Medical Report on Mr Victor Tamurrini

By

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MEDICAL REPORT

MR VICTOR TAMBURRINI

Introduction

This report was prepared by Dr Andrew J Bathgate qualified MB ChB (University of Edinburgh) 1991; Fellow of the Royal College of Physicians (UK) 2002; MD (University of Edinburgh) 2000; Certificate of Completion Specialist Training in General Internal Medicine and Gastroenterology 2000; Consultant Physician Royal Infirmary of Edinburgh March 2001 to date. Scottish Representative on UK Transplant Liver Advisory Group.

My clinical interests include all aspects of clinical hepatology, particularly liver transplantation and viral hepatitis.

This report has been based on the clinical records of the Scottish Liver Transplant Unit

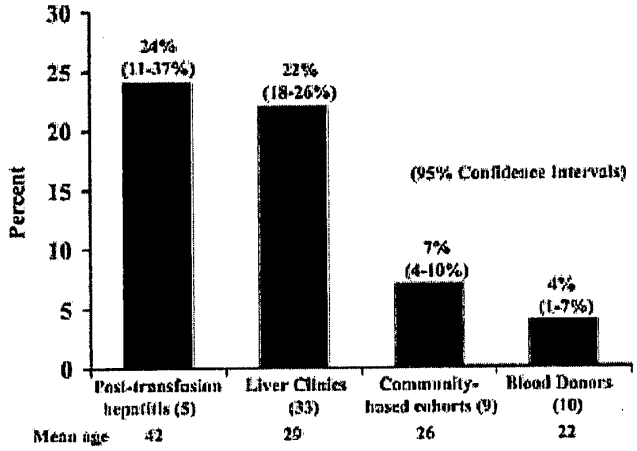
1. Background information about hepatitis C infection
2. Brief summary of medical records
3. Medical Opinion on specific questions asked

Background Information

Hepatitis C is a RNA virus that infects humans. It is transmitted through contact with infected body fluids. The commonest routes of infection are blood product transfusion before 1991 and intravenous drug use. In Scotland the most common route of transmission is sharing needles between intra-venous drug users. In most infections there is no acute illness and the infection is only discovered if a specific blood test is performed. This test first looks for the antibody to the virus and then for the virus itself. If the virus is found then the individual is said to be suffering from chronic hepatitis C infection.

The virus has six major genotypes (strains) of which 3 are commonly found in Scotland. The significance of the genotype is in the response to treatment. Genotype 1 responds less well to treatment than genotypes 2 and 3. The other genotypes 4-6 are rare in Scotland.

The rate at which the liver is damaged by the hepatitis C virus is variable. The virus causes inflammation (hepatitis) and scarring (fibrosis) of the liver. The end-stage of scarring is termed cirrhosis. The rate at which cirrhosis occurs depends on the age of the individual at the time of infection and the route of transmission. The table below indicates the rate of progression to cirrhosis over a period of twenty years.



The main co-factor in hastening progression is alcohol with even moderate amounts contributing significantly to fibrosis progression.

Following the development of cirrhosis the liver may continue to work well for a number of years with only 20% having a significant deterioration in 10 years. Individuals with cirrhosis that is deteriorating (decompensating) are usually considered for liver transplantation if suitable candidates.

Treatment

A small number of individuals get rid of the virus by themselves with time. The rate of spontaneous clearance is greatest in those with symptomatic acute hepatitis and in young females. The rate of clearance varies between studies with studies in the United Kingdom showing rates as low as 3% in 8 years while longer term studies report rates of clearance around 40% at 17 years. The treatments to attempt to improve the

clearance of the virus have developed over the past 12 years or so. The standard therapy at present has been available now for around 5 years and consists of pegylated interferon and ribavirin. Interferon is required to be injected once per week under the skin and ribavirin is an oral medication taken twice daily. Both medications have adverse affects with interferon causing severe fatigue, fever, flu-like illness and depression. Ribavirin causes anaemia by inducing the red blood cells to burst (haemolyse). In most centres this means that around 30% of patients started on treatment fail to complete therapy.

The duration of therapy depends on the genotype (strain) of the virus. Genotype 1 requires 12 months of therapy whereas genotypes 2 and 3 requires 6 months. The response to treatment also varies with genotype 1 being successful in clearing the virus in less than 50% of cases whereas genotypes 2 and 3 are cleared in approximately 80%. Treatment is less effective in individuals with cirrhosis and in the post-liver transplant setting.

Summary of Liver Transplant Notes

February 2002	Referred by Dr Stanley for consideration of liver transplantation as a treatment for his end-stage liver disease related to chronic hepatitis C infection and harmful alcohol misuse. Decision to pursue medical therapy.
August 2002	Re-assessed for liver transplantation as high alphafetoprotein and concern over possible malignancy. Listed for transplant.
October 2002	First liver transplant performed with no evidence of malignancy in explanted liver.
March 2003	Biliary anstomotic stricture stented at ERCP
November 2003	Graft cirrhosis related to recurrent hepatitis C infection diagnosed on liver biopsy.
February 2004	Second liver transplant- indication graft failure related to recurrent hepatitis C infection.
March 2004	Started on therapy for recurrent hepatitis C infection

June 2004	Liver biopsy revealing aggressive recurrent hepatitis C infection
September 2004	Further liver biopsy demonstrating no improvement in graft fibrosis despite hepatitis C therapy.
November 2004	Death from graft failure consequent upon recurrent hepatitis C infection

Specific Questions

1. What is the significance of the reference to Hepatitis C on the death certificate?

2. What are the potential sources of Mr Tamburrini's chronic hepatitis C infection?

Opinion

Recurrent hepatitis C infection following liver transplantation is virtually universal. The rate of progression of this recurrent infection to graft failure is very variable. There is a proportion of around 5-10% that develop a rapidly progressive fibrosis resulting in graft failure within a number of months. The majority of patients however develop a slowly progressive loss of graft function resulting in graft failure after a median of 8 years following transplantation.

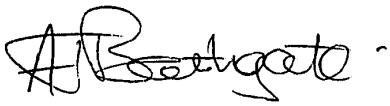
The available treatments for chronic hepatitis C are not as effective following transplantation with approximately 1 in 4 patients responding. There is no doubt that Mr Tamburrini was at the worst end of this spectrum of disease. His first graft failed within 12 months of transplantation and he was re-transplanted a few months later. It was hoped that treatment with pegylated interferon and ribavarin would prevent rapid graft failure with recurrent hepatitis C in the second graft. However this was not the

case and it was not felt appropriate to offer a further transplant as the risk of recurrent hepatitis C leading to graft failure was high.

There is no doubt that Mr Tamburrini's death was related to hepatitis C causing failure of his liver transplant. If he did not have hepatitis C it is more likely than not that he would not have required transplantation and he certainly would not have died from graft failure.

The answer to the second question is not as straightforward. Hepatitis C is a blood borne virus with the only potential source of infection being the infected body fluid of another human being. Throughout Mr. Tamburrini's notes it is indicated that the likely source of infection was infected plasma products following treatment for burns in 1984. This is certainly a potential source if infection but I am unable to comment on the exact risk as it is beyond my area of expertise as to the treatment of plasma products prior to administration to patients. The other common source of infection in Scotland is by way of sharing injecting equipment in the context of intravenous drug abuse. There is absolutely no suggestion in the notes that this was a possible risk factor. Sexual transmission of hepatitis C is not common and again there are no documented reports of this being a potential risk. The blood transfusions administered in 1998 would be an unlikely source of hepatitis C infection as every unit was screened for antibody to hepatitis C at that time. It would also be extremely unlikely from the liver point of view that an infection in 1998 would lead to liver failure four years later even in the context of alcohol as a co-factor.

The source of hepatitis C infection would, in my opinion, be likely to be related to his plasma products administered in 1984. If the expert in this area declares this to be an impossibility then the source would then be unidentified.



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