neuroimaging was contemplated, but the weight limits for the tables in our CT and MR scanners are 485 lb and 350 lb respectively and the girth of the patient would also have precluded MR imaging. Using a veterinary scanner was considered; however, the nearest one was over 600 kilometres away.

We asked the patient if he could put his head in the gantry while standing and bending forward behind the CT gantry. The patient had been medicated for nausea, and was alert, oriented and very cooperative; he agreed to attempt it. To better enable the patient to do this, we chose the CT scanner which had a narrower gantry (Siemens Sensation 64). We asked the patient to stand behind the CT gantry and place his head into the headrest of the scanning table (Figure 1a). The patient was told about the table movement with the scan, and allowed his head to move with the slow movement of the table. The images were acquired in the caudo-cranial direction, with the patient position designated as face down and leg first. Helical imaging was used to reduce movement artefact.

The images showed minimal motion artefact but were adequate for the diagnosis of haemorrhage in the suprasellar cistern and anterior interhemispheric fissure (Figure 1b), along with a large sellar-suprasellar mass, possibly pituitary macroadenoma, extending towards the left cavernous sinus (Figure 1c). The haemorrhage could be secondary to pituitary apoplexy, or could still be aneurysmal. A CT angiogram was felt necessary to answer this question. The table movement and expected sensation during the CT angiogram was discussed with the patient, and once again he agreed to proceed. The patient was placed in the same position behind the gantry (Figure 1a) and intravenous contrast media was injected to acquire the CT angiogram. Timing had to be estimated. The images were suboptimal due to motion artefact. A possible anterior communicating (ACom) artery aneurysm was suspected, which in retrospect was not present (Figure 1d). The patient underwent left pterional craniotomy and resection of tumor with direct decompression of the optic nerves, optic chiasm, and left oculomotor nerve which was compressed between the skull and the hemorrhagic tumor. The region of the anterior communicating artery was explored intraoperatively and no aneurysm was seen. The third nerve palsy recovered completely.

### Discussion

The current CT and MRI scanners in our institute have a weight limit of 485 lb and 350 lb respectively. With the increasing incidence of obesity in North America, we require new imaging solutions for patients who exceed these limits. A mobile CT scanner or an open MR scanner may be an option in these patients. Manufacturers may also consider making scanners with a mobile gantry and static patient table in the future. These will be useful even in injured or unconscious patients who are not able to stand. In cooperative patients who can stand, our method can be used with any existing CT scanner to obtain a plain head CT as well as more elaborate imaging such as CT angiogram of the head. Similar technique has been previously reported in the literature where only plain head CT was done using the standing technique.[1]

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### Reference

1. Goldsmith P, Patel A, Farmer R, Wright G, Brown J. A novel technique for CT imaging the brain of the obese patient. Clin Radiol. 2008 May;63(5):575-6.

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### To the Editor

## Chemotherapy-Associated Steatohepatitis with Temozolomide and Dexamethasone

The addition of temozolomide (TMZ) to the therapeutic armamentarium of glioblastoma multiforme (GBM) over the past decade has been a significant clinical advance. Used concurrently with radiation therapy and adjuvantly thereafter, TMZ is a well-tolerated oral therapy which provides meaningful clinical and survival benefits in patients with GBM. As TMZ has been associated with hepatotoxicity, oncologists commonly monitor liver function tests (LFT's) as a surrogate marker of liver health. Occasionally, dose reductions and/or brief drug holidays are required in order to reverse the transaminitis and potentially permanent hepatic dysfunction.[1]

The most severe forms of chemotherapy-induced liver injury can manifest as either steatohepatitis or vascular sinusoidal damage. The histologic pattern of injury in chemotherapy-associated steatohepatitis (CASH) resembles findings in non-alcoholic steatohepatitis (NASH), a form of steatohepatitis described in patients with obesity, dyslipidemia and diabetes. To date, CASH has been mainly characterized in colorectal cancer, where pre-operative irinotecan was associated with a 20% incidence of steatohepatitis.[2] In this report, we present the first known description of CASH attributable to concurrent TMZ and dexamethasone use in a patient with GBM.

### Case History

A previously healthy 46-year-old male, who took no regular medications, presented with progressive word-finding difficulties and dysgraphia. Family history was remarkable for type 2 diabetes mellitus and a history of GBM diagnosed in his father. Physical examination was unremarkable, and revealed a

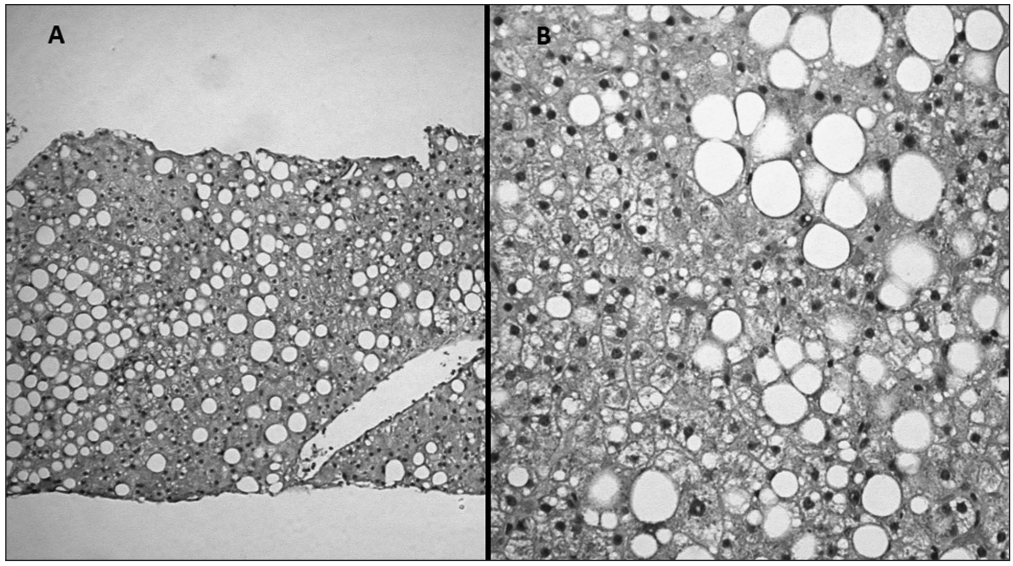


***Figure:*** *Histology of liver biopsy (H&E stain). A) demonstrates macrovesicular steatosis involving more than 80% of hepatocytes. (10 x). B) demonstrates hepatocyte ballooning. (20 x).*

well-appearing male with a weight of 111.4 kg. Brain magnetic resonance imaging (MRI) revealed a left parietal lesion. The patient underwent a subtotal resection of the parietal mass on May 3, with pathology consistent with GBM. Post-operatively, the patient was started on dexamethasone 12 mg daily, which was gradually tapered down to 4 mg daily. Within four weeks of surgical resection, the patient commenced concurrent chemoradiotherapy (CRT) with low-dose daily TMZ as per routine protocol, from June 6 to July 11.

One month following the completion of CRT, the patient presented with confusion, expressive aphasia and new frontal headaches. The dexamethasone dose was increased from 4 mg to 8 mg daily, and the patient was started on the first cycle of adjuvant TMZ at a standard dose of 150 mg/m$^2$, on Days 1-5 every 28 days. On Day 14, the patient's dexamethasone dose was increased to 12 mg daily because of recurring headaches, ongoing aphasia and confusion. By the end of the first cycle (September 12), he reported improvement in his headache but worsening comprehension and proximal motor weakness. For cycle 2, the TMZ dose was increased to 200 mg/m$^2$ on Days 1-5 every 28 days as per protocol, and his dexamethasone was further increased to 16 mg daily. Although the treatment was well-tolerated, by the end of cycle 2, he developed worsening motor weakness and a new liver transaminitis. Further TMZ administration with cycle 3 was held. The pattern of liver enzyme abnormalities is outlined in the Table. A tentative diagnosis of steroid-induced proximal myopathy was made, and the dexamethasone dosage was decreased to 12 mg PO daily (on

**Table: Temporal relationships between liver panel and drug administration (reference values in brackets)**

| Date | Aug 17 | Sept 12 | Oct 11 | Oct 18 | Oct 31 | Nov 17 | Nov 22 | Nov 28 | Dec 2 |
|---|---|---|---|---|---|---|---|---|---|
| ALT (1-60 U/L) | 60 | 122 | 355 | 290 | 314 | 220 | 204 | 138 | 134 |
| ALP (30-145 U/L) | 56 | 56 | 83 | 95 | 147 | 140 | 161 | 143 | 136 |
| Bilirubin total (0-24 umol/L) | 5 | 4 | 13 | 11 | 13 | 13 | 13 | 9 | 9 |
| AST (8-40 U/L) | 26 | - | - | - | - | 102 | - | 71 | 42 |
| Temozolomide (mg/m$^2$) | 150 | 200 | - | - | - | - | - | - | - |
| Dexamethasone (mg) | 8 | 16 | 16 | 16 | 16 | 12 | 8 | 4 | 4 |



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November 1). Bloodwork also identified fasting hyperglycemia, and insulin therapy was eventually instituted (December 1).

Just after the end of cycle 2 (October 18), an abdominal ultrasound was performed which identified increased hepatic echogenicity consistent with fatty infiltration, with no evidence of focal abnormalities or biliary duct dilatation. An ultrasound guided liver biopsy was performed on November 8. Pathologic examination revealed severe steatohepatitis, consistent with CASH. Severe steatosis (grade 3) was seen to involve more than 80% of hepatocytes. Lobular inflammation, moderate hepatocellular ballooning, and mild zone 3 perisinusoidal fibrosis were also identified. Liver biopsy pathology is shown in the Figure. Following pathologic confirmation, the Hepatology service was consulted regarding management recommendations. Temozolomide was continued to be held, a dexamethasone taper at a rate of 2 mg every three days was undertaken, and vitamin E 800 IU daily and ursodeoxycholic acid 1250 mg daily were added. Over a course of several weeks, the patient's liver enzymes, fatigue and cognitive status gradually improved, and on December 9, the patient was re-started on a reduced dose of TMZ (75 mg/m$^2$) for a delayed treatment cycle 3, in conjunction with dexamethasone 4 mg daily.

## Discussion

To our knowledge, this case report represents the first described case of CASH in the setting of GBM associated with TMZ and dexamethasone use. Chemotherapy-associated steatohepatitis appears pathologically identical to NASH in which both pathological entities are characterized by steatosis, lobular inflammation, and hepatocyte ballooning. Non-alcoholic steatohepatitis is hypothesized to arise pathophysiologically as a result of two separate insults with a similar process likely responsible for the development of CASH.[3] It is postulated that the first hit results in steatosis, with the second resulting in hepatic inflammation and fibrosis.[3] In the current case, it is likely that both TMZ and dexamethasone played a complementary role in the development of CASH. Although corticosteroids have not been shown to be an independent causal factor, dexamethasone is known to aggravate underlying NASH by inducing microvesicular steatosis and fat deposition.[3] Hepatic inflammation may be related to chemotherapy-induced oxidative stress and production of reactive oxygen species through mitochondrial dysfunction.[3] The temporal relationship between elevated LFT's and systemic treatments provide some insight into this particular case. The liver enzyme abnormalities first manifested after the patient was started on adjuvant TMZ. Corticosteroids are known to play a role in exacerbating underlying NASH, and the patient was on a high dose of dexamethasone at that time. However, this was likely not the only factor since the patient had been on similar high doses of corticosteroids without LFT elevations. Taken together, it is postulated that TMZ most likely precipitated the development of CASH, which was further potentiated with the use of dexamethasone.

Two pharmacologic interventions were instituted for CASH in this patient, consisting of vitamin E and ursodeoxycholic acid, the latter a bile acid modulating agent. In NASH, vitamin E and ursodeoxycholic acid have been shown to result in improvements in biochemical profiles.[4,5] However, neither have been shown to be of benefit in terms of fibrotic changes in the liver.[4,5] In this case, a decrease in liver enzymes occurred after initiating vitamin E and ursodeoxycholic acid. However it is important to note that the decrease in liver enzymes had already begun to occur after stopping TMZ and reducing the dexamethasone dose. Therefore, this suggests that removing the offending drug agents is important in the management of CASH.

Currently, no standard treatment guidelines exist in the management of CASH. Given our experience with this patient, we advocate early consideration of hepatic imaging to confirm steatosis, especially if LFT's remain elevated despite dose reductions and even discontinuation of TMZ. Tapering the dose of dexamethasone is felt to be essential, in addition to consultation with a Hepatologist. Finally, for patients with evidence of steatosis, there may be a potential role for the addition of vitamin E and ursodeoxycholic acid, in conjunction with chemotherapy treatment modification. If a decrease in LFT's is observed with these treatment measures, then further administration of TMZ, with close monitoring of serial LFT's, would likely be worthy of consideration given the paucity of current treatment options in patients with GBM.

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## References

1. Goldbecker A, Tryc AB, Raab P, Worthman H, Herrmann J, Weissenborn K. Hepatic encephalopathy after treatment with temozolomide. J Neurooncol. 2011; 103(1): 163-6.
2. Vauthey JN, Pawlik TM, Ribero D, et al. Chemotherapy regimen predicts steatohepatitis and an increase in 90-day mortality after surgery for hepatic colorectal metastases. J Clin Oncol. 2006; 24(13): 2065-72.
3. Stravitz RT, Sanyal AJ. Drug-induced steatohepatitis. Clin Liver Dis. 2003; 7(2): 435-51.
4. Lindor KD, Kowdley KV, Heathcote J, et al. Ursodeoxycholic acid for treatment of nonalcoholic steatohepatitis: results of a randomized trial. Hepatol. 2004; 39(3): 770-8.
5. Sanyal AJ, Chalasani N, Kowdley KV, et al. Pioglitazone, vitamin E or placebo for nonalcoholic steatohepatitis. New Engl J Med. 2010; 362(18): 1675-85.