The potential influence of interferon-α on the growth of the growing teratoma: A case report

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1. Introduction

Growing teratoma syndrome (GTS) is rare. It is fatal if the teratoma is unresectable. A standard systemic therapy is not established. The efficacy of interferon-alpha (IFN-α) for GTS was described but the treatment periods were relatively short. A 23-year-old Japanese male with bulky retroperitoneal lymph node and multiple lung metastases that progressed to GTS was administered 6 × 10^6 units of natural IFN-α 2 × /week. Since the IFN-α treatment suppressed both lesions’ growth, it was continued for >10 years. The patient is well with controlled metastases (135 months since the IFN-α’s initiation). This is apparently the longest follow-up of INF-α treatment for GTS.

2. Case presentation

A 23-year-old man with right testicular cancer was referred to Teikyo University School of Medicine after a high orchiectomy. Computed tomography (CT) revealed multiple lung metastases and bulky retroperitoneal lymph node (RPLN) metastasis. Laboratory tests showed an alfa-fetoprotein (AFP) level of 548 ng/mL, other tumor markers were within normal range. After two cycles of bleomycin, etoposide, and cisplatin (VIP), the patient’s lung metastases stabilized. The growth of the RPLN mass continued to grow. The AFP fell to within the normal range after two cycles of etoposide, ifosfamide and cisplatin (VIP), but the metastases continued to progress as shown in Fig. 1A and B.

Although a pathological diagnosis of metastases was not made, the patient was clinically diagnosed as having GTS. Therefore, the chemotherapy was discontinued and IFN-α treatment was started. The natural IFN-α was administered twice-weekly at the dose of 6 × 10^6 units for 2 years. The toxicity of IFN-α was minimal. Soon after the introduction of IFN-α, the growth of the patient’s lung metastases stabilized. The growth of the RPLN metastasis gradually decreased after 15 months of IFN-α treatment.

At 2 years after the start of the IFN-α treatment, the administration of IFN-α was reduced to once a week. The RPLN and lung metastases after 50 months of IFN-α treatment are shown in Fig. 1C and D. During the treatment, lung metastases have been well controlled, whereas the diameter of the RPLN metastasis increased from 12 cm to 23 cm. Of note, dense internal calcifications were observed in the RPLN mass; this calcification newly appeared about 1 year after the start of IFN-α treatment and gradually increased. The patient continuously received the once-weekly IFN-α treatment for another 80 months.

At that point, the patient was referred to us for further treatment. We decided to re-evaluate the patient’s tumor radiographically and pathologically. Positron emission tomography (PET)-CT revealed no positive 18-fluorodeoxyglucose (18F-FDG) uptake in either the lung or RPLN.

Abbreviations: GTS, growing teratoma syndrome; IFN-α, interferon-alpha.

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metastases (Fig. 1 E, F). The dense internal calcifications were more prominent in the RPLN mass. The pathological findings from a sample collected by a CT-guided needle biopsy are shown in Fig. 2. The specimens contained fibrous tissue with a small amount of epithelia without atypia, and pieces of cartilage and bone tissue were seen. The findings were compatible with teratoma. Immunohistochemistry was performed for the four mismatch repair proteins (MLH1, MSH2, MSH6 and PMS2); it revealed no expression of any of these proteins.

The patient is doing well 135 months after the start of IFN-α treatment. Fig. 3 showed time-course changes of the maximum diameter of RPLN mass during IFN-α treatment. At 50 months from the start of the IFN-α therapy, the growth of the RPLN metastases had almost completely stopped.

3. Discussion

We have described the case of a patient with inoperable GTS who has responded well to IFN-α treatment for over 10 years. Several investigators have reported the efficacy of IFN-α for GTS, but the treatment periods were relatively short. Postovsky et al. described a patient with GTS who achieved stable disease for 4 years with IFN-α. The present report describes the longest observation period of IFN-α therapy for GTS. The frequent toxicities of IFN-α are lethargy, fever, myalgia. But, the toxicity of IFN-α was minimal in our case. The present case provides the following three interesting findings.

Fig. 1. CT images at different time points over the patient’s course. A, B: CT just before the start of IFN-α therapy showing bulky retroperitoneal lymph node (RPLN) metastasis and multiple lung metastases. C, D: At 50 months after the start of IFN-α therapy, CT showing the enlarged RPLN mass with dense internal calcifications. The lung metastases were well controlled. E, F: PET-CT at 130 months after the start of IFN-α treatment showed well-controlled RPLN and lung metastases. There was no 18F-FDG uptake in either lesion. Dense internal calcifications were more prominently seen in the RPLN mass.

Fig. 2. Pathological findings of a biopsy sample. A: Macroscopic findings. B: Fibrous tissue with a small amount of epithelia without atypia. C: Piece of cartilage tissue (arrow). D: Piece of bone tissue (arrow).

Fig. 3. The growth of the RPLN metastasis from the start of IFN-α treatment.
First, as shown in Fig. 3, the growth of the patient’s RPLN metastases had almost completely stopped at 50 months from the start of IFN-α therapy, and the growth of the lung metastases had completely stabilized at that point. This in contrast with the progression of GTS in its natural course; Lee et al. reported that the median linear growth of GTS was 0.5 cm/month.

Second, as shown in Fig. 1E and F, PET-CT revealed no positive 18F-FDG uptake in both metastases. In addition, dense internal calcifications newly appeared in the RPLN mass after the start of IFN-α therapy. Cho et al. investigated the PET-CT findings of teratoma to discriminate mature from immature teratomas. They reported that the 18F-FDG uptake was significantly higher in most of the immature teratomas than mature teratoma. The pattern of calcification was also helpful for discriminating these mature teratomas. Cho et al. pointed out that whereas the mature teratomas showed dense calcifications, the immature teratomas showed coarse and scattered calcification. Based on those observations, we conclude that the PET-CT findings in the present case are compatible with mature teratoma.

Third, we evaluated the expressions of four mismatch repair proteins in order to explore the possibility of using pembrolizumab. The immunohistochemistry revealed that these proteins were not expressed in our patient’s case. At present, there are limited data concerning the microsatellite instability of teratomas. As another systemic therapy, Narayan et al. reported the efficacy of palbociclib, a cyclin-dependent kinase 4/6 inhibitor, for unresectable mature teratoma. In Japan, palbociclib is approved only for the treatment of refractory breast cancer.

Finally, as shown in Fig. 2, biopsy specimens did not contain elements of somatic transformation. But, there is a possibility that some elements of somatic transformation exist elsewhere in the large tumor. If presented, it could pose a potential explanation for the INF-α responsiveness in our case.

4. Conclusion

The present case suggests the potential influence of INF-α on the growth of the GTS. Future studies to better elucidate the utility of INF-α in treating GTS are needed.

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Declaration of competing interest

The authors have no conflict of interest to disclose.

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