

Complete Regression of an Advanced Breast Cancer through Combined Treatment of Radiation and Immunotherapy of Mycobacterium tuberculosis-extracted Polysaccharide Complex (Tubercin®)

Kyuha Hwang, Jinhyang Jung, Hoyong Park, Youngha Lee, Tai Ho Chung*

Department of Surgery and Department of Immunology*
Kyungpook National University Hospital, Daegu

-presented at 2004 spring meeting of Korean Breast Cancer society-

INTRODUCTION

The management of locally advanced breast cancer (LABC) requires a combined modality treatment approach involving surgery, radiotherapy and systemic therapy.

With recent advances in tumor immunology, immunotherapy has now been established as the fourth column of cancer therapy besides surgery, radiotherapy and chemotherapy. Of the various types of immunotherapy, we use Mycobacterium tuberculosis extracted polysaccharide complex (Tubercin®) to activate the host immune response, especially cell-mediated immunity. Tubercin® is a polysaccharide complex free of lipids and proteins, which was isolated from Mycobacterium tuberculosis in 1974. The immunotherapeutic properties of Tubercin® were shown in many previous studies. When administered as an adjuvant treatment in 500 patients with advanced cancers, patients had a significant longer disease-free survival.

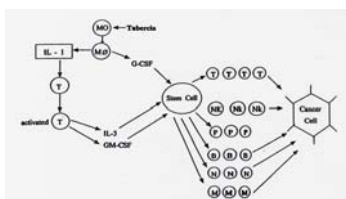
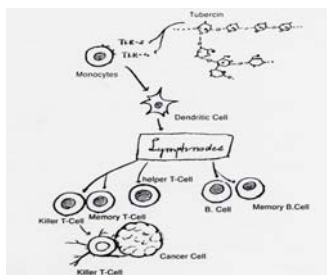


Fig 1. Tubercin® action on immune system



During the whole breast radiotherapy, she received 2nd Tubercin® treatment (2µg IM twice/week). After whole breast radiotherapy, the tumor exhibited inflammatory changes with exudate and managed conservatively. The inflammation improved and tumor reduced markedly.

And then, she received standard chemotherapy of cyclophosphamide, methotrexate, 5-FU to prevent the tumor growth, but she experienced severe myelosuppression. So, she received oral 5-FU (Furtulon®:600mg/day) chemotherapy, but experienced gastrointestinal problems. She stop the oral chemotherapy, but, 2nd Tubercin treatment continued until December 2000 with good tolerance. In May 2001, 1 year after whole breast radiotherapy, she revisited our department. She received 3rd Tubercin treatment (2µg IM twice/week) thereafter. Physical examination revealed only vaguely palpable nodule and pathologic examination revealed only fibrous changes. She persisted in remission almost 3 year later. (May, 2004)

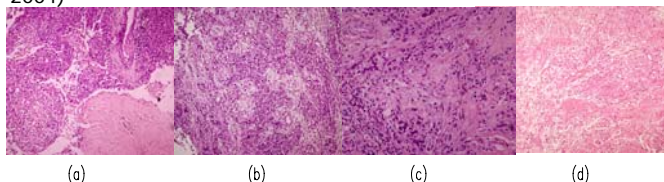


Fig. 2 (a),(b),(c) Pathologic findings in core needle biopsy: Section shows small pieces of breast tissue. Tumor cells grow in diffuse sheets, as individual cells and stroma is scanty. Tubular differentiation is barely detectable. Areas of necrosis are seen. (d) In follow-up core needle biopsy, section shows no evidence of malignancy

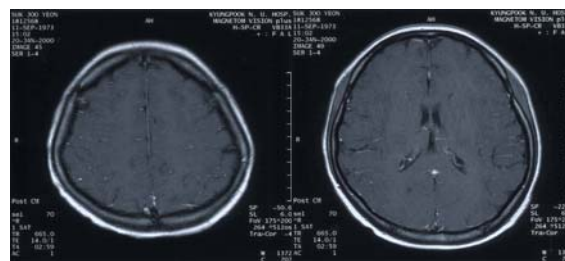


Fig. 3 MRI findings of leptomenigeal metastasis. Accentuated leptomenigeal enhancement was noted in contrast enhanced MR view.

CASE PRESENTATION

A 26-year-old unmarried woman was presented in October 1999 at Kyungpook National University Hospital with about 6×6cm sized non-tender mass in upper inner quadrant of right breast for 2 weeks. Pathologic examination with core needle biopsy revealed invasive ductal carcinoma (Fig 2). Preoperative clinical evaluation for distant metastases yielded negative results, and serum tumor markers were within normal range.

To reduce the tumor size, she received preoperative chemotherapy with epirubicin (75mg/m²) and vinorelbine (25mg/m²). However, after 3 cycle of epirubin and vinorelbine, tumor grew up to 9cm, and she received 2nd line chemotherapy with paclitaxel (80mg/m²) and vinorelbine (25mg/m²).

In January 2000, after 2 cycle of paclitaxel and vinorelbine, she was presented with seizure attack and loss of consciousness. After work-up, she was diagnosed with leptomenigeal metastasis (Fig. 3) and received whole brain radiotherapy (30Gy). During the brain radiotherapy, she started her 1st immuno-therapy with Tubercin®(2µg IM daily) for 15 days. However, in March 2000, tumor grew up to 11×8cm. Because of the progression of the disease, she received radiotherapy to whole breast (50Gy with 10Gy boost) with capecitabine chemo-therapy (2500mg/m²).

DISCUSSION

Local control rates and overall survival have improved with the use of multimodality therapy, but LABC remains problem with local recurrence and distant metastases. We recently experienced the complete pathologic regression of locally advanced breast cancer with leptomenigeal metastasis using radiotherapy and immunotherapy with Tubercin®. Although which treatment modality does contribute to the regression is not clear, immunotherapy may have considerable role in tumor regression; activation of host cellular immunity to kill the cancer cell, recovery of host immunity during chemotherapy and radiotherapy.