

Treatment of liver cancer

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A few days ago, he visited Bangladesh and was kind enough to share a few words about the treatment of liver-centric diseases, alongside some good advice on how to maintain healthier lifestyles to prevent such diseases.

What are the main causes of liver cancer?

First of all, there are two categories of liver cancer — primary liver cancer and secondary liver cancer. Primary liver cancer arises from the liver cells itself. It is the result of chronic liver injury such as chronic viral hepatitis B, or hepatitis C. It can be caused by fatty liver, which is related to diabetes, and cirrhosis caused by excessive drinking of alcohol. These are potential risk factors.

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer. HCC occurs most often in people who are carriers of hepatitis B, or hepatitis C infection.

Secondary liver cancer arises from cancer that originates outside the liver. Most often, it is either colorectal, lung, or breast cancer, which ultimately spreads to other organs



like the liver. Treatment of this type of cancer is dependent on the primary organ from where the cancer spreads.

Other rare causes of liver cancer are those related to hereditary diseases.

Has there been any recent breakthroughs in treatment?

There have been some interesting breakthroughs in the last couple of years. Liver cancer is a challenging illness to fight against, as the majority of its patients are in Asia, mostly the poor, and until recently there was very little interest from the pharmaceutical industry.

Appropriate treatment of HCC is dependent on the stage at which the cancer is diagnosed. Surgery is potentially curative in early stage HCC. There have also been breakthroughs in the treatment of intermediate and advanced stages of the cancer.

In the intermediate stage, yttrium-90, a radioactive nuclide coated in tiny spheres, is introduced via a catheter, which takes it from the artery to the tumour. This has the potential of downstaging it thus making it possible for surgical resection.

Liver cancer is often diagnosed in the intermediary stage, as there are no conspicuous symptoms in the earlier stages. Vague symptoms, like loss of appetite and malaise, exist.

In the advanced stage, there is systematic therapy, as the cancer cells can potentially be in many parts of the body. The cancer has spread in the bloodstream, making leeway to the entire body. Immunotherapy is a very promising new therapy.

How is liver cancer approached from a doctor's perspective?

Liver cancer is one of most prevailing forms of cancer in the world today. Its preventive measures need to be taken seriously with treatment if necessary. It is seen from a multi-disciplinary approach — involving medical and radiation oncologist, nuclear medicine physician, surgeon, and interventional radiologist.

How viable is the idea of liver transplant?

Liver transplants are done when the liver is not functioning well, and the best outcome occurs when it is carried out for HCC in the early stage. The rate of survival for both resection and transplant is the same in early stage HCC. Surgery is however only possible if the liver function is good. Otherwise, transplant is an option.

What are the dietary and lifestyle habits we should follow/avoid to maintain a healthy liver?

Alcohol, which causes cirrhosis, should be avoided. Hepatitis B and C are transmitted in multiple ways — sexual intercourse, sharing needles, sharing toothbrushes, etc. Hepatitis B is genetic in some cases as well, and that is called vertical transmission.

If the mother is a carrier of hepatitis B, the child must be vaccinated at birth. There should be strict diet regulation and exercise to reduce the risk of fatty liver. It also helps to avert the risk of diabetes. High carbohydrate intake increases the chances of having fatty liver.

Fitness should always be a high priority, and for that, proper diet plan should be implemented with regular exercise. Given that time for exercise is short for many, the focus on diet should be at the 80 percent threshold, and the rest for exercise.

What preventive measures can be taken?

When it comes to primary liver cancer, it is best to avoid the risk factors stated above. This is the primary prevention.

The secondary prevention is that known carriers of hepatitis B must receive treatment and go for regular blood screening and imaging every six months.

Those diagnosed with hepatitis B are more prone to liver cancer, and screening must involve two modalities — ultrasound and alpha-fetoprotein. Both should be used in case there is a chance of false reading. Crosschecking should be done.

By Israr Hasan

New light on an existing therapy

Two landmark studies led by SingHealth researchers show interesting new findings on a liver cancer therapy that has been in use for more than a decade.

The therapy — Y90-SIRT — refers to Selective Internal Radiation Therapy (SIRT) with yttrium-90 (or radio embolization), which is a way of controlling the growth of liver cancers too advanced to be removed by surgery at the time they were diagnosed.

The two studies were led by researchers from the National Cancer Centre Singapore (NCCS). The first study was a 27-centre, randomised controlled study in 11 Asia-Pacific countries. Randomised controlled trials provide the highest form of clinical evidence in medicine, known as level 1 evidence, because it compares two treatments under highly controlled conditions.

The study confirmed that the therapy is efficacious and safe for patients with locally advanced liver cancer, while the second study uncovered additional mechanisms that explain why it works so well.

The six-year randomised controlled study, which involved 360 patients, showed significant tumour regression and higher safety with Y90-SIRT compared to available oral cancer therapy.

"Tumour regression is important,

as this potentially allows patients with locally advanced liver cancer to eventually be treated with liver resection or transplantation, which are curative modalities in early-stage liver cancers. Most liver cancer patients in Singapore are diagnosed with locally advanced cancers," said Professor Pierce Chow, Senior Consultant, Division of Surgical Oncology, NCCS, who initiated both studies.

The findings were published in leading cancer journal, *Journal of Clinical Oncology* earlier this year.

While this clinical trial confirmed that the therapy leads to good response in patients and is safe, it is the second study that explains the molecular mechanisms behind the good outcomes.

"These findings represent new advancement in the knowledge and treatment of liver cancer. They have provided us with strong scientific data that confirms and explains why this therapy works," said Prof Chow. SingHealth currently has the most experience with this therapy in the Asia-Pacific after having treated almost 500 cases.

Therapy has fewer side effects

Y90-SIRT, which delivers radioactive micro beads directly into tumours through the blood vessels leading to tumours, causes fewer side effects than Sorafenib, an oral drug for liver cancer.

Prof Chow cited the case of a patient in his '70s with an 8 cm tumour in his liver. Two weeks after the Y90-SIRT therapy, apart from a loss of appetite, he could carry on with his daily activities.

Six months later, his tumour had shrunk by half and he was downstaged to early-stage liver cancer. His cancer was subsequently resected and he remained well.

"The side effects of the standard oral cancer therapy drug include skin peeling, tiredness, diarrhoea, and so forth. But the side effects of Y90-SIRT were fewer and milder. It is a less toxic drug, and over a six-month period, the patient survival rate was much higher," said Prof Chow.

While Y90-SIRT has been used for more than a decade, level 1 evidence was only available in 2017 through the NCCS-led SIRveNIB Asia-Pacific study and the European SARAH study, which was conducted at the same time with a study design based on the Asia-Pacific one. Both studies have since been published.

The second study results

The second study found that in addition to killing cancer cells through radiation, Y90-SIRT also boosts the body's immune system, which leads to long-lasting effects.

Results, published in leading scientific journal *Gut* this year, showed that Y90-SIRT

enhanced the body's immune system to fight cancer.

Dr Valerie Chew, Junior Principal Investigator, SingHealth Translational Immunology Institute, and lead author of the study, said the Y90-SIRT therapy activates immune cells to attack cancer.

"We discovered that immune cells in the body that can fight cancer are enriched in patients who had the therapy," she said.

The discovery is important when seen in the context of immunotherapy, a treatment that harnesses the body's immune systems to recognise and attack cancer cells. But how well patients respond to immunotherapy can be limited by the number of immune cells they have. If the number of immune cells is low, even with immunotherapy, cancer treatment might not be effective.

Dr Chew said this suggests that the Y90-SIRT treatment, which induces an increase in immune cells in patients' bodies, may work very well in combination with immune-therapy.

"Y90-SIRT in combination with the existing immunotherapy may enhance the immune response in patients," she said.

The article has been re-printed from the November/December 2018 issue of Singapore Health, the flagship publication of the SINGHEALTH DUKE-NUS ACADEMIC MEDICAL CENTRE.