

Inositol hexaphosphate plus inositol induced complete remission in stage IV melanoma: a case report

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Inositol hexaphosphate (IP6) also called phytic acid is a polyphosphorylated carbohydrate naturally found in cereals, nuts, grains, and high-fiber-containing foods. It has been shown to inhibit the growth of many different tumor cell lines both *in vitro* and *in vivo* like colon, pancreas, liver, prostate, and even melanoma. Vitamin B inositol is a precursor of IP6 and another naturally occurring compound with anticancer properties. We present a case report of a patient with metastatic melanoma who declined traditional therapy and opted to try over the counter supplement IP6 + inositol instead. To our surprise, the patient achieved a complete remission and remains in remission 3 years later. On the basis of this case and previous preclinical studies, we believe further research is indicated in exploring

Introduction

Overall, 91 270 patients will be diagnosed with melanoma in the USA in 2018, with an estimated 9320 deaths [1]. Its incidence continues to rise at an overall rate of 33% in men and 23% in woman [2]. The prognosis of patients with stage IV melanoma has been historically dismal with a 5-year survival ranging between 5 and 19% [3]. With the advent of immunotherapy and targeted therapies, long-term remission for stage IV disease has now become possible for many patients. In spite of the advances, not all patients derive benefit and many do relapse. As such newer therapies/therapies to improve the efficacy of available treatment options are greatly needed. Inositol hexaphosphate (IP6), also called phytic acid, is a polyphosphorylated carbohydrate naturally found in cereals, nuts, grains, and high-fiber-containing foods. It has been shown to inhibit the growth of many different tumor cell lines both *in vitro* and *in vivo* like colon, pancreas, liver, prostate, and even melanoma [4–6]. Vitamin B inositol is a precursor of IP6 and another naturally occurring compound with anticancer properties [7]. We present a case report of a patient with metastatic melanoma who declined traditional therapy and opted to try the over the counter supplement IP6 + inositol instead. To our surprise, the patient achieved a complete remission and remains in remission 3 years later.

Case description

A written informed consent was obtained from the patient for reporting of his case and images. A 59-year-old male with a past medical history of depression, hypertension, and migraines presented in 2012 with a 5-year-old mole that has been progressively getting bigger and started bleeding

antiproliferative and potential immune stimulating effects of IP6 + inositol in patients with metastatic melanoma. *Melanoma Res* 00:000–000 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

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recently over the dorsum of his left foot (Fig. 1). Biopsy of the lesion confirmed a 1.4 mm, nonulcerated melanoma. The patient underwent wide local excision with sentinel lymph node biopsy revealing a 1.2 cm, 3.5-mm deep, nonulcerated nodular melanoma with 3 mitosis/mm², negative deep and peripheral margins, and no lymphovascular invasion or microsatellitosis. Two lymph nodes were noted to have micrometastatic foci of melanoma on sentinel lymph node biopsy. The patient was staged as pT3apN2acM0: stage IIIB melanoma. He underwent a subsequent left inguinal dissection which upgraded the stage to stage IIIC. At this time a

Fig. 1



Primary melanoma lesion over the dorsum of the left foot.

PET/CT did not show any evidence of distant metastasis. Although he was at a high risk of having melanoma recurrence, adjuvant therapy with interferon could not be offered as the patient had a history of suicidal ideations in the past. As such, he was placed on active surveillance with restaging scans every 3 months starting January 2013.

After over a year on active surveillance, the patient noticed a 4-mm pink to slightly purple, firm, centrally eroded papule over the left shin. The lesion was completely excised on 25 March 2014 and was confirmed to be in-transit malignant melanoma involving the superficial and deep dermis with negative margins. Restaging computed tomography (CT) of the chest/abdomen/pelvis showed no evidence of distant metastasis. Again given his history of depression, he was deemed not a good candidate for adjuvant interferon, and in addition, the patient denied participation on an adjuvant clinical study.

In January 2015 the patient presented with a new subcutaneous lesion in his left medial thigh that was biopsied and confirmed to be *BRAF V600E* mutant melanoma. Left medial thigh melanoma was 3 cm in size. Restaging scans of the chest/abdomen/pelvis revealed a new mediastinal and right hilar lymphadenopathy with multiple pulmonary nodules (Fig. 2). Lactate dehydrogenase was within normal limits and he was staged as having a stage IVB disease. The patient was offered systemic therapy with both immunotherapy and targeted therapy but he declined both and instead elected to pursue the combination vitamin IP6 + inositol (800 mg/220 mg), five tablets in the morning and five in the evening daily. To our surprise, restaging scans 6 months later showed significant improvement. Subsequent CT scans showed continued response with a decrease in the size of the hilar and mediastinal lymph nodes and shrinkage

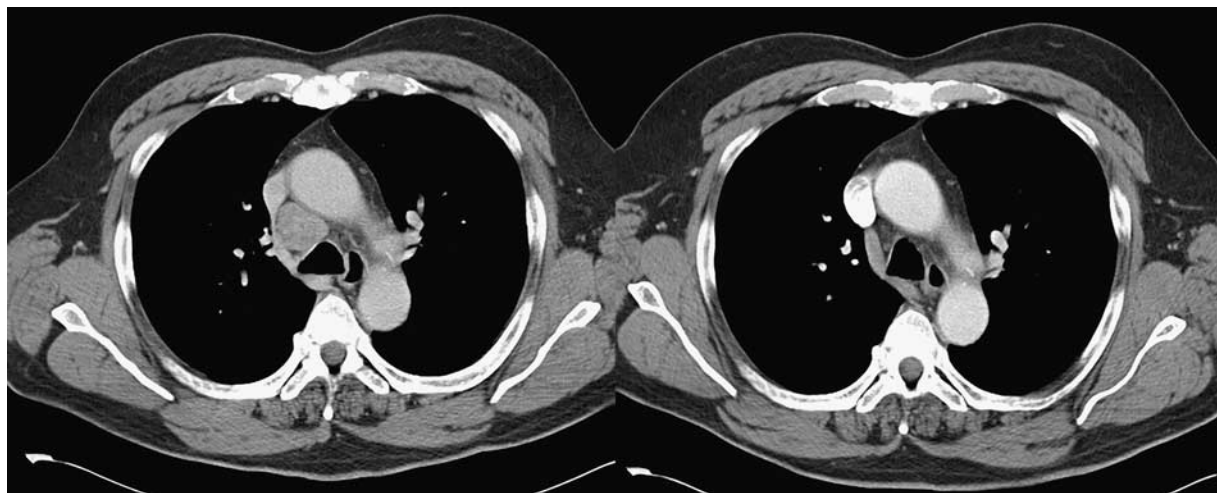
of the left medial thigh in the transit lesion. The patient went into complete clinical and radiological remission after being on the vitamin combination for 2 years (Fig. 2). Three years after relapse, the patient remains in complete remission and continues to take IP6 + inositol daily. We have not seen any subjective or objective evidence of side effects that can be attributed to high doses of daily IP6 + inositol intake so far.

Discussion

IP6 also called phytic acid is a polyphosphorylated carbohydrate naturally found in corn, soybeans, wheat bran, cereals, nuts, grains, and high-fiber-containing foods [4]. Inositol phosphates are common molecules found in mammalian cell systems. IP6 regulates a number of biological processes including cell cycle, signal transduction, intracellular protein transport, RNA splicing, and vesicle-mediated transport [8,9]. Interestingly, it has been shown to inhibit growth of many different tumor cell lines both *in vitro* and *in vivo*, like colon [10–13], pancreas [14], liver [15,16], breast [17–21], prostate [22–28], leukemia [29], and melanoma [5,6,30]. Many mechanisms have been proposed to explain its antitumor activity including gene alterations with stimulation of tumor suppressor genes like *p53* and *p21 WAF1/Cip1* [12], by arresting cell cycle in G0/G1 phase [31], decreasing VEGF production [28,30,32], inducing differentiation [29,33], and even apoptosis at high doses with no effect on normal cells [11,34]. Its antioxidant properties have been known for a long time [35,36]. In addition, a direct correlation has been found between increased NK cell activity [37] and tumor suppressive effect of IP6 in in-vivo studies.

Vitamin B inositol is a precursor of IP6 and another naturally occurring compound, which has also been shown to have anticancer properties [7]. Animal studies have shown that the combination of IP6 + inositol provides additive anticancer

Fig. 2



Computed tomography with the contrast of the chest before (left) and 2 years after (right) starting inositol hexaphosphate + inositol showing complete radiologic resolution of the upper right hilar lymph node.

properties than each given individually [38]. A phase 1 study evaluating the efficacy of IP6 + inositol in the treatment of breast cancer patients receiving chemotherapy, showed that IP6 + inositol as an adjunct therapy ameliorated the side effects and improved the quality of life among patients treated with chemotherapy [17].

Although this is a single clinical case showing IP6 + inositol's potential role in controlling our patients stage IV disease and spontaneous regression of primary melanoma, and rarely metastatic melanoma has been reported in literature [39,40], we believe that there are ample preclinical and clinical data to suggest that this nontoxic, readily available supplement should be evaluated in clinical trials for its antitumor activity. Further research is also indicated in exploring the anti-proliferative and potential immune stimulating effects of the IP6 in patients with metastatic melanoma.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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