Questionable Interpretation of Results of ACTIVE Study on Matrix Coils by Boston Scientific

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Posterior Column Involvement in Miller Fisher Syndrome or Dorsal Root Ganglion Neuronopathy?

The case of posterior column involvement in Miller Fisher syndrome (MFS) reported by Inoue et al (1) is interesting and important. Although central nervous system involvement was reported in MFS, the posterior column lesion due to inflammatory pathogenesis is worthy of debate in terms of differential diagnosis on radiology and prognosis. The main point is whether the posterior column involvement of this patient is a part of MFS or dorsal root ganglion neuronopathy accompanied with MFS. The patient had the triad of ophthalmoplegia, areflexia, and ataxia of MFS, and recovery of ophthalmoplegia is typical of MFS. Recovery of ataxia, however, is poor disproportional to ophthalmoplegia, which is also contradictory to the benign courses of MFS (2). The authors also discussed the debates on lesion localization of ataxia in MFS. We believe that the ataxia of this patient is the manifestation of dorsal root ganglion (DRG) neuronopathy accompanied with MFS incidentally, rather a part of MFS pathogenesis. This may explain why this patient is different to those of benign courses.

Lack of vibratory sensation and no response on somatosensory evoked potential examination on follow-up may not only arise from posterior column lesion. Indeed, areflexia on the background of mild weakness also suggests there may be some peripheral involvement. We think the posterior column damage is a dying back–type degeneration, which might arise from DRG cells following an inflammatory neuronopathy accompanied with MFS, rather than secondary to initial involvement of posterior nerve roots of cauda equina as a part of MFS as the authors imply. The MR imaging abnormality throughout the posterior columns is homogeneous and extends from the level of C1–T12. Retrodegeneration of nerve roots of cauda equina is not a sound explanation for such an extensive lesion. In humans, deep sensory tracts from the lower limbs travel through the fasciculus gracilis and those from the upper limbs and trunk through the fasciculus cuneatus. Thus, we would like to know whether there are some abnormalities in the nerve roots of cervical enlargement at presentation and on follow-up. Cauda equina enhancement is not uncommon in Guillain-Barré syndrome (GBS), but severe ataxia is seldom seen as a consequence. Whether cauda equina enhancement is an early marker of inflammatory pathogenesis of DRG neuronopathy awaits prospective investigation. Homogeneity of hyperintense lesion confined to the spinal posterior column and no apparent abnormalities on T1-weighted images or on gadolinium enhancement study at 5 months after onset is the typical feature of neuronopathy. For the evidence of DRG or peripheral nerve involvement, sensory nerve action potentials of both upper and lower extremities should be reported and discussed in detail. If they were not available, a sural nerve biopsy would retrospectively demonstrate the extent of peripheral nerve involvement.

Posterior column MR imaging abnormalities following DRG degeneration and neuropathy have been previously reported. DRG neuronopathy due to inflammation may occur simply after acute infection or along with other diseases (3). The most commonly reported DRG involvement due to immunocompromise is sensory neuronopathy with Sjögren syndrome, which trigeminal ganglion neuronopathy may accompany (3). The extent of posterior column lesions may reflect the degree of neuronopathy associated with Sjögren syndrome, hence, makes a helpful marker for estimating severity (4). A patient with subacute progressive sensory ataxic neuronopathy after *Rickettsia conorii* infection was also reported. Histologic studies revealed profound loss of myelinated fibers due to primarily axonal degeneration. The clinical course and the electrophysiologic and histologic findings suggest primary involvement of the dorsal root ganglion (5). Professor Yu-pu Guo, of Beijing Union Hospital (personal communication), once had an acute severe ataxia patient with sensory neuronopathy after diarrhea. MR imaging revealed homogeneous T2-weighted hyperintense lesions of the posterior column. Autopsy revealed DRG degeneration with secondary degeneration of posterior column. The acute course suggests the inflammatory reaction is severe enough to induce more complete degeneration of posterior column than that found in the more chronic courses in Sjogren syndrome. Experimental sensory neuronopathy may be induced with GD1b (6). In this model, axonal degeneration was present in the dorsal column of the spinal cord, in the dorsal roots, and in the sciatic nerve. Some of the nerve cell bodies in the dorsal root ganglia had degenerated and disappeared. Clinically impaired deep sensation was noted in GBS patients with GD1b antibodies (7). In this sense, MFS may overlap with sensory neuronopathy theoretically, because there is cross-reactivity between GQ1b and GD1b (7). Severe ataxia on follow-up, however, is rare even in GBS patients with GD1b antibodies, and there was little evidence of DRG neuronopathy in GBS patients. Thus, we believe ataxia of this patient was caused by DRG neuronopathy accompanied by MFS incidentally.

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Reply

We thank Drs. Lia and Xie for their valuable comments on our case report. They describe that the ataxia in our patient must have been caused by dorsal root ganglion (DRG) neuropathy incidentally accompanied by Miller Fisher syndrome (MFS). We, however, maintain that MFS can be associated with DRG involvement. Our patient manifested rapidly progressive ocular signs and severe ataxia simultaneously, although

the prognosis of his ataxia was worse than for that of other MFS patients. It has recently been suggested that the lesion responsible for the ataxia manifestation in MFS is located in the DRG (1). Also, it has been documented that large neurons in the DRG from MFS patients are positive for anti-GQ1b antibody (2). Thus, it is plausible that MFS could be associated with the DRG lesion attributable to anterograde degeneration of the spinal posterior column, as shown in our patient. Nevertheless, the site of lesions causing ataxia in MFS still remains to be elucidated. Further studies should be necessary to clarify this intriguing issue.

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Concha Bullosa and Nasal Septal Deviation

We read with interest Stallman et al's report on the incidence of concha bullosa and its relationship to nasal septal deviation (1). They mentioned the fact that, to their knowledge, no study had evaluated concha bullosa in relation to nasal septal deviation. It would seem to have been appropriate for these authors to cite a previous report, by Elahi et al, about paraseptal structural changes and chronic sinus disease in relation to the deviated septum (2), because Elahi et al indicate the relationship between nasal septal deviation and concha bullosa. Elahi et al concluded that increasing angles of septal deviation are associated with bilateral sinus disease and contralateral middle turbinate abnormalities (including concha bullosa) and ethmoidal bulla prominence (Table 1). Their study methods differed from Stallman et al's by grouping the nasal septal deviation according to deviation angles and definition of concha bullosa.

Although Stallman et al's literature search missed Elahi et al's report, we congratulate them on their well-written and nicely illustrated study.

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Reply

We thank Dr. Arslan for his letter regarding our recent article on "concha bullosa." We apologize for not citing the article by Elahi et al, as it does pertain to the problem of concha bullosa. There were, however, many articles regarding this topic and we had to cite only those that we thought were most closely related to our article and how we performed our study. Of necessity, this meant that not all previous works could be cited. We do thank Dr. Arslan for his kind comments regarding our work.

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Questionable Interpretation of Results of ACTIVE Study on Matrix Coils by Boston Scientific

We fully agree with Raymond et al (1) that "new embolic agents should first demonstrate safety characteristics that are equivalent to standard platinum coils before considering a widespread application" and "worse, their use could be associated with early rebleeding when lesions are treated after rupture" (p. 1129).

These concerns are even more important and urgent when companies of embolic agents provide us with questionable interpretations of study results. In the 2004 *Matrix Newsletter,* the results of the so-called ACTIVE Study are presented (2). Matrix coils are coated with a biologically active substance and proved to accelerate healing of intracranial aneurysms in swine, and it is concluded that these coils may prevent aneurysmal recanalization after endovascular treatment of cerebral aneurysms (3).

The first page of the newsletter states, "The ACTIVE Study represents the first prospective multicenter trial designed to evaluate the benefit of the Matrix Detachable Coil for the treatment of cerebral aneurysms and was sponsored by Boston Scientific, Neurovascular, Fremont, CA."

On the second page, it is reported that 3% of the patients treated with Matrix coils suffered a fatal early rebleeding (three of 100). On closer inspection, however, only 44 of these 100 patients were treated after aneurysmal rupture. Thus, the early fatal rebleeding rate should have been reported to be 7% (three of 44) instead of 3%. In the ISAT study (4), in which the patients were treated with standard platinum coils, 10 of 1005 patients suffered an early rebleeding after coiling of a ruptured aneurysm (1%).

Apart from the fact that this 7% of rebleeding rate after treatment with Matrix is unacceptably high, these findings are not surprising after review of the remaining part of the newsletter: it is reported that 67% of the coiled aneurysms still show residual aneurysm filling on the immediate postembolization angiogram. On the 12-month follow-up angiogram, 49% of the aneurysms show "progressive thrombosis." Apparently the Matrix coils allow residual filling of the aneurysmal sac over an unknown period of time and during this period the patient is not protected against a rebleeding.

Middle-turbinate abnormalities (percentage) (from Reference 2)

	Group 1 (0–9°)		Group 2 (10–15°)		Group 3 (>15°)	
	Ipsilateral	Contralateral	Ipsilateral	Contralateral	Ipsilateral	Contralateral
Hypertrophy	9	22*	9	24*	5	55*
Impaction	15	14	21	18	18	32*
Concha bullosa	18	26	24	38	23	45*
Paradoxic deviation	14	17	9	6	0	5

*Statistical significance ($P < .05$).

In the evaluation of these new coils that possibly improve long-term results, the most important goal of ruptured aneurysm treatment—that is, to exclude the aneurysm from the circulation to prevent early rebleeding—is clearly ignored.

So do these new coils at least perform better in the long term than they were designed to? On page 3, the results of follow-up angiography after 12 months are discussed. In a complex and confusing way, an attempt is made to compare these findings on follow-up with historical data, but in a presentation by the company we find out that 16% of the followed patients had to be retreated with coils (5). The retreatment rate after treatment with standard platinum coils is in the range of 10% (6).

The conclusion of the ACTIVE Study should therefore not be that "the results of 1st treatment with 1st Generation Matrix Detachable Coils are favorable," but that Matrix coils offer no benefit over standard platinum coils and that these coils should not be used to treat recently ruptured cerebral aneurysms.

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Fatal Ethibloc Embolization of Vertebrobasilar System Following Percutaneous Injection into Aneurysmal Bone Cyst of the Second Cervical Vertebra

Peraud et al (1) reported a fatal injection of Ethibloc into an aneurysmatic bone cyst of C2 due to inadvertent embolization in the vertebrobasilar system. The embolization material was found in a small branch artery of the vertebral artery at the C2 level. The authors suspect that the embolizing material passed into a side branch of the vertebral artery running into the aneurysmatic bone cyst. Our own experience with intravertebral contrast injection supports this theory. Within the vertebroplasty of osteolytic lesions of C2, we routinely perform vertebral phlebography. The contrast is injected via the needle placed to inject the bone cement. The background for this routine is the experience that osseous pathology in vertical vertebral bodies often is supplied by arterial branches of the vertebral arteries. In one patient with an osteolytic lesion from breast cancer, we could prove a retrograde filling of the left vertebral artery and subsequently the basilar artery by injection of contrast into the osteolytic lesion of the second vertebra. We found an impressive amount of contrast filling the posterior circulation (Fig 1). Direct arterial puncture could be excluded by needle position.

Consequently, we did perform vertebroplasty under biplanar fluoroscopy by using a higher viscosity of the bone cement than normally used. The patient was treated successfully and without any complication.

Anatomically, the vertebral arteries supply the bone in the cervical spine. Under normal conditions, the selective angiography of the vertebral arteries cannot visualize the vertebral supply, but highly perfused bone tumors (eg, metastases) in the cervical spine show tumor blush via selective vertebral injec-

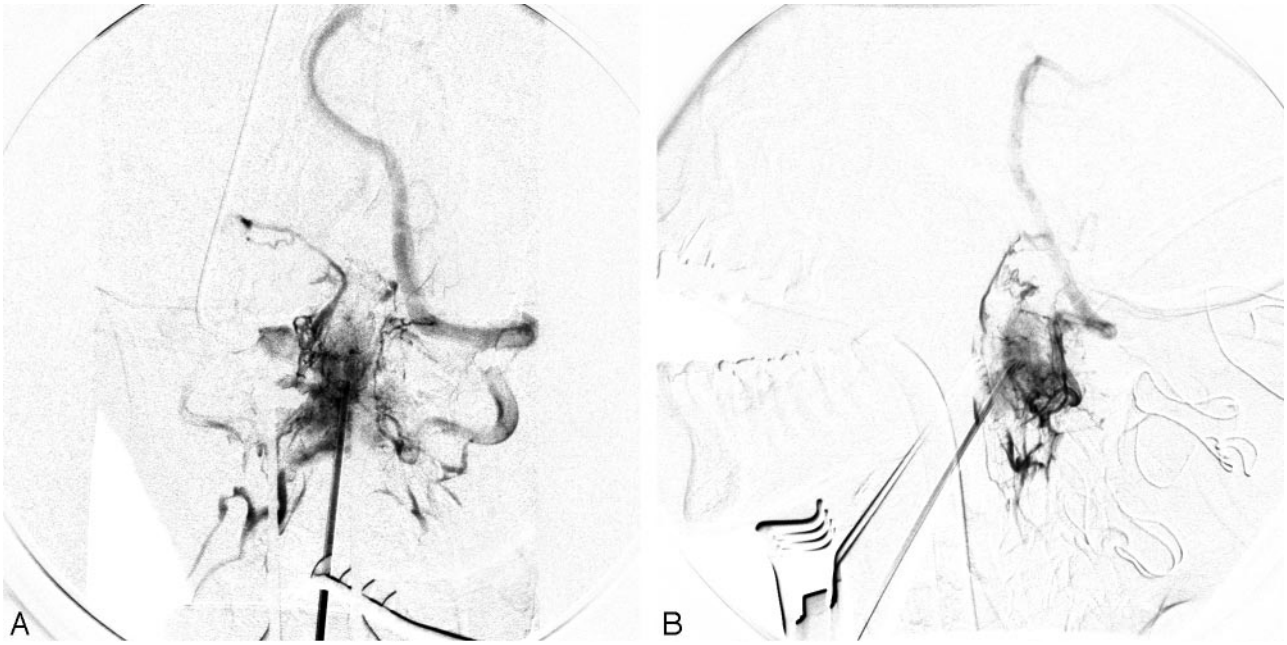

FIG 1. Anteroposterior (*A*) and lateral (*B*) views of contrast injection into C2. The arrows mark the needle and instruments of the surgical access, which normally is used at our institution to perform vertebroplasty of C2. There is an early filling of the left vertebral artery and the basilar artery via small arterial branches.

tion. We do think that enlargement of anatomically normal arterial vessels supplying the vertebral bone due to pathologic structures in the bone are the basis for functional relevant connections between the osseous structures of the cervical spine and the posterior arterial circulation. We suggest performing contrast injection before embolization or cement injection into cervical vertebral bodies, regardless of individual pathology. Furthermore, biplanar fluorscopic control may help to avoid inadvertent embolization of the basilar artery.

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Errata

Due to an oversight, Riyadh Al-Okaili's name was misspelled in the published list of authors for the article "**Transient Traumatic Spinal Venous Hypertensive Myelopathy**" in the August 2005 issue. The correct author list should be:

Mark A. Auler, Riyadh Al-Okaili, and Zoran Rumboldt. (*AJNR Am J Neuroradiol* 2005;26:1655–1658.)

Due to an oversight, the Letter entitled "**Concha Bullosa and Nasal Septal Deviation**" in the August 2005 issue (*AJNR Am J Neuroradiol* 2005;26:1882) listed an incorrect affiliation for the first author and omitted the name of the second author. The correct attribution for this letter should be:

Gokhan Arslan and Kamil Karaali, Radiology Department, Akdeniz University School of Medicine, Antalya, Turkey

Due to an oversight, the author affiliations for the article "**Predominant Cerebellar Volume Loss as a Neuroradiologic Feature of Pediatric Respiratory Chain Defects**" in the August 2005 issue (*AJNR Am J Neuroradiol* 2005;26:1675–1680) were incorrect. These should be:

From the Departments of Molecular and Human Genetics (F.S., L.-J.C.W.) and Radiology (J.V.H.), Baylor College of Medicine, and the Texas Children's Hospital (F.S.), Houston, TX; and the Department of Pediatrics (G.D.V.), State University of New York at Buffalo, Buffalo, NY.

Also in this article, the legend for Figure 3 on page 1678 was incorrect. It should be:

FIG 3. Sagittal midline T1-weighted (*A*) and coronal fluid-attenuated (*B*) inversion recovery images demonstrate evidence of progressive cerebellar atrophy when compared with interval sagittal T1-weighted midline image (*C*). Note evidence of pontine involvement with T1-weighted hypointensity returned from a pons diminished in size.

Also in this article, a sentence in the third paragraph in the left column of page 1679 was incorrect. It should be:

"Our patient with LS due to cytochrome c oxidase-associated *SURF1* deficiency displayed progressive cerebellar atrophy and ataxia as presenting features."

Due to an author oversight, reference 9 in this article was incorrect. It should be:

9. Van der Knaap M, Valk J. **Magnetic resonance in mitochondrial disorders.** *Euromit* 6; Nijmegen, the Netherlands, July 2004.

Tissue at Risk Is Overestimated in Perfusion-Weighted Imaging: MR Imaging in Acute Stroke Patients without Vessel Recanalization
Thomas Kucinski, Dirk Naumann, René Knab, Volker Schoder, Susanne Wegener, Jens Fiehler, Amitava Majumder, Joachim Rother, and Hermann Zeumer

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Due to reinspection of our original data, we recently encountered deviations between the initial measurements and the file used for statistical analysis. Two columns of figures of CBV values (lesion and control of the surviving tissue, ST7) have been interchanged with corresponding columns of CBV, but from day 1 instead of day 0. Hence, the given value of the rCBV of ST7 in Table 2 has to be changed from 1.02 ± 0.12 to 0.87 ± 0.10. Consequently, there is no longer a statistical difference between the rCBV of those regions evolving to infarction more than 24 hours after onset, ie, between day 1 and 7, and the surviving tissue. The ROC analysis now reveals a value of 0.75 with a sensitivity of 0.44 and specificity of 0.94 (originally published data: 0.82, sensitivity 0.56 and specificity 0.95). Although the tenor of our work is still accurate, we now have to point out, that there is no reliable threshold discriminating survival against death of tissue for any of the perfusion parameters rCBV, rCBF, rTTP or rMTT.