Cameo

# Regression of an acral lentiginous melanoma with an immunotherapy using a Mycobacterium tuberculosis-extracted polysaccharide complex (Tubercin)

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A 77-year-old-female presented with a painless, pigmented lesion, which had been present for approximately 10 years but had increased significantly in size during the last 3 months. Her past history was unremarkable, but she had been a farmer for more than 50 years and was routinely exposed to excessive amounts of sunlight. On examination, a lesion measuring 11 × 15 mm was noted on the base of left thumb. The lesion was black, slightly elevated and irregularly shaped with a relatively demarcated border. Histological examination of the biopsy specimen was consistent with an acral lentiginous melanoma (ALM) with a thickness of 4 mm. Whole body computed tomographic examination and bone scan demonstrated no distant metastases.

The patient refused not only the surgical treatment but also the recommended chemotherapeutic regimen due to her advanced age. She was then referred to the WHO Collaboration Viral Hepatitis Center at Kyungpook National University for consideration for immunotherapy with Tubercin.

The patient consented to a trial of Tubercin, which was initiated on December 24, 1999. She received three 0.3 mL subcutaneous intralesional injections of Tubercin and 2 mL intramuscular injections on the buttock every other day. After 10 months of treatment the lesion appeared as a faint brown-colored macule and almost complete regression was noted. The follow-up histological examination performed after 1 year showed no evidence of melanoma (Fig. 1). The treatment regimen was reduced to biweekly treatments consisting of two 0.2 mL intralesional injections and one 2 mL intramuscular injection. After an additional year, the treatment will be further reduced to a biweekly 1 mL intramuscular injection. The patient has remained free of any metastases and demonstrated no local or systemic reactions.

## Discussion

Malignant melanoma is an immunogenic tumor to which various types of immunotherapy have been applied.[1] Several attempts with nonspecific immune adjuvants such as BCG[2] and levamisole[3] were not convincing. Recent studies have demonstrated that high dose interferon (IFN)-alpha has been reported to improve overall survival rate[4] but the IFN treatment must be considered in relation to its availability, cost and significant toxicities. Given these limitations, other therapeutic regimens are still being actively pursued.

Tubercin is a polysaccharide complex free of lipids and proteins, which was isolated from Mycobacterium tuberculosis (H37RV) in 1974.[5] The immunotherapeutic properties of Tubercin were shown in many previous studies. When administered as an adjuvant treatment in 500 patients with advanced cancers, including melanoma, patients had a significantly longer disease-free survival.[6,7] During this trial, no significant adverse effects were noted. A significant number of anergic patients with various malignant diseases developed a delayed cutaneous hypersensitivity reaction to 2,4-dinitrochlorobenzene after treatment with Tubercin. Interestingly, the development of a hypersensitivity reaction in these patients positively correlated with an improved survival rate[8] suggesting that Tubercin may restore the impaired cell-mediated immunity. This hypothesis is further supported in this case. The follow-up histological examinations after Tubercin treatment showed the appearance of many tumor-infiltrating lymphocytes around melanoma cells which was absent before treatment.

Acral lentiginous melanoma (ALM) is relatively uncommon in Caucasians, but frequently seen in all pigmented races. While a few cases of melanoma have been reported to regress spontaneously, ALM is a more aggressive tumor with a higher mortality rate and no reported cases of spontaneous regression.[9] In the present case, after 1 year of an aggressive treatment with

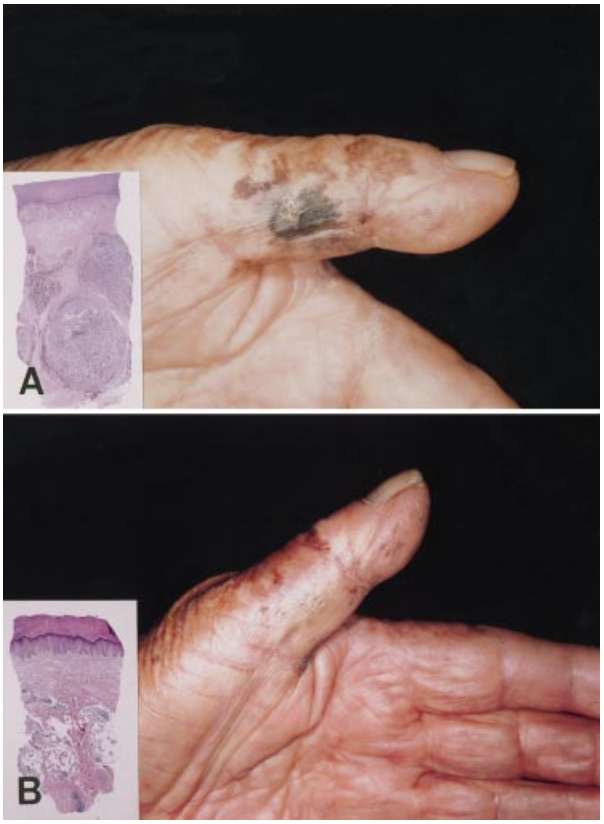


**Figure 1** Gross and histologic findings of the melanoma before (A) and after (B) Tubercin treatment

Tubercin, the primary tumor became histologically undetectable and she has remained free of any known metastases. Furthermore, she has demonstrated no local or systemic reactions. We suggest that Tubercin, which is safe and easily administered at a relative low cost, may be efficacious as an immunotherapeutic agent for malignant melanoma.

## References

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