Case report: on the benefits of screening – hepatocellular cancer complicating hepatitis C

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INTRODUCTION

A middle-aged man was referred from general practice with deranged liver function tests (alanine aminotransferase 310 IU/L, alkaline phosphatase 114 IU/L, gamma-glutamyl transferase 430 IU/L, bilirubin 16, total protein 88g/L and albumin 44g/L). He had previously lived elsewhere and had been diagnosed with the hepatitis C virus in 1994. The infection was genotype 1B, and at the time of diagnosis an ultrasound scan (USS) and biopsy of the liver were taken, which both confirmed advanced stage liver cirrhosis. At the time of diagnosis, he was eligible for, and opted to have, treatment which consisted of daily ribavirin and thrice-weekly alpha-interferon. However, despite an incomplete course of treatment, due to non-response, he was placed on surveillance.

At the time of his new patient clinic review, he was on no medications, had no allergies, was an ex-smoker, and teetotal. On examination, he was haemodynamically stable and there were no stigmata of chronic liver disease.

With the agreed intention of treating him, there was a need to determine his infective status. His screen for hepatitis C antibodies was positive and his hepatitis C polymerase chain reaction 5,000,000iu/ml: consistent with viraemia and active infection. Alpha-fetoprotein was raised at 181ng/ml and a repeat liver USS reported no cirrhosis and no liver nodules. He was commenced on peginterferon 150mcg weekly and ribavirin 600mg twice daily.

During the course of treatment, he developed an interferon-induced neutropenia and the treatment was halted temporarily. Despite the treatment pause he responded well, which was evidenced by the fall in his viral load to 788,000 iU/ml.

Figure 1. Ultrasound scan of liver showing coronal section through liver and large hepatoma. Coarse echotexture consistent with cirrhotic change

After ten weeks of treatment, he began to experience insufferable headaches, nausea and fatigue, and therefore was unable to tolerate continuation of the treatment. At this stage, he was placed on annual clinic review with six-monthly interim checks on his alpha-fetoprotein in general practice. Interim alpha-fetoprotein was not conducted and one year later it was still raised at 200.1ng/ml. Figures 1 and 2 show the result of the corresponding USS of his liver.

Figure 2. Coronal section through liver on ultrasound showing multiple low-density lesions in the liver

He then had a computed tomography (CT) staging scan, which showed multifocal arterially enhancing liver lesions with rapid washout. These features are consistent with a multifocal hepatocellular carcinoma. He was referred and discussed at a regional multidisciplinary team hepato-biliary unit. He was diagnosed with multifocal hepatocellular carcinoma (HCC), without vascular invasion and without extra-hepatic disease. There were eleven lesions in total and the consensus was for five courses of transcatheter arterial chemoembolisation (TACE) as he was not suitable for liver grafting. He has now completed his course of cisplatin-based TACE and is doing remarkably well. He continues under active follow-up at the regional centre.

DISCUSSION

Hepatitis C is a common infection affecting males more than females. More than 50% of cases are encountered between the ages of 25-44 years.⁽¹⁾ It is described as a major health concern in the UK with between 200,000-400,000 infected individuals.⁽¹⁾ There are reported to be 170 million cases worldwide.⁽¹⁾ The most common presentation is with chronic carriage and can manifest as either chronic liver disease, cirrhosis and/or HCC. It is an RNA virus and its usual mode of transmission is parenterally, especially in blood products prior to 1991, intravenous drug users and unsanitary tattoos.

There are six genotypes that exist, the most common being type 1 which accounts for 40-60% of all hepatitis C infections and is the most difficult to clear.⁽¹⁾ If the diagnosis is suspected, this is confirmed by an ELISA hepatitis C virus antibody, which if positive requires an estimation of the viral load to be made.⁽¹⁾ This is conducted via hepatitis C PCR, which is indicative of active viraemia if greater than or equal to two million copies per ml.⁽¹⁾ Liver biopsy is then indicated to ascertain the extent of liver inflammation, fibrosis and cirrhosis. Then lastly, in order to direct treatment course, genetic testing must be conducted. Treatment license lies with peginterferon and ribavirin in combination, and duration is dictated by genotype: type 1, 12 months; and types 2 and 3, six months.⁽¹⁾

For a certain proportion of those with chronic type 1 hepatitis C infection, the NS3/4A serine protease inhibitors boceprevir or telaprevir can be administered, in conjunction with peginterferon and ribavirin. Licensing is restricted towards those who are either previously untreated or have experienced treatment failure.^(2,3) The cost implications are up to £2,800 for 28 days' treatment and up to £30,800 for a full 44 weeks' course. In comparison, the full course of peginterferon and ribavirin alone can cost up to £11,000, this value being additive to the cost of the protease inhibitors.^(2,3) There is data to suggest that combined there is greater efficacy.^(2,3)

For a proportion of those with chronic carriage of hepatitis C infection, HCC will develop. HCC is one of the most common malignant diseases worldwide.⁽⁴⁾ It is reported to cause 1,500 deaths a year in the UK.⁽⁴⁾ Worldwide, the prevalence of HCC parallels that of hepatitis C and B infections.⁽¹⁾ Other risk factors in the development of HCC are excess alcohol consumption, haemochromatosis and, rarely, primary biliary cirrhosis.⁽⁴⁾

As with hepatitis C, more males are affected than females. In the UK, the mean age is 66 years and it is, in fact, rare below the age of 45 years.⁽⁴⁾ Cirrhosis is associated with up to 95% of cases of HCC and formerly was a contraindication to treatment. HCC develops as small nodules taking many years to grow.⁽⁴⁾ The doubling times are estimated between 1-19 months, with a median of six months.⁽⁴⁾ The HCC data on survival suggests a hampering owing to both the severity of the underlying liver disease and the tumour size at initial detection. Another consideration in survival is that a proportion of these patients are asymptomatic. This is the realm where screening can assist. Screening is recommended for all alcohol abstinent cirrhotics and consists of six-monthly alpha-fetoprotein and liver USSs.⁽¹⁾ An alpha-fetoprotein >400ng/ml is highly suggestive of HCC, although 20% of these tumours do not

secrete it.⁽⁴⁾ Liver USS has a high sensitivity and specificity for lesions that are 3-5cm in size. If a tumour is detected, then a CT scan is required for staging the tumour.

Treatment options are directed by genetic status, stage and patient preference. Surgical options are only viable if there is a single lesion <5cm, or up to three lesions <3cm.⁽⁴⁾ Chemoembolisation, as utilised in this case, has 63% survival.⁽⁴⁾ It involves the direct delivery of the chemotherapy agent to the site of the tumour and the side effect profile is related to the type of chemotherapy agent used. If the HCC is at the advanced stage, then the targeted multikinase inhibitor sorafenib can be used.⁽⁴⁾

CONCLUSION

HCC is on the increase, as are the hepatitis viruses which lead to it. Some cases are asymptomatic, but for those that can be screened this should occur by means of alpha-fetoprotein and liver USSs. Screening tests are useful but are not absolute, so if the index of suspicion is high enough then consider closer monitoring with more detailed tests. This is a clear case of where a screening system in place has worked to detect cancer earlier than it would have ordinarily been identified. The case reflects the potential dangers of patients, particularly those with high-risk psychosocial factors, being lost to follow-up. Clinicians need to maintain a level of 'ownership' in monitoring, so that we do not lose patients, especially the potentially curative ones, to follow-up.

REFERENCES

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