been irradiated to any significant dose. Without supporting dose/volume information, brain irradiation as an aetiological factor remains just a possibility.

It may be that authors feel that the significant pathophysiology relates to irradiation of major blood vessels outside the CNS although the article fails to clearly make this distinction. If so, there is no need to invoke the notion of radiation 'spreading' to the brain. If this is the hypothesis, then knowledge of the patient's smoking habits and alcohol intake (both strongly associated with squamous cell carcinoma of the upper aero-digestive tract in a 71-year-old male who also has diffuse white mater changes suggestive of ischaemia) would be pertinent, as would the presence or absence of carotid bruits. None of these details are mentioned. The time course of the events makes this possibility less likely as large vessel damage after radiotherapy often takes years to develop rather than the weeks in this case.

It may be that radiotherapy contributed to events but the evidence presented fails to support this assertion. I would therefore question whether this does constitute the first case of serotonin syndrome secondary to fluoxetine precipitated by a radiation induced cerebral vasculopathy to be described. Was the treating clinical oncologist consulted?

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Lesson of the month (2)

Editor – I read with interest Chirwa *et al*'s lesson of the month (*Clin Med* February 2008 pp 107–8). I feel, however, that the authors' premise of the underlying pathophysiology of radiation-induced cerebral vasculopathy is flawed.

Insufficient clinical details were given in order to determine the specifics of the radiotherapy their patient may have received. In general, radiotherapy for a tonsillar carcinoma is delivered to the primary tumour, or tonsillar bed if given post-operatively, and to the cervical lymph nodes at risk. These would include the ipsilateral level Ib-IV nodes (T1–2, N0) or bilateral Ib-V nodes if T3–4 or N+.

Radiotherapy is precisely delivered to a specific target volume. The target volume as defined above would usually be delineated on planning a computed tomography scan and it would be unusual to include any cerebral tissue within the treatment field.

Radiotherapy has both early and late effects. Early normal tissue toxicity occurs during radiotherapy and in the 90 days following radiotherapy. Late toxicity is defined as changes persisting or occurring more than 90 days after completion of radiotherapy.[1]

Stenosis and occlusion of vessels has been reported as late toxicity and would usually develop within the first eight years after treatment, with a latent period reported as 2–25 years.[2] Although this gentleman may be at risk of carotid artery stenosis and thus potential cerebral hypoxia, we would not anticipate the development of this within the time frame of 12–16 weeks post treatment.

The authors cite the paper by O'Connor *et al* in support of the argument for cerebral vasculopathy.[3] This paper, however, discusses radiotherapy for central nervous system neoplasms and cerebral arteriovenous malformation and as outlined above we would not expect the cerebral vasculature to receive a significant radiotherapy dose in the treatment of a tonsillar carcinoma.

I would therefore challenge the authors' claims that radiation induced vasculopathy is the underlying mechanism responsible for the development of their patients acute neurological deterioration.

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References

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2 Bitzer M, Topka H. Progressive cerebral occlusive disease after radiation therapy. *Stroke* 1995;26:131–6.
3 O'Connor M, Mayberg M. Effects of radiation on cerebral vasculature: a review. *Neurosurgery* 2000;46:138–51.

In response

Many thanks to Button and Dorey for comments on our article on serotonin syndrome. We are grateful for the points raised. I agree that no mention of our patient's smoking and alcohol ingestion habits were mentioned, as well as the dose/volume of radiation administered for the treatment of the tonsillar ca and these were important in this case. I can, however, say that the patient was an ex-smoker and clinically he had no carotid bruits.

The point you made of large vessel damage due to radiation being a delayed response is entirely true hence the 12–16 week period in this case could not account for this. There are case reports where the large vessel vasculopathy occurred as long as twelve years later. However, it is also well known that endothelial cells are perhaps the most radiation-vulnerable elements of the mesenchymal tissue and that the injuries occur often in capillaries, sinusoids and small arteries in that order. Our hypothesis therefore is that the radiation precipitated these events by the injury caused to small vessels with subsequent damage to the endothelium hence affected serotonin metabolism.

The conclusion in our discussion paragraph states that cerebral vasculopathy precipitated the events and this was drawn from this hypothesis.

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