SUMMARY OF THREE TALKS PRESENTED TO AMMF AT IMPERIAL COLLEGE LONDON, ON 12 MARCH 2010, OUTLINING THE PROGRESS OF CHOLANGIOCARCINOMA RESEARCH WORK THE CHARITY IS HELPING TO FUND

1. Epidemiology, Diagnosis and Proteomic Profiling in Cholangiocarcinoma, Dr Shahid Khan

Dr Khan is interested in finding a new method for diagnosing cholangiocarcinoma earlier than is currently possible.

Cholangiocarcinoma is the second most common primary liver cancer and has a very poor prognosis. Worryingly the number of deaths from the disease is increasing, for example from 36 in the UK in 1968 to 1003 in 2004, an increase of 30 fold. Furthermore, cholangiocarcinoma is extremely difficult to diagnose. Disease is often identified too late for surgery and currently there are no other effective treatments. Dr Khan emphasises that earlier diagnosis may be the key to increasing survival from this disease.

A diagnosis of cholangiocarcinoma is made after finding particular tumour markers in the blood, however the same markers can also indicate the presence of several different cancers and even non-cancerous bile duct disease.

In the study presented, Dr Khan tried a new method to identify different tumour markers to diagnose cholangiocarcinoma more accurately. Blood from 10 people with cholangiocarcinoma was investigated for new tumour markers of interest and compared to that from 9 people with gall bladder stones. Dr Khan found that levels of several new protein markers were different between the two patient groups allowing reliable differentiation between cancerous and non-cancerous bile duct disease.

In the future this work may pave the way for a new, faster and more accurate method to diagnose cholangiocarcinoma.

2. Genetic Factors in Cholangiocarcinoma, Dr Chris Wadsworth

Dr Chris Wadsworth is trying to find answers to two of the biggest questions relating to cholangiocarcinoma: Why do people get it? And, are some people genetically predisposed to it?

It is known that disorders which cause long-term inflammation of the bile ducts, including liver fluke infection and chronic liver disease are associated with about 20% of cases of cholangiocarcinoma, but that leaves 80% of cases with no apparent cause.

Some parts of bile itself are harmful when exposed to the cells lining the bile duct and can cause damage resulting in inflammation. Usually these harmful bile salts are wrapped up into parcels, or micelles, with other ingredients including cholesterol, so as to protect the vulnerable bile duct cells. However, if the proportions of bile ingredients are wrong some harmful bile salts are left unwrapped.

It has been suggested that people with cholangiocarcinoma may have genetic mutations leading to differences in their bile composition. In the study presented, the largest of its kind, Dr Wadsworth looked at DNA from 173 patients with cholangiocarcinoma and compared it to DNA from 265 similar but healthy people.

He found that people with cholangiocarcinoma were significantly more likely to have a genetic difference leading to reduced secretion of the bile ingredient phosphatidylcholine, thus causing a change in the overall bile composition. Interestingly this genetic mutation is also associated with increased risk of accumulation of toxic bile products in pregnancy.

Although future work is needed to confirm this finding, this work suggests that people who get cholangiocarcinoma may be predisposed to make a type of bile which causes irritation and inflammation in the bile duct thus increasing the likelihood that cancer will develop.

Comment regarding the above two studies from Dr Shahid A Khan, Clinical Senior Lecturer & Consultant Physician, Department of Medicine, Imperial College London:

"Support from AMMF directly funded the preliminary study of proteomic profiling in bile, the results of which formed the basis of a successful application for a substantial British Liver Trust Research Award for us to take these studies to the next level and investigate in larger numbers of patients.

AMMF support also directly paid for much of the genetic analyses carried out by Dr Wadsworth. The final results will be used in a major project grant application to the Medical Research Council.

These two studies would not have been possible without AMMF support and we are very grateful."

3. Microcoil Development for Biliary Imaging, Dr Chris Wadsworth

Currently, diagnostic imaging of the bile duct is difficult because the ducts are small and hidden deep inside the body. In the second of his talks, Dr Wadsworth introduced his solution to this problem: a tiny imaging probe placed within the bile duct itself.

MRI is the best way to make images of the body's soft tissues, but this technique is unable to provide images of a good enough resolution to diagnose bile duct abnormalities. Part of the problem is that the detector is too far from the site of interest. To overcome this problem, Dr Wadsworth and colleagues at Imperial's Department of Electronic Engineering have developed an MRI detector probe that sits directly inside the bile duct. The proximity of the probe to the site of interest massively increases the resolution of the images achieved compared to conventional MRI. To date the probe has been tested inside various isolated organs including liver, pancreas and kidney, as well as a sardine!

Next the group hope to use the probe to look at the oesophagus and bile ducts in living patients. The potential diagnostic benefits of such a tool are clear.

AMMF has helped fund this project, and will continue to do so.

We are grateful to Dr Ruth Corrigan MA (Cantab), for her kind help in the technical translation of these talks.

AMMF
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