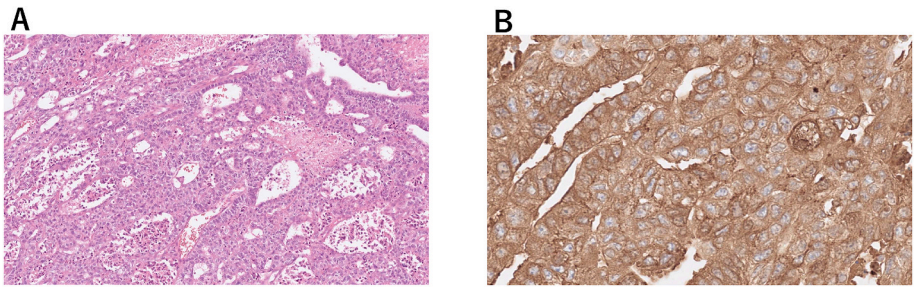

Fig. 3. Pathological findings of the resected lymph node. **A:** Hematoxylin and eosin stain. **B:** Immunohistochemistry with AFP antibodies. Germ cell tumor cells diffusely infiltrated into the lymph node. The cells were strongly positive for AFP.

In our patient's case, the pathological diagnosis of the LR tumor was YST. There have been few reports about the histologic types of LR tumors. In 2000, Michael et al. evaluated the pathology of 91 cases of LR and reported that teratoma was the most common; 60% of the patients had teratoma including 20 patients (24%) in whom teratoma was the only element.[5] Next to teratoma, YST was the most commonly observed type. Overall, 46% of the patients had YST, including 32 patients (35%) in whom YST was the only element. Their study was the first to report the high frequency of YST in LR tumors. For our patient, although the tumor's pathology was viable YST, we did not perform adjuvant chemotherapy. His tumor relapsed after second-line chemotherapy, which highly suggested chemoresistance. In addition, his serum AFP normalized postoperatively, and we thus considered that the patient would probably not benefit from adjuvant chemotherapy.[1]

4. Conclusion

In the present patient, FDG-PET identified the target lesion of a later relapse that had been preceded by long-term AFP elevation, and this use of FDG-PET made it possible to perform effective salvage surgery.

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Declaration of competing interest

The authors have no conflict of interest to disclose.

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