Author’s response to reviews

Title: The use of a lumbar drain for management of pseudotumor cerebri caused by All-trans retinoic acid

Authors:

Fahid T Rasul (fahidrasul@doctors.org.uk)
Ahmed K Toma (ahmedktoma@yahoo.com)
Akbar A Khan (akbaralikhan77@hotmail.com)
Gordon T Plant (gordon.plant@uclh.nhs.uk)
Laurence D Watkins (laurence.watkins@uclh.nhs.uk)

Version: 3 Date: 13 September 2012

Author’s response to reviews: see over
To Whom It May Concern:

Re: The use of a lumbar drain for management of pseudotumor cerebri caused by All-trans retinoic acid

I attach a revised manuscript following editorial review and comments. Here I outline the revisions made:

Editor comment:

*Promyelocytic leukemia is known to be associated with venous sinus thrombosis. In fact this has been the cause of death and failure. Dural venous sinus thrombosis is a known cause of pseudotumor. We do not know why retinoic acid can be the cause of this condition but if it is the cause the pseudotumor resolves in a very short period of time. The time course of the pseudotumor is consistent with recanalization of a dural venous sinus after thrombosis and is a much more likely cause of the condition. If a venous study was done and showed no thrombosis the report should include that statement. If it was not done the alternative explanation of venous sinus thrombosis must be included. I also would like to understand what the lumbar drain did to reverse the condition other than decrease ICP.*

Our reply:

We agree with the comments and have looked in further detail for the evidence for dural venous sinus thrombosis as the cause of PTC in our case. No CT venogram was performed as this would not have altered our management strategy. This is discussed in full detail in the discussion section including an appreciation of the value of CT venogram in such cases. We have also discussed the possible reasons for the significant improvement observed in such a short space of time.
Editor comment:

The authors report their management of a case of pseudotumor cerebri associated with ATRA use. They demonstrate that a temporizing measure (lumbar drainage) may be useful in this usually self-limited disease. Useful points to discuss would be:
1. Over what period of time were the 5 cycles of intrathecal chemo given? Did the papilledema remain stable during this time?
2. Is it possible that lumbar drain insertion "broke the cycle" of the PTC, as we postulate occurs in some idiopathic cases?
3. Such a rapid resolution of papilledema with lumbar drainage is interesting, as in my experience, ONSF can give such a day-to-day measurable change, while CSF diversion can take weeks to be effective.

Our replies:
1. We have included specific details of the period of time that the intrathecal chemo was given including a comment on the stability of papilledema during this period.
2. We have commented on the possibility that the lumbar drain ‘broke the cycle’. This is included with a fuller discussion of the possible aetiology (dural sinus thrombosis) for the PTC.
3. We have postulated our idea(s) for why such a rapid improvement was observed and commented on the fact that this is unusual with lumbar drains and much more likely with optic nerve sheath fenestration.

Editor comments:

The authors report as if lumbar drainage treated the persistent pseudotumour cerebri. This is likely to be an incorrect surmise. The lumbar drain was a method for controlling the intracranial pressure (ICP) and it in itself is unlikely have caused the amelioration of the underlying pathology (secondary to retinoic acid) which had caused the pseudotumour cerebri.

Our reply:
We have made explicit that it is likely that the effect of the lumbar drain was to reduce ICP rather than treat the PTC.

Editor comments:
1. Spelling mistake in the title. It Should be ‘promyelocytic leuk(a)emia’ (not ‘lukaemia’)
   a. The Authors state of the ‘apoptotic’ mechanism. The Main mechanism of the drug is to cause differentiation of haemopoietic cells
3. Insufficient information provided:
   a. No CT Scan of the head
   b. No visual field chart
   c. No specific values from the visual acuity tests
   d. Serial lumbar puncture:
      i. How often was this done?
      ii. What gauge of spinal needle used and how was the bevel angled?
      iii. What was the opening and closing pressures?

4. “CT scan confirmed normal appearances of CSF space”: in pseudotumour cerebrie, I would expect the subarachnoid spaces (particularly the cortical sah spaces) to be effaced; ventricles to be small.

5. Papilloedema
   a. The authors report that they could discern acute improvement in papilloedema (following lumbar drainage of CSF). Most would be surprised by this. They should acknowledge this concern and try to explain why there was acute improvement in papilloedema in their patient.

Our replies:
1. Spelling mistake amended
2. The differentiation mechanism has been included with referencing
3. As follows
   a. No CT head included.
   b. Visual field chart prior to lumbar drain removal now included
   c. Specific values from visual acuity tests included
   d. Serial lumbar puncture details included as recommended.
4. Following further specialist neuroradiology review this has been amended to include mild reduction in ventricular size and moderate effacement of cortical subarachnoid spaces
5. We have commented and discussed in detail the possible reasons for seeing an acute improvement in papilloedema in our patient.

Thank you for once again for considering publishing our article in your journal. We look forward to hearing from you.

With best wishes
Yours sincerely

Mr Fahid Rasul (MRCS, MBBS, BSc)
Victor Horsley Department of Neurosurgery
National Hospital for Neurology and Neurosurgery
Queen Square
London, UK.
(on behalf of all the authors)