Potential Role of Human Growth Hormone in Melanoma Growth Promotion

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Background: Human growth hormone (HGH) and insulin-like growth factor-1 (IGF-1) have been shown to play a role in the malignant transformation and progression of a variety of cancers. HGH is also known to up-regulate molecular signaling pathways implicated in the pathogenesis of melanoma. Although HGH has previously been implicated in promoting the clinical growth of both benign and malignant melanocytic neoplasms, to our knowledge there are no conclusive studies demonstrating an increased risk of melanoma following HGH therapy. Nevertheless, there are reports of melanoma developing subsequent to HGH coadministered with either other hormones or following irradiation.

Observation: A 49-year-old white man presented with a new pigmented papule that was diagnosed as melanoma. The patient reported using HGH for 3 months prior to the diagnosis. His 51-year-old wife, who also was white, had also been using exogenous HGH for 3 months and had been diagnosed as having a melanoma 2 weeks prior.

Conclusions: Given the unlikelihood of 2 unrelated people developing melanoma within a short time span, it is reasonable to assume that a common environmental component (HGH or other shared exposure) contributed to the development of both melanomas. Because of the increased use of exogenous HGH as an antiaging agent, it is important to be aware of the growth-promoting effects of this hormone. Until better data are available that determines the true risk of exogenous HGH, its use as an antiaging agent merits increased surveillance.


WE REPORT 2 CASES OF new-onset cutaneous melanoma subsequent to the initiation of exogenous human growth hormone (HGH), an anabolic peptide hormone synthesized by the anterior pituitary gland. Endogenous HGH secretion is regulated by growth hormone–releasing hormone (GHRH) produced in the hypothalamus. Most of HGH’s effects on growth and metabolism are mediated by insulin-like growth factor 1 (IGF-1). IGF-1 is produced primarily in the liver following stimulation by HGH. The use of exogenous HGH as an antiaging agent is gaining acceptance and increasing in prevalence despite its negative adverse effects, including oncogenic transformation and neoplastic progression.

Human growth hormone’s direct effects are predominantly mediated through the mitogen-activated protein kinase/extracellular–signal–regulated kinase (MAPK/ERK) and janus kinase signal transducer and activator of transcription (JAK-STAT) pathways. IGF-1 directly up-regulates the MAPK/ERK and phosphoinositide 3-kinase (PI3K) pathways. Given that overstimulation of these pathways has been implicated in the pathogenesis of melanoma, there may be indication to closely monitor patients using exogenous HGH for development of malignant disease.

REPORT OF A CASE

A 49-year-old white man presented with a new pigmented papule on his left lower back (Figure 1 and Figure 2). A biopsy was performed, and findings were consistent with a diagnosis of melanoma (Breslow depth, 0.32 mm) (Figure 3). Although there was no family history of melanoma among his genetic relatives, his 51-year-old wife, who also was white, had been diagnosed as having a melanoma on the right arm 2 weeks prior (Breslow depth, 0.75 mm). Both patients noted that 3 months previously they had begun an antiaging regimen that included exogenous HGH for development of malignant disease.
cluded daily subcutaneous injection of HGH (0.58 mg) and testosterone. His wife’s regimen included daily subcutaneous administration of HGH (0.29 mg) plus topical testosterone, progesterone, and estrogen to her inguinal region and axillae. On discovery of the melanomas, both discontinued their exogenous hormone regimens.

There is one similar report in the literature of a 26-year-old woman who developed melanoma following hormone therapy with HGH, thyroid hormone, and estrogen.9 Although this report suggested that estrogen replacement was the causal agent, it could not rule out the role of HGH via the Naranjo adverse drug reaction causality algorithm. Although estrogen has been implicated as a risk factor in the development of melanoma,10 subcutaneously administered exogenous HGH was the only agent common to all 3 regimens.

It is well established that pigmentation is regulated by a variety of signaling pathways, including peptide hormones.11 Consequently, it is possible that there exists a direct correlation between exogenous HGH administration and the development of melanoma. This correlation may also extend to benign melanocytic neoplasms. Supporting evidence includes a previous study that demonstrated that administration of exogenous HGH accelerates the rate of nevus growth.12 There is also evidence that nevi in individuals treated with HGH exhibit abnormal melanosome architecture, increased Ki-67 staining, and increased anisokaryosis compared with matched controls.13 However, it should be noted that other studies of patients failed to confirm this correlation.14-16

Although the aforementioned series did not demonstrate the development of melanoma in any of the patients younger than 18 years, there is a report of malignant melanoma developing in both a 9-year-old girl and 15-year-old boy following 3.0 and 1.5 years of exogenous HGH replacement, respectively.16 One aspect unique to both of these cases was that the patients had previously received craniospinal irradiation. Consequently, an underlying mutation generated by irradiation could have primed the melanocytes to grow in re-
Curiously, melanoma may have an endogenous growth promoting loop for the HGH/IGF-1 pathway. Supporting evidence includes the presence of GH-Rs on melanoma cells and the fact that melanoma cells synthesize IGF-1. It is also interesting to note that melanomas express growth hormone–releasing hormone receptors (GHRH-Rs). Although, to our knowledge, direct production of HGH by melanoma cells has not been noted in the literature, activation of the GHRH-Rs has been shown to have growth-promoting functions in other tumors. Given the proliferative effects of each member of this pathway, specific antagonists to each receptor may also have a therapeutic benefit in melanomas.

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Top-Accessed Article: UV Light Tanning as a Type of Substance-Related Disorder


In this article, Warthan and colleagues demonstrate the addictive nature of indoor tanning booth use. Of 145 beachgoers, 26% met the modified CAGE (Cut down, Annoyed, Guilty, Eye-opener) criteria, and 53% met the modified Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, criteria. Furthermore, they suggest that tanning booth use should be considered a novel type of substance-related disorder. This proposition poses a compelling argument to restrict tanning booth use in minors, similar to restrictions imposed on alcohol and tobacco use.

Warthan and coauthors’ article is significant because it highlights the challenges that we clinicians face in deterring tanning booth use in our patients despite increasing evidence of associated health risks. It is imperative for practitioners to appreciate the possible addictive behaviors involved in tanning booth use in order to focus on patient education and prevention efforts.

From October 2010 to August 2011, this article was viewed 1667 times on the Archives of Dermatology website.

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