Possible vaccine for mesothelioma proven safe

March 4 2010

Researchers have demonstrated the safety of a potential vaccine against mesothelioma, a rare cancer associated primarily with asbestos exposure. The vaccine, which infuses uses a patient's own dendritic cells (DC) with antigen from the patient's tumor, was able to induce a T-cell response against mesothelioma tumors.

"[This] is the first human study on DC-based immunotherapy in patients with mesothelioma," wrote Joachim G Aerts M.D., Ph.D., a pulmonary physician at Erasmus Medical Center in the Netherlands.

The findings have been published online ahead of print publication in the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

The U.S. and other developed countries have prohibited the use of asbestos for decades, but the time between asbestos exposure and diagnosis of mesothelioma can up to 50 years. The incidence of mesothelioma, therefore, is still on the rise and expected to continue to increase until 2020. Once diagnosed, mesothelioma has a median survival time of 12 months. The standard chemotherapeutic treatment only improves survival time by about three months.

The anticipated increase in the incidence of mesothelioma, together with the paucity of treatment options, has spurred considerable interest in the development of new therapies. Immunotherapy, which uses the body's own immune system to target and destroy cancer cells, has been shown

to have some promise.

"The possibility to harness the potency and specificity of the immune system underlies the growing interest in cancer immunotherapy," said Dr. Aerts. "One such approach uses the patient's own DC to present tumor-associated antigens and thereby generate tumor-specific immunity."

Building upon their previous research which demonstrated that DC vaccinations induced anti-tumor immunity and conferred a survival benefit in mice, Dr. Aerts and colleagues sought to test the clinical relevance of their finding. After recruiting 10 human patients recently diagnosed with malignant pleural mesothelioma of the epithelial subtype, they cultured immature DC from their blood and exposed the DC to the antigen produced by the patients' tumors. The DC were also exposed to keyhole limpet hemocyanin (KLH), which was used as a surrogate marker to show an immune response. The DC were then matured and injected back into the patients in three doses over a two-week interval.

Serum samples from all patients showed a significant increase of pre- versus post-vaccine antibodies to KLH. In the four patients whose tumor material was sufficient for testing, there was clear induction of cytotoxicity against their own tumors after vaccination. Three patients showed signs of tumor regression, though this could not be conclusively or directly attributed to the vaccine.

Encouragingly, while eight of the patients developed flu-like symptoms in response to the vaccinations, the symptoms normalized after one day in all but one of the patients. There were no signs of autoimmune diseases in the patients provoked by the vaccination, nor other serious side effects.

"The major problem in mesothelioma is that the immunosuppressive

environment caused by the tumor will negatively influence our therapy so we are now working on a method to lower this immunosuppressive environment," said Dr. Aerts. "We hope that by further development of our method it will be possible to increase survival in patients with mesothelioma and eventually vaccinate persons who have been in contact with asbestos to prevent them from getting asbestos related diseases."

Provided by American Thoracic Society