CASE REPORT

Hepatocellular carcinoma in a patient with chronic lymphocytic leukaemia involving the liver

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SUMMARY

A relationship between hepatocellular carcinoma and chronic lymphocytic leukaemia has been reported. This is a case of a 75-year-old woman with stable chronic lymphocytic leukaemia, not on treatment with an increased activity of serum alkaline phosphatase and negative liver disease work up. A liver biopsy revealed leukaemic infiltration without evidence of cirrhosis or fatty liver. Four years later, she presented with a rapidly progressive liver mass which was diagnosed as hepatocellular carcinoma histologically.

BACKGROUND

This case is important as it confirms the coexistence of two malignancies in one liver, which may identify a common oncogenic pathway between chronic lymphocytic leukaemia and hepatocellular carcinoma.

CASE PRESENTATION

In 2008, a 75-year-old Hispanic woman presented to our hospital for an oncology evaluation. She was previously diagnosed with chronic lymphocytic leukaemia by elevated peripheral blood cell count, also confirmed by bone marrow aspiration and biopsy 4 months prior to this visit. Comorbidities included diabetes mellitus, hypertension, hyperlipidaemia and migraine headaches. There was no family history of malignancies. She denied alcohol and drug use. She denied fever, chills, night sweats, weight loss and abdominal pain. Her weight was 62.1 kg with height of 1.55 m and body mass index was 25.8 kg/m². Examination of the cervical, axillary and inguinal lymph nodes was negative. The liver and spleen were normal in size. Laboratory showed white blood cells of $15 \times 10^9/L$ with no anaemia. Lactate dehydrogenase was normal at 179 U/L (normal 100–190 U/L). Her serum alkaline phosphatase activity ranged from 288 U/L to 440 U/L (normal 50–136 U/L). Lipid profile showed high-density lipoprotein of 91 mg/dL (normal 33–92 mg/dL), total cholesterol of 229 mg/dL (normal 0–200 mg/dL), triglycerides of 87 mg/dL (normal 60–240 mg/dL) and low-density lipoprotein of 121 mg/dL (normal <130 mg/dL). The rest of the laboratory investigations were within normal limits. Viral hepatitis, autoimmune and metabolic liver diseases were excluded. Her MR cholangiopancreatography was normal. Owing to unexplained high level of serum alkaline phosphatase activity, a CT-guided biopsy of the liver parenchyma was performed revealing dense infiltrate of monotonous population of small lymphocytes and

Figure 1 Liver biopsy on H&E staining (x100) showing liver parenchyma with dense infiltrate of monotonous population of small lymphocytes (arrows) without any fatty changes. Immunohistochemical stains were positive for CD20, PAX-5, CD5, CD23, CD43 and BCL-2.

no fatty changes. Immunohistochemical analysis showed positivity for CD20, PAX-5, CD5, CD23, CD43 and BCL-2 consistent with B-small lymphocytic lymphoma/chronic lymphocytic leukaemia (figure 1). She was followed by the oncology service and had serial imaging every 6 months demonstrating intra-abdominal lymphadenopathy, but there was no radiological suggestion of cirrhosis or fatty liver. She did not meet criteria for treatment at this time.

Four years after the diagnosis of B-small lymphocytic lymphoma/chronic lymphocytic leukaemia, as part of a routine evaluation of her intra-abdominal lymphadenopathy, a CT scan of the abdomen showed an 8 cm right lobe liver mass. Two weeks later she presented with right upper quadrant abdominal pain accompanied by malaise, constipation and loss of appetite. Physical examination was notable for submandibular lymphadenopathy and right upper quadrant tenderness. She had no cutaneous stigmata of chronic liver disease.

INVESTIGATIONS

The presence of a liver mass with prior liver histopathology consistent with B-small lymphocytic lymphoma/chronic lymphocytic leukaemia first suggested a rapidly growing lymphoma of the liver; however, a repeat CT-guided biopsy of the new liver mass instead revealed hepatocellular carcinoma. α -Fetoprotein was 3.2 ng/mL (normal 0–10 ng/mL). The tumour size increased to 16 cm within the span of 2 months, occupying the entire

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Figure 2 CT scan showing liver mass with extensive involvement of both right and left lobe. Biopsy of the liver mass showing necrotic hepatic tissue with malignant cells.

right lobe of the liver, with left lobe and portal vein involvement (figure 2).

TREATMENT

Owing to the extent of the hepatocellular carcinoma, the patient was started on sorafenib, which she received for 3 weeks.

OUTCOME AND FOLLOW-UP

The patient's condition deteriorated rapidly. She elected to be placed in hospice care and died 2 weeks later. Postmortem biopsy was not performed.

DISCUSSION

Chronic lymphocytic leukaemia is one of the chronic lymphoid neoplasms characterised by accumulation of incompetent lymphocytes. It is predominantly a disease of the elderly and is considered to be identical to the mature B-cell small lymphocytic lymphoma, an indolent kind of non-Hodgkin lymphoma. Survival ranges from months to decades after the diagnosis and treatment regimens are based on clinical staging and laboratory findings showing disease progression, which our patient had not exhibited over the years of follow-up.

In the absence of known risk factors for developing hepatocellular carcinoma, the question of what could have predisposed this patient to this type of tumour arises. Common oncogenic cellular pathways may contribute to the development of hepatocellular carcinoma and chronic lymphocytic leukaemia. The relationship between non-Hodgkin lymphoma and hepatocellular carcinoma^{1 2} has been published. However, no conclusions can be drawn from these studies as some of the patients reported had serology consistent with prior viral hepatitis infection, which can be associated with both types of malignancies. One report has suggested that non-Hodgkin lymphoma involving the liver may constitute a risk factor for the development of hepatocellular carcinoma however a rationale for this speculation was not provided.³ A common link that may stimulate oncogenic pathways related to both malignancies could contribute to their development. In this context, the extracellular signal-regulated kinase (ERK) pathway has been implicated in the development of both cancers.^{4 5} Additionally, there may be a genetic predisposition for both tumours. Interestingly, sorafenib, an inhibitor of RAF serine/threonine kinase isoforms, which are known to regulate the Raf kinase/mitogen-activated Erk kinase/extracellular signal-regulated kinase (RAF/MEK/ERK) pathway and which is approved for the treatment of

hepatocellular carcinoma is being studied for the treatment of chronic lymphocytic leukaemia because of its proapoptotic properties.⁶ Thus, the possibility exists that sorafenib may be an effective drug for this rare combination of cancers, hepatocellular carcinoma and chronic lymphocytic leukaemia.

Learning points

- ▶ There might be a relationship between chronic lymphocytic leukaemia and hepatocellular carcinoma.
- ▶ Common oncogenic cellular pathways to both malignancies have been suggested to explain this relationship.
- ▶ Non-Hodgkin lymphoma has been described as a possible predisposing factor for the development of hepatocellular carcinoma in the absence of known risk factors. This case further illustrates this possibility.
- ▶ The potential therapeutic effect of sorafenib in chronic lymphocytic leukaemia, and its approved treatment for hepatocellular carcinoma may reveal common oncogenic pathways to both cancers.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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