Promising developments in early diagnosis and treatment of mesothelioma

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New results presented at 3rd European Lung Cancer Conference in Geneva, Switzerland show important steps being made to improve the diagnosis and treatment of malignant pleural mesothelioma, an aggressive cancer of the outer lining of the lungs caused by asbestos exposure.

Micro RNAs speed diagnosis

Australian researchers have identified a small molecule that is more abundant in the blood of people with the deadly lung disease mesothelioma than in healthy people. Their findings bring scientists a step closer to being able to diagnose mesothelioma earlier than is currently possible.

At present diagnosing mesothelioma depends on the availability of a lung biopsy that contains enough tumor tissue. However suitable biopsies are not always available, which can leave doctors uncertain about the patient's diagnosis, sometimes resulting in a delay to the start of treatment. "If doctors could use a diagnostic marker based on a simple blood test to help with diagnosis, it could circumvent the problem of availability of tumor tissue and help to accelerate the diagnostic process," says Dr Michaela Kirschner from the Asbestos Diseases Research (Concord Hospital Campus) in Sydney, who reported the new findings.

So far a number of proteins have been proposed as blood-based markers for malignant pleural mesothelioma; however none of these has so far reached the accuracy required for routine clinical use.

In the new study, Dr Kirschner and colleagues explored whether molecules known as microRNAs in blood could serve as a diagnostic marker for the disease. Studying 5 patients with malignant pleural mesothelioma and 3 healthy controls, they identified 17 microRNAs with significantly differential abundance in the two groups. They then validated these miRNAs in a series of blood samples from 15 patients and 13 controls. These studies revealed that the level of a particular microRNA known as miR-625-3p was four-fold higher in the blood of mesothelioma patients.

Measuring levels of that molecule in blood samples allowed the researchers to discriminate between MPM patients and controls with an accuracy of 82.4%.

"Detailed analyses of our two independent sample series have shown that miR-625-3p performs as well as any previously proposed protein marker for detecting mesothelioma," Dr Kirschner said. "However, like most diagnostic markers, miR-625-3p is not 100% accurate, and therefore there is a chance the assay will produce both false positives as well as false negatives. Further studies on larger sample sizes are needed to see whether the accuracy of miR-625-3p can be confirmed or even turn out to be better than currently observed."

"Should further studies prove that microRNAs in plasma are accurate enough for the diagnosis of malignant pleural mesothelioma, this will lead to the development of a diagnostic test for routine clinical use," Dr Kirschner said. "This test would then represent a relatively simple way to circumvent the problems associated with obtaining a tissue biopsy. For a patient this would mean that appropriate treatment could be instituted at

an earlier stage."

High-dose radiotherapy gives good response rates

Despite a widespread belief that mesothelioma does not respond to radiotherapy, Australian researchers have found that it may have the best response rates of any single treatment for patients with disease largely confined to one side of the chest.

Between 2003 and 2011, Dr Malcolm Feigen and colleagues from Austin Health Radiation Oncology Center in Melbourne gave radiotherapy to 45[1] patients aged 45 to 74 with doses of between 45 and 60 Gy to one side of the chest over six weeks. The radiation was administered using 3D-conformal or intensity-modulated radiotherapy. None had surgery to remove their affected lung. At the beginning of treatment more than 80% of patients had the more advanced stage III or IV disease, and all had prior chemotherapy and/or surgery, except for two.

The median survival for the patients was 12.4 months from starting radiotherapy, ranging from 2 to 87 months, the researchers say. There were no life-threatening or fatal toxicities from treatment.

"Many believe mesothelioma to be radioresistant and that toxicity is prohibitive if high doses are given with the affected lung in situ," Dr Feigen and colleagues say.

"Our experience provides clear evidence that radiation is arguably the most effective single agent for mesothelioma and new technologies including intensity-modulated radiotherapy allow high doses to be delivered safely."

Blood markers identified

Swiss, Italian and US researchers report that they have tested another group of potentially useful blood markers for mesothelioma.

Dr Ferdinando Cerciello from the Swiss Federal Institute of Technology and the University Hospital Zurich and colleagues studied 56 candidate biomarker peptides that they isolated from laboratory samples of mesothelioma and tested in the blood of patients with mesothelioma, healthy donors and non-small-cell lung cancer patients.

The study "revealed potential candidate biomarkers in serum, accessible simultaneously by mass spectrometry," the authors report. At the meeting, they will report the strategy for the selection and measurement of their 56 peptides in serum as well as the results of an evaluation in 75 blood samples.

Sorafenib well tolerated

The drug sorafenib is well tolerated in patients with mesothelioma after completion of platinum containing chemotherapy, British investigators report.

In a phase II trial of sorafenib following first-line chemotherapy in 53 patients with malignant mesothelioma, 34% of patients were progression-free after six months.

Dr Sophie Papa and Dr James Spicer from Kings College London and colleagues say that the drug was well tolerated and offered a length of progression-free survival that "compares favorably" to other targeted agents in this disease.

"Mesothelioma, one of the most important occupational diseases, is attracting more and more attention nowadays," noted Prof Paul Baas from the Department of Thoracic Oncology at The Netherlands Cancer

Institute, member of the ESMO Chest Tumors Faculty Group. "New developments in the diagnostics and treatment of this disease are really important, including those presented during the ELCC 2012 meeting: improvements in the diagnosis by simply measuring biomarkers in peripheral blood samples will identify patients who may be candidates for new studies or financial reimbursement by their employers. The developments in molecular biology allow us now to detect circulating fragments of (micro)RNA and peptides that may play an important role. Furthermore the understanding that radiation therapy and targeted agents can be given to these patients will lead to new, promising, studies."

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