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**CASE STUDY: MALIGNANT MELANOMA MANAGEMENT USING THE
INTEGRATED HEALTH CLINIC APPROACH**

Introduction

Melanoma is the most serious form of skin cancer and the sixth most common cancer in North America¹. In comparison to other skin neoplasms, melanoma is especially aggressive and capable of spreading in an unpredictable manner to virtually any organ in the body¹. Prognosis is dependent upon primary tumor thickness, presence of ulceration, mitotic rate, and presence/extent of metastatic disease². Risk factors include UV exposure, genetic susceptibility, history of non melanoma skin cancers, and immunosuppression^{3,4,5}. Treatment options depend on the presence of metastasis but may include surgical resection, immunotherapy, targeted inhibition of MAP kinase pathways, and/or radiation over affected sites⁶. Despite the multitude of treatment options available, the incidence of melanoma continues to drastically rise with no appreciable reduction in mortality rate. Smaller scale studies have noted tumour cell response to integrative modalities including injection therapies, targeted supplementation, hyperthermia and off-label pharmaceuticals. In this report, we present a case of malignant melanoma treated at the Integrated Health Clinic (IHC), that responded incredibly well to advanced naturopathic protocols including hyperthermia, in conjunction with disease-specific dietary, supplementary, injection and intravenous therapies.

Case history:

J.B., a 54 year-old female who was originally diagnosed with melanoma in June 2011. She initially presented at the IHC with a lesion on the posterior right scalp, which was excised with a deep margin and 1mm clearance. Pathology revealed the melanoma with a Breslow depth of 5 mm. Three sentinel lymph nodes were removed. All negative for metastatic deposits. In September 2011, J.B. underwent a re-excision biopsy of the lesion which showed no residual melanoma.

She remained symptomatically well until November 2013, when a new 9 mm nodular lesion was again noted on the scalp, this time located anteriorly on the right temporal region. A biopsy confirmed invasive melanoma, with a Breslow depth of 10mm. In preparation for further surgery, J.B. had a staging workup in November 2013 consisting of a chest x-ray (CXR) and abdominal ultrasound. Although CXR was clear, abdominal ultrasound showed multiple target-like hypoechoic lesions seen within both lobes of the liver measuring up to 1.6cm in size. A follow up CT of the head, neck, chest abdomen in December 2013 noted two intracranial lesions in the right parietal region measuring 1.4cm (Fig. 1.), and basal frontal region measuring

5mm (Fig. 2.). JB was recommended neurological resection followed by whole brain radiation, but declined due to the possible side effects.

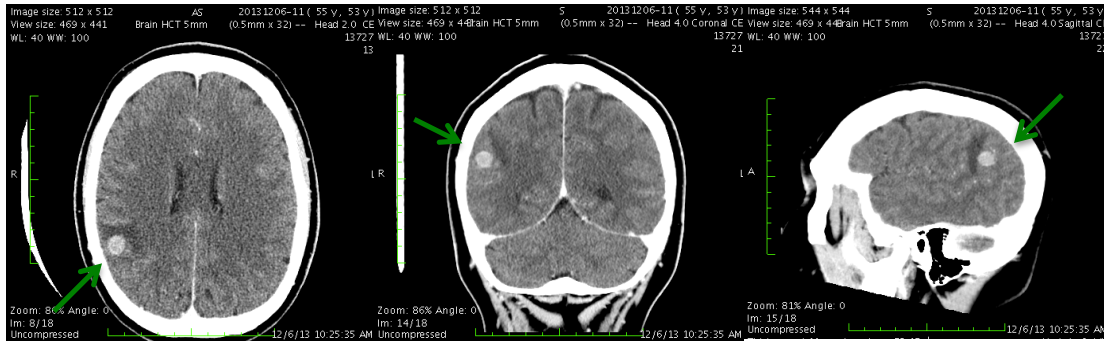


Fig. 1. - CT of head - lesion at right parietal region - December 2013



Fig. 2. - CT of the head - lesion at basal frontal region - December 2013

These lesions were not visualized with a follow up PET/CT and MRI of the head from January 2014 of the head (Fig 3 & Fig 4)

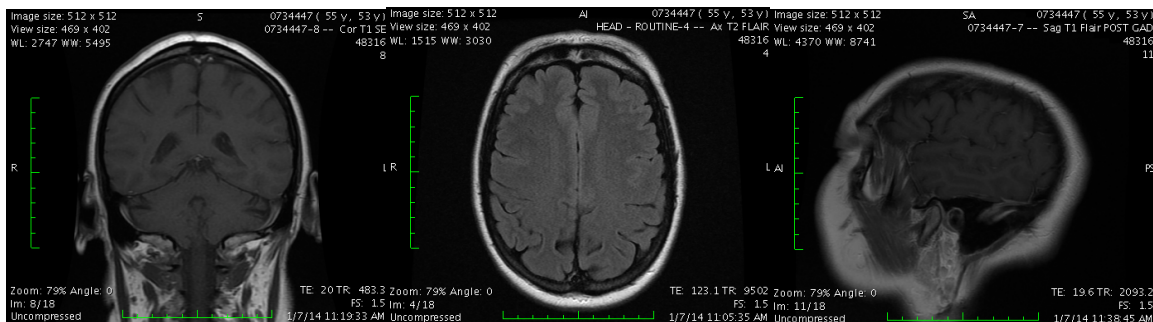


Fig. 3. MRI of the head - no lesion at right parietal region - January 2014

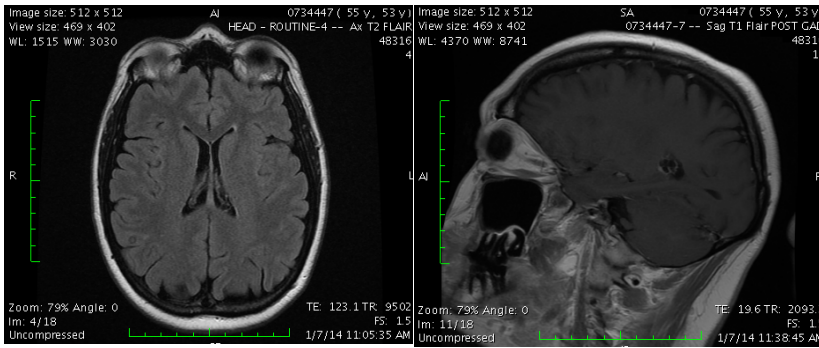


Fig. 4. MRI of the head - no lesion at basal frontal region - January 2014

Increased SUV uptake was noted in the right pre-auricular nodes and cervical lymph nodes of the right neck, as well as in the porta hepatis. (Fig. 5.).

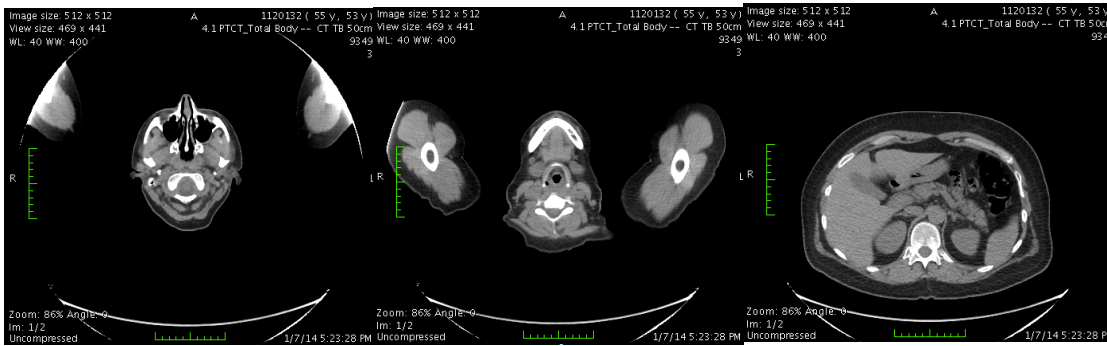


Fig. 5. - PET scan whole body - January 2014

JB was recommend to start her naturopathic intervention in January 2014 (Table 1.)

Table 1. - Treatment Protocol

Medication Prescription	Dosage	Effect
I.V. dichloroacetate (DCA)	2x/week with LRHT	Inhibits pyruvate dehydrogenase thereby inhibiting glycolysis. Causes favoring of aerobic respiration, which reverses the suppression of apoptotic pathways. Increased tumor apoptosis shrinks tumor size ⁷ . Inhibits angiogenesis,

		alter expression of HIF, and alter pH regulators V-ATPase and MCT1 ⁸ .
I.V. ascorbic acid (25G)	1 x/week with LRHT	Improve quality of life, decrease tumor size and prolong relapse interval ⁹ . Alleviates cancer and chemotherapy related symptoms ¹⁰ .
Can-Arrest (Curcumin 200mg, Boswellia 200mg, Quercetin 100mg)*	2 capsules p.o. BID	Inhibit cyclooxygenase-2 (COX2) enzymes. Blocking COX 2 has been shown to decrease tumor invasiveness ¹¹ . Inhibition of the transcription factor NF-κB to arrest tumor growth and its progression ¹²
Aspirin (ASA)*	81mg p.o. daily	Associated with decrease in melanoma incidence ¹³ Inhibit chemically-induced carcinogenesis of epithelial tumors ¹⁴ .
Nutra-QOL (Fermented Wheat Germ)*	1 sachet p.o. daily	Anti-tumoral, Immune-modulation. Improve quality of life ¹⁵ . Induced apoptosis and exert significant antitumor activity ¹⁶
Iscador S.Q. injections *	Twice weekly	Prolong survival time and stimulate self-regulation ¹⁷ . Early cycle inhibition followed by apoptosis in a dose dependent manner ¹⁸
IHC multi-vitamin	1 capsule p.o. BID	Raises tissue cofactor concentrations and thereby increases the activity of defective enzymes ¹⁹ . Micronutrient deficiencies, both individually and in combination leads to DNA damage which can lead to

		cancer ²⁰ .
Vitamin D3	4,000 I.U. tablet p.o. BID	Potent anticancer activity with inhibition of melanoma growth ²¹ . Promotes apoptosis and prevents angiogenesis ²²
Melatonin	10mg capsule p.o. h.s.	Immunomodulatory. Augment production of T-lymphocytes and NK cells. Oncostatic properties in melanomas and tumors of epithelial origin ²³ . Benefits seen on survival rates, treatment response rates, disease progression, and toxicity profile ²⁴ .
Erfa Thyroid	30mg p.o. OD	Suppresses TSH, which is shown to induce proliferation of melanoma cells ²⁵ .

* Taken 30-45 minutes before LRHT

On February 4, 2014, J.B. began heat therapy consisting of loco-regional (LRHT) and fever range-whole body hyperthermia (FR-WBHT) in addition to the oral and injection protocols. Thereafter, a diagnostic linear endoscopic ultrasound in March 2014 revealed normal findings, with no evidence of remaining disease. In April 2014, a CT of the abdomen and pelvis showed a non-enlarged and normal appearing porta hepatis node, with no other evidence of intra-abdominal malignancy. On follow-up, physical findings showed no evidence of the previously visible and palpable lesions in the right temporal region and pre-auricular nodes except for a small solitary soft nontender lymph node in the right infra-auricular area.

Since May 2014, J.B. has received 16 LRHT treatments to the scalp and cervical chain and three FR-WBHT treatments. She tolerated both forms of hyperthermia well with no observed or reported adverse effects. It should be noted that J.B. did experience a flare of her dormant rheumatoid arthritis, possibly a result of immune therapies including the oral supplements, injection therapies and FR-WBHT. She received 25gm IVAA and IVDCA without adverse side effects. J.B. has continued the oral regimen and occasional IVAA infusions. As of September 2015 she remains free of disease.

J.B. is an encouraging case of malignant melanoma. Borrowing the statement of her medical oncologist, her outcome is truly a "miracle." She has declined conventional treatment such as radical surgery, immunotherapy or molecularly targeted

treatments. Judging from the imaging, laboratory results, and her signs and symptoms, her clinical course from the start of the treatment at the IHC shows that there is no remaining evidence of disease. J.B. continues to respond well to the treatment protocol consisting of LRHT, FR-WBHT, injection therapies, medications and supplementation and remains in complete remission with no evidence of disease (Fig. 6 & 7).



Fig. 6. CT/PT scan whole body – July 2015

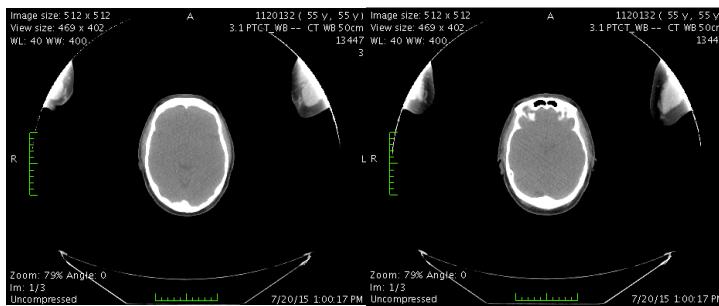


Fig 7. CT/PT scan whole body – July 2015

Discussion:

The incidence of melanoma continues to rise and despite efforts to heighten early screening techniques, there has been no reduction in mortality¹. United States epidemiological studies from 1982 to 2011 reported a 2 fold increase in melanoma cases²⁶. Given these staggering statistics, it seems prudent to investigate adjunctive therapies for melanoma. This case report demonstrates the potential utility of an integrative plan for malignant melanoma. The mechanisms and effects of targeted supplementation and injection therapies on melanoma have been presented in Table 1.

Hyperthermia as a singular modality has shown improvements in both partial and complete response rates for several malignancies including squamous cell cancers, adenocarcinomas, and melanomas²⁷. The effect of hyperthermia depends on the temperature and exposure time. A likely mechanism for tumour cell death is protein denaturation, observed at temperatures greater than 40°C which can lead to alterations in multimolecular structures including cytoskeleton and membranes, changes in enzyme complexes for DNA synthesis and repair²⁸. Hyperthermia relies

on the unique characteristics of malignant cells, and acts on these mechanisms to inhibit its growth. Compared to healthy tissue, malignant cells are more sensitive to high temperatures. Tumor cell architecture and vasculature is more chaotic compared to healthy tissue, and this leads to an immature, structurally defective microvascular system that is less resilient to perfusion shifts. The morphology, membrane fluidity and gene expression of a cancer cell also differs from normal cells. Heat increases membrane fluidity and instability of cancer cells, leading to cell death directly or indirectly through increased delivery of cytostatic chemotherapy agents. Heat induces expression of p53, a tumor suppressor transcription factor that is mutated or decreased in cancer cells. Hyperthermia also induces protective anti-tumor immune responses by presenting the tumour peptides to naïve T-cells in the draining lymph nodes. The lymphocytes will mature and proliferate into cytotoxic T lymphocytes and CD4+ helper cells, mounting an adaptive immune response against tumour cells²⁷. Elevated temperatures influence lymphocyte transformation and mitogenesis, both of which increase the activity of the immune system. The systemic activation of the immune system by hyperthermia may help target metastatic tumour cells²⁹. Hyperthermia clinically if properly used is free of serious side effects, and when utilized with chemotherapy and radiotherapy can increase their anti-tumoural effects³⁰.

Conclusion:

This case report demonstrates that integrative oncology treatment is safe and effective for the management of metastatic melanoma. Melanoma being an aggressive disease should be managed using all possible resources. The use of naturopathic treatments played an important role for the patient's wellness and quality of life. Hyperthermia in combination with targeted supplementation has shown to be effective in the management of malignant melanoma with fewer side effects.

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