Case Report

Long term survival with the combination of interferon and chemotherapy in metastatic melanoma

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Abstract  The prognosis of metastatic melanoma is poor. Pre-targeted treatment era, the combination of interferon-α (IF-α) plus chemotherapy had been used and have generally short response duration. Herein, we present a metastatic melanoma case that achieved long-term durable complete response (CR) IF-α plus chemotherapy and IF-α maintenance therapy and had lower Regulatory T (Treg) cells. A fifty-year old woman was admitted to the hospital with metastatic melanoma. Lactate dehydrogenase (LDH) level was 660 U/L. The percentage of CD4+CD25+ Treg cells was 2.4% in CD4+ lymphocytes. The IF-α plus chemotherapy and IF-α maintenance were administered. After six courses of chemotherapy, CR was achieved. Vitiligo and hypothyroidism occurred. The patient has remained in CR for approximately 7 years until second pleural metastases were detected and death. The patient has positive prognostic factors such as induction of autoimmunity, small tumor volume, mild elevated LDH level, and lower Treg cell percentage. She survived long term with CR after IF-α treatment with concurrent chemotherapy and maintenance. IF-α plus chemotherapy may be a treatment option for metastatic melanoma in selected cases who cannot reach new targeted drugs.

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Introduction

Metastatic melanoma is an aggressive disease with poor prognosis. Median survivals are 6–15 months [1]. Melanoma is less sensitive to chemotherapy or radiotherapy than other cancers. Interferon-α (IF-α) treatment is a treatment option and has a response rate of 16% (one-third complete response) for advanced melanoma. The median duration of response is
approximately 4 months. Its combination with chemotherapy had been frequently used in treatment of metastatic malignant melanoma until new agents such as Raf kinase inhibitors, Mek inhibitors and ipilimumab were discovered.

Herein, we present a metastatic melanoma case that achieved long-term durable complete response (CR) IF-α plus chemotherapy and IF-α maintenance therapy and had lower Regulatory T (Treg) cells.

Case report

A fifty-year old woman was admitted to our clinic with right pleural and multiple skin recurrences of melanoma (DFS: 28 months). Lactate dehydrogenase (LDH) level was 660 U/L. CD4+ lymphocyte ratio among lymphocytes was 26.75%. The percentage of CD4+CD25+ Treg cells was 2.4% in CD4+ lymphocytes (Fig. 1).

The biochemotherapy was administered with dacarbazine (DTIC) 300 mg/m², cisplatin 30 mg/m² days 1–3 every 21 days, and INF-α2b 5 MU subcutaneously three times a week, then treatment was maintained with INF-α2b 5 MU three times a week. After six courses of chemotherapy, complete response (CR) was achieved. Vitiligo and hypothyroidism occurred. The patient has remained in CR for approximately 7 years. Pleural relapse was detected. She deceased after ipilimumab and vemurafenib treatment.

Discussion

Before the era of new molecular targeted agents, combinations with biologic agents and chemotherapy have been extensively investigated for metastatic melanoma. Firstly, addition of IF-α to DTIC has increased response rate in phase II studies, but phase III trials failed to confirm survival advantage [2,3]. Thereafter, survival advantage of a combination of CVD (cisplatin, vinblastine, and DTIC) chemotherapy plus IL-2 and IF-α has been shown [4]. EORTC 18951 study evaluated addition of IL-2 to cisplatin, DTIC plus IF-α, however, they did not show survival advantage [5].

Although biochemotherapy studies did not support survival benefit, the presented case survived for 7 years in CR after combination of chemotherapy and IF-α. This duration is longer than survival data of two large studies (9.1 and 3.9 months). This may be due to IF-α maintenance, although the effect of biologic agent maintenance has not been well known. Some predictive factors such as small volume skin or soft tissue metastases, LDH level, performance status, hypothyroidism, vitiligo occurrence have described for long term survival [6–8]. Our case had also mild elevated LDH, good performance status, only skin and soft tissue metastases, hypothyroidism, and vitiligo.

Treg cells are another prognostic factor of cancer patients. They have a role in self-tolerance and immune homeostasis and mediate immunosuppression against tumor. It is reported that Treg cells increase in peripheral blood and tumor microenvironment of melanoma patients [9]. Their increase is associated with poor prognosis in melanoma [9]. Treg cell percentage of the patient (2.4% in CD4+ lymphocytes) was lower than reported range of melanoma patients (4.9–16%) and data of our previous lung cancer study [10]. This may be one of the explanations of long durable response. This observation should be confirmed by prospective clinical trials.

In conclusion, she survived long term in CR after IF-α treatment with concurrent chemotherapy and maintenance. The studies showing whether the patients are responsive to chemoimmunotherapy, are required. IF-α plus chemotherapy may be a treatment option for metastatic melanoma in selected cases who cannot reach new targeted drugs.

Conflict of interest

The authors have no conflict of interest statement to make.

Reference


