Journal of Cancer Therapy, 2011, 2, 381-383
doi:10.4236/jct.2011.23052 Published Online August 2011 (http://www.SciRP.org/journal/jct)

Primavist™ in the Diagnosis of Oxaliplatin Induced Sinusoidal Obstruction: A Case Report

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Received April 25th, 2011; revised June 9th, 2011; accepted June 18th, 2011.

ABSTRACT

This is a case report of a patient who underwent Oxaliplatin based neo-adjuvant chemotherapy for colorectal liver metastases, and subsequently developed sinusoidal obstruction, which was detected by Primavist enhanced MRI scan.

Keywords*: *Oxaliplatin, Sinusoidal Obstruction, Liver Injury

1. Introduction

This is a case report of a gentleman who was initially diagnosed with and sigmoid colon carcinoma, and subsequently treated with a sigmoid colectomy in December 2008. Histology of the lesion demonstrated a pT_3N_1 tumour with 3 of 48 lymph nodes positive for metastasis. At the time of operation he was noted to have synchronous liver metastases which were initially deemed to be resectable.

Unfortunately, in February 2009, the patient underwent a repeat CT scan, which demonstrated that new metastases had appeared in the liver, and had made the lesions non-resectable. He was trialled with adjuvant chemotherapy, and demonstrated good response to six cycles of Oxaliplatin based chemotherapy.

A subsequent Primavist MRI scan demonstrated 3 lesions in segment VI and VII, as well as changes consistent with Oxaliplatin related sinusoidal obstruction (**Figure 1**).

These 'Blue Liver' changes were confirmed at operative intervention, where the patients had a segment VI and a partial Segment VII resection. Changes consistent with Oxaliplatin therapy was also demonstrated in the histology specimen obtained (**Figure 2**).

The patient underwent regular follow up, and in January 2010 was found to have a rise in serum CEA of 3.6 compared to 1.3 in December 2009. Repeat Primavist MRI scan demonstrated recurrence in segment II and III, however, the Oxaliplatin based injury had resolved on imaging (**Figure 3**).

The patient underwent curative resection in July 2010, and histology demonstrated changes consistent with fibrosis secondary to Oxaliplatin therapy (**Figure 4**).

2. Discussion

Oxaliplatin is a cytotoxic platinum compound, originally discovered by Professor Yoshinori Kidani at the Nagoya City University. It exerts its action by cross linking DNA strands, thereby, preventing division and replication. It is primarily used in the treatment of advanced colorectal carcinoma which has metastasised to local/regional lymph nodes as part of the FOLFOX regime (Folic acid, 5-FU and Oxaliplatin).

The main side effect of Oxaliplatin is that of neurological impairment, however, it also causes sinusoidal obstruction, leading to the phenomenon of the 'Blue Liver Syndrome' and subsequent nodular regenerative hyperplasia [1]. The presence of sinusoidal obstruction increases the risks of surgery, as the liver is more friable and easily damaged.

This phenomenon has been widely described in the literature. In a case series by Rubbia *et al.* [1], the incidence of sinusoidal obstruction has been demonstrated to be as high as 54% and subsequent nodular regenerative hyperplasia in up to 24.5%. Unfortunately diagnosis is usually only established at laparotomy.

Numerous studies undertaken have endeavoured to highlight any possible indicators that may be used to diagnose whether sinusoidal obstruction is present. Biochemical analyses have potentially yielded some promising results. Soubrane *et al.* [2] demonstrated in their case series that sinusoidal obstruction should be suspected in patients who have a low platelet count or a high aspartate

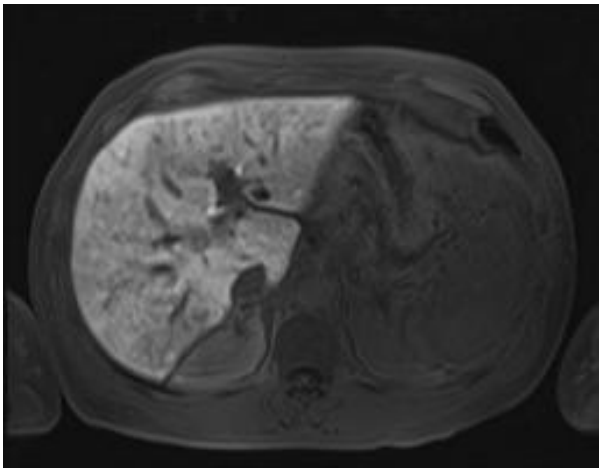

Figure 1. Primavist™ MRI demonstrating post oxaliplatin treatment coarse liver.

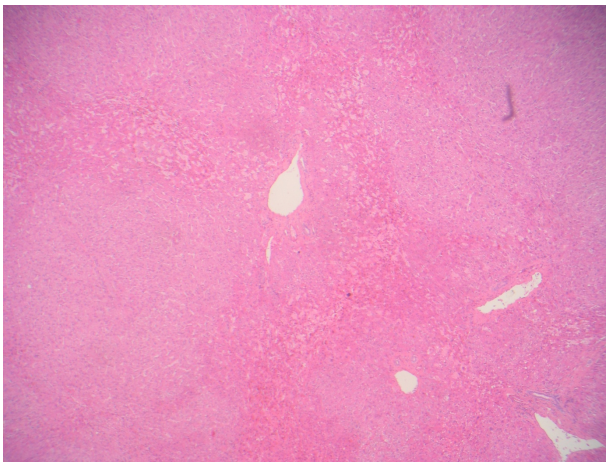

Figure 2. Histology of Oxaliplatin induced liver injury; dilation of the sinusoids and vascular congestion.

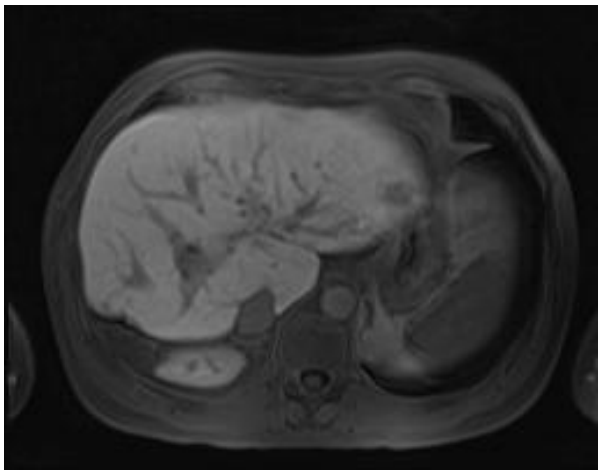

Figure 3. Primavist™ MRI demonstrating resolution of Oxaliplatin induced liver injury.

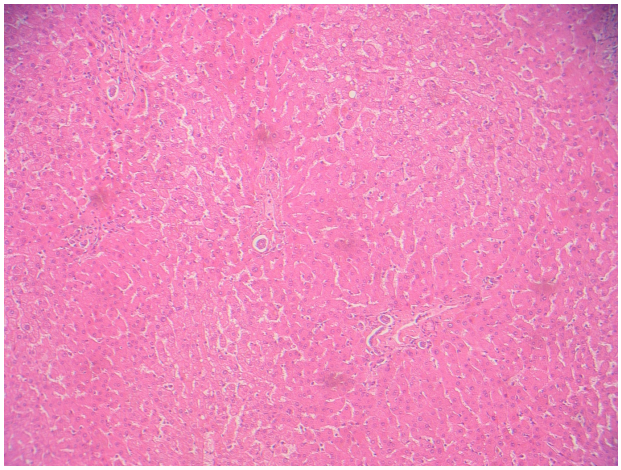

Figure 4. Histology demonstrating resolution of Oxaliplatin induced liver injury.

aminotransferase, leading to a high aspartate amnotransferase to platelet ratio index (APRI). Liver function test monitoring is also corroborated by Arotcarena *et al*. [3], who recommend the monitoring of gamma glutamyl transferase and alkaline phosphatise in diagnosing sinusoidal obstruction.

As in our case report, radiology can be a fundamental role in diagnosis of sinusoidal injury and nodular regenerative hyperplasia. Rha *et al*. [4] demonstrated that in the presence of NRH, spiral CT demonstrates multiple enhancing nodules during the hepatic arterial and portal venous phases. MR images showed multiple hyper-intense nodules on T1-weighted images and hypo/isointense nodules on T2-weighted images.

Simpler radiological tests can be used to establish whether this phenomenon is present. Sinusoidal obstruction may be suspected in patients who develop splenomegaly during the period of the chemotherapy [5]. Elastography [6] has been implicated as a useful tool; a mechanical pulse is generated at the skin surface, which is propagated through the liver. The velocity of the wave is measured by ultrasound. The velocity is directly correlated to the stiffness of the liver, which in turn reflects the degree of fibrosis.

Our patient had a Primovist™ enhanced MRI scan which demonstrated diffuse abnormalities in what was supposed to be normal liver parenchyma during the period of chemotherapy, then after cessation of treatment, the liver was radiologically and biochemically normal.

Primovist™ is a relatively new contrast agent for the imaging of liver conditions, including liver tumours, both malignant and benign. It has demonstrated it is well tolerated with high safety margins [7]. Primovist™ brightens the signal of T1 weighted MR images immediately after contrast administration. The normal hepatocytes

have increased uptake compared to abnormal hepatic tissue and therefore, will have increased the signal intensity of normal liver parenchyma. This results in improved lesion-to-liver contrast because damaged liver parenchyma contains dysfunctional hepatocytes.

This has demonstrated potential for determining patients who have had sinusoidal injury and subsequent resolution, which plays an important role in the timing of operative intervention as sinusoidal injury may complicate operative intervention.

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