Metachronous testicular seminoma occurring 8 years after treatment of extragonadal nonseminomatous germ cell tumor in the retroperitoneum

Kosuke Shibamori · Toshiaki Tanaka ·
Hiroshi Kitamura · Naoya Masumori ·
Taiji Tsukamoto

Received: 1 October 2012 / Accepted: 22 November 2012 / Published online: 20 December 2012
© The Japan Society of Clinical Oncology 2012

Abstract We report a case of metachronous testicular seminoma occurring 8 years after treatment of extragonadal nonseminomatous germ cell tumor in the retroperitoneum. A 29-year-old male Japanese patient presented with a bulky tumor in the left obturator fossa. The serum levels of alpha-fetoprotein and lactate dehydrogenase were extremely high. He underwent open tumor biopsy and the pathological finding was immature teratoma. After three cycles of BEP therapy (bleomycin, etoposide, cisplatin), we performed retroperitoneal lymph node dissection and tumor resection. We added one cycle of VIP therapy (vinblastine, ifosfamide, cisplatin) as a salvage therapy because the pathological examination demonstrated immature teratoma with suspicious viable germ cell tumors. Eight years after surgery, the patient noticed that the left testis was swollen. All tumor markers were within normal limits. We performed a left radical orchiectomy, and pathological examination revealed pure seminoma with invasion of the rete testis. We emphasize the necessity of self-examination after treatment of extragonadal germ cell tumor.

Keywords EGGCT · Metachronous · Seminoma · Germ cell tumor

Introduction

Extragonadal germ cell tumor (EGGCT) is rare and accounts for 2–5 % of cancer diagnosis in all germ cell

tumors [1]. Metachronous testicular tumor after EGGCT is also rare. To the best of our knowledge, 35 cases were reported in the literature [2–14]. Herein we report a case of metachronous testicular pure seminoma occurring 8 years after treatment of immature teratoma in the pelvis.

Case report

The patient was previously reported as a case with EGGCT arising in an unusual site [15]. He noticed left inguinal and hip pain at the age of 29 years old. Magnetic resonance imaging (MRI) showed a bulky tumor in the left obturator fossa (Fig. 1). The size of the tumor was $10 \times 6 \times 10.5$ cm, and the para-aortic lymph node was also swollen (4×3 cm). Serum levels of AFP (alpha-fetoprotein) and LDH (lactate dehydrogenase) were extremely high (12946.2 ng/ml and 508 IU/L, respectively). On the other hand, the serum level of beta human chorionic gonadotropin was within the normal limits.

Open tumor biopsy revealed it was immature teratoma (Fig. 2). Radiographic and physical examination revealed no abnormal findings in the bilateral testes, including burnout tumor. After three cycles of BEP therapy (bleomycin, etoposide, cisplatin) and normalization of tumor markers, we performed retroperitoneal lymph node dissection and tumor resection. The pathological examination demonstrated immature teratoma with suspicious viable germ cell tumors, and the main tumor was located in an extralymphatic site. Then we added one cycle of VIP therapy (vinblastine, ifosfamide, cisplatin) as a salvage therapy.

There had been no findings suggestive of recurrence and metastasis after the initial treatment. Eight years after surgery, however, the patient noticed the left testis swollen without scrotal pain. The size of left testis was 5.5×3.2 cm,

K. Shibamori (✉) · T. Tanaka · H. Kitamura · N. Masumori ·
T. Tsukamoto
Department of Urology, Sapporo Medical University School
of Medicine, S1W16, Chuo-ku, Sapporo 064-8543, Japan
e-mail: shibamori.k@gmail.com

Fig. 1 MRI findings before BEP therapy. There was a solid, bulky tumor (10 × 6 cm) in the pelvis with a heterogeneous area

Fig. 2 Macroscopic findings of pelvic tumor show mature and immature ductal structure composed of columnar epithelium and squamous epithelium

and ultrasonography showed a heterogeneous solid mass. There was no abnormal finding in the right testis and no radiographic evidence of metastatic disease. All tumor markers were within normal limits. We performed a left radical orchiectomy, and pathological examination revealed pure seminoma with invasion of the rete testis (Fig. 3). After that, we added two cycles of carboplatin as adjuvant chemotherapy because we decided he was at high risk of developing recurrence. He was free from disease 10 months after surgery.

Discussion

Metachronous testicular tumor after EGGCT is rare. To the best of our knowledge, 35 cases were reported in the

Fig. 3 Macroscopic findings of metachronous testicular tumor show clear cytoplasm with big nuclei and infiltration by lymphocytes, i.e., pure seminoma

literature, as summarized in Table 1 [2–14]. Hartmann et al. [8] reported that the cumulative risk for development of metachronous testicular cancer 10 years after diagnosis of EGGCT is 10.3 %. Also they reported that metachronous testicular cancer occurred in 14.2 % of retroperitoneal EGGCT and 6.2 % of mediastinal EGGCT cases. The cumulative risk of seminomatous EGGCT was 1.4 %, whereas that of nonseminomatous EGGCT was 14.3 %.

It is controversial whether EGGCT is a primary tumor or metastasis of testicular intraepithelial neoplasia (TIN). We did not perform testis biopsy when he developed EGGCT. He might have had TIN in the left testis and presented with a late relapse this time. In our patient, however, microscopic examination revealed that the tumor in the pelvis grew outside the lymphatic tissue, whereas the left obturator lymph node did not contain the tumor tissue. This finding suggested that the pelvic tumor was of extragonadal origin rather than the result of lymph node metastasis. Therefore, we concluded that the testicular seminoma was a metachronous tumor.

Interestingly, the combination of nonseminomatous EGGCT and metachronous seminoma, similar to our case, was the most common in the reported cases. The mechanism of the trend to develop this combination is unclear. Oosterhuis et al. [16, 17] showed that the primitive germ cell tumor could differentiate into seminoma, and seminoma could differentiate into nonseminoma in stages. We hypothesized that EGGCT would be asymptomatic until it grew bulky because of its development deep in the body, so that it would tend to differentiate into nonseminoma at the time of diagnosis. On the other hand, MTT would be detected more easily in the early period because it is palpable in the scrotum and would be noticed in the follow-up for EGGCT.

Table 1 Summary of reported cases of EGGCT with metachronous testicular tumor

No.	Author	Years of publication	Age	Primary site of EGGCT	EGGCT histology	MTT histology	Elevated markers (EGGCT)	Elevated markers (MTT)	Interval between EGGCT and MTT	follow up period after diagnosis of MTT
1	Quintela AG	1991	44	rp	Sem	Non-sem	LDH, β -hCG	AFP	7 yrs.	3 yrs.
2	Lokich J	1994	22	rp	Non-sem	Sem	normal	normal	14 yrs.	unknown
3	Hayashi T	1996	18	unknown	Non-sem	Sem	LDH, AFP	LDH, β -hCG	7 yrs.	unknown
4	Gerl A	1996	Unknown	rp	Non-sem	Sem	Unknown	Unknown	35 mo.	30 mo.
5	Gerl A	1996	Unknown	rp	Non-sem	Sem	Unknown	Unknown	42 mo.	49 mo.
6	Gerl A	1996	Unknown	rp	Non-sem	Sem	Unknown	Unknown	77 mo.	106 mo.
7	Allaway M	2000	22	unknown	Non-sem	Sem	AFP	normal	7 yrs.	30 mo.
8	Daniel C	2001	24	rp	Sem	Non-sem	β -hCG	hCG	5 yrs.	7 yrs.
9	Daniel C	2001	23	rp	Non-sem	Non-sem	Unknown	normal	23 mo.	10 yrs.
10	Hartmann JT	2001	28	rp	Non-sem	Sem	β -hCG	Unknown	74 mo.	51 mo.
11	Hartmann JT	2001	19	med	Non-sem	Sem	AFP, β -hCG	Unknown	80 mo.	35 mo.
12	Hartmann JT	2001	33	rp	Non-sem	Non-sem	AFP, β -hCG	Unknown	30 mo.	40 mo.
13	Hartmann JT	2001	40	rp	Non-sem	Sem	normal	Unknown	100 mo.	66 mo.
14	Hartmann JT	2001	49	rp	Non-sem	Sem	normal	Unknown	88 mo.	115 mo.
15	Hartmann JT	2001	24	med	Sem	Non-sem	β -hCG	Unknown	41 mo.	51 mo.
16	Hartmann JT	2001	29	rp	Non-sem	Non-sem	AFP, β -hCG	Unknown	30 mo.	102 mo.
17	Hartmann JT	2001	22	rp	Non-sem	Sem	AFP	Unknown	48 mo.	4 mo.
18	Hartmann JT	2001	23	rp	Non-sem	Sem	AFP	Unknown	14 mo.	74 mo.
19	Hartmann JT	2001	26	med	Non-sem	Non-sem	AFP, β -hCG	Unknown	84 mo.	18 mo.
20	Hartmann JT	2001	48	med	Non-sem	Sem	normal	Unknown	72 mo.	1 mo.
21	Hartmann JT	2001	34	rp	Non-sem	Sem	AFP, β -hCG	Unknown	35 mo.	68 mo.
22	Hartmann JT	2001	Unknown	rp	Non-sem	Sem	AFP	Unknown	102 mo.	22 mo.
23	Hartmann JT	2001	30	rp	Non-sem	Sem	normal	Unknown	42 mo.	153 mo.
24	Hartmann JT	2001	34	rp	Non-sem	Sem	normal	Unknown	78 mo.	108 mo.
25	Hartmann JT	2001	22	rp	Non-sem	Non-sem	β -hCG	Unknown	39 mo.	7 mo.
26	Mindrup SR	2004	42		Non-sem	Non-sem	AFP, β -hCG, LDH	normal	50 mo.	unknown
27	Kuroda	2004	32	rp	Non-sem	Sem	normal	normal	4 yrs.	unknown
28	Ando	2007	22	unknown	Non-sem	Sem	β -hCG, LDH	normal	8 yrs.	6 mo.
29	Yamada	2008	30	rp	unknown	Sem	AFP, β -hCG, LDH, DUPAN2, CA19-9	LDH, β -hCG	8 yrs.	15 mo.
30	Kawamura	2009	33	rp	Sem	Non-sem	normal	LDH, HCG	8 yrs.	10 mo.
31	Hashimoto	2010	27	rp	Non-sem	Sem	Unknown	HCG	120 mo.	4 mo.
32	Hashimoto	2010	30	rp	Sem	Non-sem	Unknown	HCG	96 mo.	30 mo.
33	Hashimoto	2010	28	rp	Non-sem	Sem	Unknown	HCG	64 mo.	16 mo.
34	Hashimoto	2010	32	rp	Non-sem	Sem	Unknown	HCG	15 mo.	30 mo.
35	Hashimoto	2010	47	rp	Non-sem	Non-sem	Unknown	HCG	21 mo.	4 mo.
36	Present case	2012	29	rp	Non-sem	Sem	AFP, LDH	normal	8 yrs.	10 mo.

Age age at EGGCT diagnosis, EGGCT extra gonadal germ cell tumor, MTT metachronous testicular tumor, Sem seminoma, Non-sem non-seminoma, LDH lactate dehydrogenase, HCG human chorionic gonadotropin, β -hCG human β -chorionic gonadotropin, AFP α -fetoprotein, CA19-9 carbohydrate antigen 19-9, rp retroperitoneum, med mediastinum, yrs years

In this case, although serum AFP levels were extremely elevated, open biopsy revealed no component other than immature teratoma. The tumor possibly had components of embryonal carcinoma or a yolk sac tumor that were not detected by sampling. Furthermore, the necessity for an appropriate regimen of salvage chemotherapy for patients with immature teratoma only proven in the residual mass had not been established at that time. Recently, two cycles of cisplatin-based chemotherapy were recommended for patients with proven viable cancer cells or immature teratoma found by residual mass resection [18]. However, the number of cycles was determined empirically [19] and is not well validated. Although we performed only one cycle of VIP therapy, the treatment strategy may not have affected the metachronous recurrence in this case.

Given that patients with germ cell tumors have a high risk of metachronous testicular tumor [8], we emphasize the necessity of self-examination of the testes as well as long-term follow-up with both physical and tumor marker examinations by medical doctors after treatment of EGGCT.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Bokemeyer C, Nichols CR, Droz JP et al (2002) Extragenadal germ cell tumors of the mediastinum and retroperitoneum: results from an international analysis. *J Clin Oncol* 20:1864–1873
2. Quintela AG, Bonet EL, Roman L et al (1991) Testicular germ cell tumor seven years after a retroperitoneal germ cell tumor. *Eur Urol* 19:336–338
3. Lokich J (1994) Metachronous gonadal and extragonadal primary germ cell tumors: two case reports. *Cancer Invest* 12:406–408
4. Hayashi T, Mine M, Kojima S et al (1996) Extragenadal germ cell tumor followed by metachronous testicular tumor. *Urol Int* 57:194–196
5. Gerl A, Clemm C, Lamerz R et al (1996) Cisplatin-based chemotherapy of primary extragonadal germ cell tumors. A single institution experience. *Cancer* 77:526–532
6. Allaway M, Nseyo UO (2000) Primary testicular seminoma in a patient with a history of extragonadal non-seminomatous germ cell carcinoma. *Urology* 55:949–950
7. Daniel C, Fizazi K, Culine S et al (2001) Metachronous gonadal and extragonadal primaries, or late relapse of germ cell tumor? *Urol Oncol* 6:49–52
8. Hartmann JT, Fossa SD, Nichols CR et al (2001) Incidence of metachronous testicular cancer in patients with extragonadal germ cell tumors. *J Natl Cancer Inst* 93:1733–1738
9. Mindrup SR, Konety BR (2004) Testicular recurrence from “primary” retroperitoneal germ cell tumor. *Urology* 64:1031–1032
10. Kuroda I, Ueno M, Mitsuhashi T et al (2004) Testicular seminoma after the complete remission of extragonadal yolk sac tumor: a case report. *BMC Urol* 4:13
11. Ando R, Yasui T, Tozawa K et al (2007) Testicular seminoma occurring 8 years after treatment of a metastatic extragonadal germ cell tumor. *Int J Urol* 14:85–86
12. Yamada Y, Tomita K, Fujimura T et al (2008) Metachronous testicular tumor developing eight years after retroperitoneal extragonadal germ cell tumor. *Int J Urol* 15:267–269
13. Kawamura N, Yamamoto K, Yoshioka I et al (2009) A case of metachronous testicular tumor developing seven years after complete remission of retroperitoneal extragonadal germ cell tumor. *Hinyokika kyo* 55:635–638
14. Hashimoto K, Fujimoto H, Kouno T et al (2012) The incidence and management of metachronous testicular germ cell tumors in patients with extragonadal germ cell tumors. *Urol Oncol* 30:319–324
15. Tanaka T, Kitamura H, Masumori N et al (2006) Retroperitoneal extragonadal germ cell tumor presenting as a bulky pelvic mass of the obturator fossa. *Int J Urol* 13:180–182
16. Oosterhuis JW, Castedo SM, de Jong B et al (1989) Ploidy of primary germ cell tumors of the testis: pathogenetic and clinical relevance. *Lab Invest* 60:14–20
17. Oosterhuis JW, Looijenga LH (2003) Current views on the pathogenesis of testicular germ cell tumors and perspectives for future research: highlights of the 5th Copenhagen workshop on carcinoma in situ and cancer of the testis. *APMIS* 111:280–289
18. Albers P, Albrecht W, Algaba F et al (2011) EAU guidelines on testicular cancer: 2011 update. *Eur Urol* 60:304–319
19. Fizazi K, Tjulandin S, Salvioni R et al (2001) Viable malignant cells after primary chemotherapy for disseminated nonseminomatous germ cell tumors: prognostic factors and role of post-surgery chemotherapy—results from an international study group. *J Clin Oncol* 19:2647–2657