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Stroke following chiropractic manipulation of the cervical spine

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Abstract We analyzed the clinical course and neuroradiological findings of ten patients aged 27–46 years, with ischemic stroke secondary to vertebral artery dissection (VAD; $n = 8$) or internal carotid artery dissection (CAD; $n = 2$), all following chiropractic manipulation of the cervical spine. The following observations were made: (a) All patients had uneventful medical histories, no or only mild vascular risk factors, and no predisposing vascular lesions. (b) VAD was unilateral in five patients and bilateral in three. VAD was located close to the atlantoaxial joint in all eight patients and showed additional involvement of lower sections in six, as well as temporary occlusion of one vertebral artery in three. (c) Nine of ten patients had brain infarction documented by magnetic resonance imaging or computed tomography. (d) Onset of symptoms was immediately after the manipulation ($n = 5$) or within 2 days ($n = 5$). (e) Progression of neurological deficits occurred within the following hours to a maximum of 3 weeks. (f) Maximum neurological deficits were severe in nine of ten patients. (g) Outcome after 4 weeks–3 years included no or mild neurological deficits in five patients, marked deficits in three, persistent locked-in syndrome in one, and persistent vegetative state in one. (h) Informed consent was obtained in only one of ten patients. Thus, patients at risk for stroke after chiropractic manipulation may not be identified a priori. Neurological deficits may be severely disabling and are potentially life threatening.

Key words Stroke · Vertebral artery dissection · Chiropractic manipulation · Carotid artery dissection · Cervical spine

Introduction

Vertebral or carotid artery dissections (VAD, CAD) are rare causes of stroke. In the younger adult population under the age of 45 years, however, as many as 20% of strokes are associated with arterial dissection [4, 20]. Dissections have been known to occur after chiropractic manipulations and after abrupt spontaneous movements of the cervical spine [1, 11, 13, 15, 19]. Their incidence appears to be increasing [23]. At present, however, it is unclear whether this is a result of improved noninvasive methods of neuroradiological diagnosis such as magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA), increased awareness of its relevant symptoms, or an increasing number of chiropractic cervical spine manipulations, which have been identified as one of the major causes [7]. Up to now no reliable statistics about the number of chiropractic manipulations performed are available in Germany. Here we analyze the clinical course and neuroradiological findings in ten patients treated at our institutions for stroke based on VAD or CAD following chiropractic manipulation of the cervical spine. Special interest was directed to the

evaluation of risk factors, the development of neurological deficits, neuroradiological findings, and long-term outcome.

Patients

We studied ten patients (three men, seven women) aged 27–46 years (mean: 34) with VAD ($n = 8$) or CAD ($n = 2$) following chiropractic manipulation of the cervical spine. Five of the patients were referred to us in the acute state over a period of 14 months, and the other five visited us as outpatients only several months after the vascular accident had occurred. They had been alerted by an evening television broadcast on the subject that reached about 1.5 million persons. In these five patients, data were accumulated from personal interviews, examinations, and medical documentation obtained at other neurological hospitals at the time of the vascular accident. Two of the patients (nos. 7 and 8) were treated at neurological rehabilitation hospitals by one of us (K.-D. B. or P.-W. S). All patients (except no. 7 who was in a persistent vegetative state) gave informed consent for utilization of data.

Results

Chiropractic manipulation

The indication for the chiropractic maneuver was neck pain in nine patients associated with headache in two or headache alone in one (Table 1). The manipulations were performed outside our institution by orthopedists in seven patients, a physiotherapist in one, and health practitioners who are not physicians in two. The chiropractic maneuver type was described by the patients since medical documentation of it was not available in any case. Descriptions of the maneuvers preceding the stroke differed in all patients. Elements of abrupt or extreme head rotation were reported by nine patients, abrupt extension by four, extreme anteversion by one, forceful tilting by one, and thrusts to the mastoid by one. One patient remembered that a major manipulation had been performed but was unable to recall an exact description because of nausea, neck pain, and possibly impaired consciousness which had developed immediately.

Six patients developed neurological deficits after the first manipulation, and four had had at least one and up to approximately ten preceding manipulations. In patient no. 2 symptoms of brainstem and cerebellar ischemia, as shown in Table 1, began 1.5 h after his first chiropractic manipulation. Computed tomography at that time demonstrated cerebellar infarction. After 6 years he had a second chiropractic manipulation of the neck and developed a minor brainstem stroke with similar symptoms but complete recovery after 4–5 weeks. Patient no. 4 had experienced symptoms of a brainstem transient ischemic attack (TIA) during one of her previous chiropractic manipulations but recovered within 2 h at that time.

Table 1 Patients and manipulation characteristics (*VA* vertebral artery, *IC* internal carotid artery, *r* right, *l* left, *bi* bilateral, 1+1: complications after first and second manipulations)

Patient no.	Sex	Age (years)	Dissected artery	Indication for manipulation	Vascular risk factors	Manoeuvre type	Manipulation (*n*)	Latency to onset
1	F	34	VA/r	Migraine, neck pain	None	Rotation, extension, tilting	6	Immediate
2	M	40	VA/r	Neck pain	Mild hypertension	Forceful rotation and extension at the same time	1 + 1	1.5 h; second: 2–3 h
3	F	27	VA/bi	Neck and shoulder pain	None	Right and left rotation, extension	1	1 day
4	F	29	VA/l	Neck pain	Smoking 1 or 2 cigarettes/day	Rapid, repeated right-left turning	Approx. 10	2 days
5	F	29	VA/bi	Neck pain, headache	Mild hypertension	Right-left rotation, abrupt extension, two or three thrusts to the mastoid	2	Immediate
6	F	35	VA/l	Neck pain	None	Forceful rotation to left side three or four times	5	Immediate
7	F	31	VA/l	Neck pain	None	Abrupt forceful rotation to the right	1	Immediate
8	F	34	VA/bi	Neck pain	Mild hypertension	Forceful rotation to right and left once	1	16 h
9	M	35	IC/r	Headache	Smoker, hypercholesterolaemia	Anteversion of head and shoulder, head rotation to both sides	1	Immediate
10	M	46	IC/l	Neck pain	None	Unclear	1	16 h

Neurological deficits

Moderate vascular risk factors were present in five of the ten patients (Table 1). None had cerebral or other vascular accidents or any other relevant disease in their past medical or family history. In addition to oral contraception, taken by patient nos. 1, 3, and 6, none was on any regular medication.

The onset of symptoms was immediately after the procedure in five patients and within 2 days in the remaining five. The first symptoms were: vertigo (n = 7), nausea (n = 6), vomiting (n = 3), unusual, sudden and severe cervico-occipital pain (n = 4), brief syncope (n = 2), or respiratory arrest and coma within minutes (n = 1). A progressive and sometimes fluctuating deterioration in neurological deficits was observed during the following days in all but one patient. The maximum neurological deficit is shown in Table 2 and was severe in all patients except patient no. 9.

In four patients the following additional abrupt stepwise deterioration was observed: Patient no. 3, who had severe cervico-occipital headache immediately right after the chiropractic manipulation, experienced a vertebrobasilar TIA including loss of consciousness and tetraparesis the following day and recovered within hours with vertigo and tinnitus remaining. On day 8 after the manipulation,

Table 2 Clinical and neuroradiological findings (*r* right, *l* left, *bi* bilateral, *VAR/VAL* right/left vertebral artery, *ICR/ICL* right/left internal carotid artery, *MCA* medial cerebral artery, *AG* conventional angiography, *DA* digital subtraction angiography, *MRA* magnetic resonance angiography)

Patient no.	Neurological deficits	Residual neurological deficits	Observation period	Infarction on CT/MRI	Vascular pathology
1	Nausea, vertigo, syncope, hemiparesis, l hemihypesthesia, diplopia, blurred vision	None	12 m	Pontine r	AG: irregular VAR wall upper 1/3; Doppler: temporary occlusion VAR with reperfusion after 3 days; MRA after 6 mo: asymmetry r < l
2	Vertigo, tetraparesis, dysarthria, dysphagia, tortional nystagmus in all positions of gaze, ataxia, horizontal gaze paresis, Horner's syndrome, facial palsy r	Intermittent vertigo	First: 60 m; second: 10 m	Cerebellum r at first manipulation; none after second manipulation	AG: dissection of VAR with high degree stenosis at several sections; Doppler: flow difference r < l
3	Initially neck pain; after 1 day, impaired consciousness, tetraparesis; after 8 days: locked-in syndrome	Locked-in except minimal movement of lips	25 m	Pons + cerebellum	AG: Subintimal bleeding of VAL, irregular stenosis at several sections of VAR, complete reperfusion after 2 weeks
4	Nausea, vertigo, falling to right side, after 3d completion to Wallenberg's syndrome	Vertigo, tinnitus, diplopia, hypesthesia for pain and temperature	4 m	Lateral medulla l	AG: high degree stenosis of VAL at C7, poststenotic dilatation, irregular wall up to atlas
5	Nausea, vertigo, dysarthria, paresis l arm, hypesthesia l body half	Hypesthesia l, asthenia, dysmetria left arm, headache	3 y	Medulla l	AG day 3: occlusion of VAR with a 15-mm stump, irregular wall of AVL with up to 90% stenosis, retrograde filling of BA, AG day 9: recanalization of VAR, orthograde filling of BA
6	Initially: vertigo, nausea, vomitting, paresis r arm, bilateral paresthesias, after 21 days: additional r hemiplegia, dysarthria, hyperhidrosis	Medium degree r hemiparesis	6 m	Medulla bi, thalamus r	AG: AVL wall irregularities; cross-section MRI: semicircular wall haematoma at atlas sling of AVL
7	Nausea, vertigo, vomiting, respiratory arrest, coma	Persistent vegetative state	9 m	Pons, cerebellum, medulla, secondary hydrocephalus	MRA: dissection VAL with haematoma of wall, VAR hypoplasy, BA occlusion and retrograde filling; Doppler: occlusion VAL + occlusion BA
8	Initially: intensifying neck pain, nausea, vertigo, vomiting, intermittend diplopia; day 10: r hemiplegia, nystagmus, l hypoglossal nerve paresis, r hemihypesthesia	Hemiplegia r, r hemihypesthesia, r hemihypalgesia, depression	12	Cerebellum l, medulla	MRA: VAL occlusion at upper 1/3, VAR: long-stretch of approximately 50% stenosis; Doppler: reperfusion of VAL beginning after day 12 with remaining stenosis after 12 m
9	Hemicrania r, nausea, photophobia	None	4 w	None	DA: dissecion of ICR 2 cm after carotid bifurcation
10	Aphasia, hemianopia, headache, dysarthria	Dysarthria, mild degree dysphasia	6 m	$2 \times 3 \times 3$ cm^3 + 3 small volumes within l central MCA territory	MRI: hematoma of wall of ICL at scull base; MRA after 6 mo: lumen of ICL < ICR; Doppler: dissection high degree stenosis

brainstem infarction occurred, leaving the patient with a persistent locked-in syndrome. Patient no. 4 had nausea and vertigo and tended to fall to the right side within minutes after the manipulation. On day 3 her condition deteriorated. Neurological deficits now were those of complete Wallenberg's syndrome. Patient no. 6 had nausea, vomiting, vertigo, paresis of the right arm, and paresthesias in all limbs immediately after the manipulation. After 3 weeks of a fairly stable course she suddenly developed an additional right hemiplegia, hyperhidrosis, and severe dysarthria. Patient no. 8 developed an intensifying neck pain, nausea, vertigo, vomiting, and intermittent diplopia 16 h after the manipulation. MRI demonstrated an infarction of the cerebellum on day 6. Vertebrobasilar TIA occurred on day 8 and a brainstem infarction on day 10, with right hemiparesis, right hemihypesthesia, and left hypoglossal nerve palsy. An additional infarction within the medulla oblongata and onset of reperfusion in the previously occluded left vertebral artery was demonstrated by MRI and MRA on day 12.

Neurological outcome

Residual deficits are shown in detail in Table 2. Two patients (nos. 1 and 9) had no persistent neurological deficit. Patient nos. 2, 5, and 10 had mild deficits with slight impairment of daily life. Three patients (nos. 4, 6, and 8) had moderate deficits with marked impairment of daily life. Patient nos. 3 and 7 had a very severe outcome with persistent locked-in syndrome or persistent vegetative state and total dependency.

Medical treatment

The time course of treatment differed in all patients. Anticoagulation was administered to all patients with full-dose heparin to increase the prothrombin time to the two to threefold of its original value. Despite high-dose anticoagulation with heparin patients no. 6 and 8 developed brainstem infarction. Onset of treatment varied from 1 to 6 days after the initial symptoms. Anticoagulation treatment was switched to phenprocoumon after 13–28 days and maintained for 6–14 months in all patients. In patient nos. 1, 2, and 4–10, phenprocoumon was then replaced by 100–300 mg aspirin per day. In patient no. 3 a local intraarterial lysis with 300,000 UI urokinase over 6 h was attempted in the occluded vertebral artery on the same day that she developed the locked-in syndrome, without alteration in the neurological condition or vascular status and without complications occurring.

Neuroradiological and sonographic findings

MRI revealed brainstem infarction in seven of eight patients with VAD (Table 2). The MRI of patient no. 2 depicted cerebellar infarction only. Additional infarctions within the cerebellum were shown in three patients and in the thalamus in one. In patient no. 10, with CAD, MRI demonstrated a $2 \times 3 \times 3\,cm^3$ infarcted brain volume within the central medial cerebral artery territory and three small areas of infarction in the ipsilateral parietal lobe.

The arterial dissection was demonstrated by conventional angiography or digital subtraction angiography in eight patients, MRA in one, and MRI (wall hematoma) in patient no. 10. The appearance was typical, with wall irregularities and stenosis of varying degrees on angiography and wall hematoma on MRI [14, 20]. VAD was unilateral in five patients and bilateral in three. VAD was located near the atlantoaxial joint in all eight patients but extended to lower sections of the vertebral artery in six. In addition, complete temporary occlusion of one vertebral artery was found in patient nos. 1, 5, and 8. Follow-up investigations by duplex sonography revealed reopening of these vessels and marked reperfusion 3, 6, and 10 days later. In the two patients with CAD, the site of dissection was located 2 cm distal to the bifurcation in one patient and at the skull base in the other.

Patient's consent

Informed consent about the potential risks of the manipulation had not been obtained in nine of ten patients. Only one patient reported that he had vaguely been informed by his physician.

Discussion

The patients with stroke following chiropractic manipulation of the cervical spine described here and in the literature are generally young adults, have no or only few risk factors, and show an uneventful medical history suggesting that vascular risk factors or predisposing vascular lesions are of no relevance. In keeping with this, in a review of the literature Frisoni and Anzola [7] found strokes following VAD and CAD to occur mainly in younger and otherwise healthy adults. They identified chiropractic manipulations of the cervical spine to be the predominant cause particularly of VAD but rarely of CAD, with subsequent stroke in 60 of their 72 cases (83%). This indicates that patients at risk cannot be identified a priori on clinical terms or neuroradiological examination. Women predominated in the present series by a ratio of 7:3. This may be coincidental but is in agreement with the predominance of women seen in other young stroke patient groups.

Our data demonstrate that dissections may develop either immediately or after many uneventful manipulations. Dunne et al. [6] histopathologically found multiple recent and one old dissection in a patient who underwent several

uncomplicated chiropractic manipulations 3 years before a fatal one. We noted that there had been transient neurological symptoms in patient nos. 2 and 4 at one of their previous manipulations. It may thus be speculated that chiropractic manipulations can lead to small lesions in the arterial wall which remain asymptomatic or cause transient symptoms and act as a locus minoris resistentiae during further chiropractic manipulations. Transient symptoms at one manipulation should therefore be regarded as an absolute contraindication to any further manipulation.

The role of predisposing vertebral ligament laxity remains merely speculative but suggests avoiding cervical chiropractic manipulations in patient groups with a known hypermobility, such as Ehlers-Danlos syndrome, Marfan disease, osteogenesis imperfecta, and possibly stretch syncope [22]. Johnson et al. [9] described a massive proteoglycan accumulation in the artery wall, most likely predisposing an artery to dissection, in a patient with fatal VAD after a game of cricket and chiropractic neck manipulation. A heritable factor in the pathogenesis of spontaneous cervical artery dissection has been suggested by a study by Majamaa and colleagues [12]. However, no evidence of a mutation of the type 3 collagen, known to be involved in the genesis of Ehlers-Danlos syndrome, has been found in a group of patients with spontaneous cervical arterial dissection [24].

By far the most vulnerable site during chiropractic manipulation of the cervical spine is the vertebral artery, particularly at the atlantoaxial joint. Here its course changes from vertical, passing through the transverse foramina to a horizontal loop penetrating the oblique ligament of the atlas before entering the skull. At this particular site, rotation may cause a shearing force at the vessel wall producing intimal tearing, dissection, intramural hematoma, and subsequent thrombus formation. In addition, many reports and the neuroradiological findings shown here indicate that the entire length of the vertebral artery, and also the internal carotid artery may be affected [3, 7, 17]. As opposed to VAD following chiropractic manipulation, spontaneous VAD does not show a preferred site of dissection [20].

From previous reports there is evidence that the neurological deficits usually develop in several steps [5]. Immediately after the manipulation the initial lesion of the vertebral artery may cause the sudden cervico-occipital pain or a brief syncope. The lesion may remain subclinical or cause further immediate nonspecific symptoms such as nausea, tinnitus, and vertigo. These initial symptoms have been reported to precede manifestation of objective neurological deficits [8] or remain the only symptoms [25]. After a period lasting from minutes to days and even weeks objective neurological deficits may appear if the dissection causes lumen obliteration or thrombus formation and subsequent infarction in the vertebrobasilar territory. A slow progression of neurological deficits during the hours and days to follow may be attributed to either enlargement of the dissection, including the intramural hemorrhage or appositional growth and propagation of a thrombus.

Both mechanisms may be paralleled by an exceedingly critical perfusion of the dependent arteries, and this could explain the sometimes gradual and fluctuating progression of the neurological deficits. The abrupt, secondary deterioration, as seen in four of our patients, may be best explained by arterial thrombembolism in some cases, possibly associated with the onset of reperfusion of an obliterated vessel after some days [10, 16]. Brain infarction has been shown to occur in the brainstem in roughly three-fourths of patients and to involve the cerebellum, the occipital lobe, or diencephalic structures in the remainder [21]. Unawareness of these pathoclinical correlations and especially the interval until clearcut neurological deficits develop may delay diagnosis and therapy. It may also obscure the chiropractic manipulation as having been the initial etiological factor. From spontaneous trauma with minor head injuries it has become clear that this latency maybe as long as 7 weeks [2].

Few data are available on long-term neurological outcome. In our series long-term outcome varied from unimpaired to very severely impaired with total dependency. In the overview of reported cases summarized by Frisoni and Anzola [7], 8 of 39 (21%) patients died and 3 more (8%) were left with persistent locked-in syndrome [18].

No controlled studies are yet available to confirm the efficacy of cervical spine manipulation for any indication, for example, neck pain. Furthermore, as long as there are no detailed descriptions and standardized protocols of the manipulation, it is impossible to assess whether there are safe manipulation techniques. From theoretical considerations and memory reports of our patients rotation seem to be crucial.

Nine of our ten patients had not been informed about the potential hazards of chiropractic cervical spine manipulation. Since possible complications cannot be predicted and may be very severe, it seems of utmost importance to carefully evaluate the benefit-risk ratio of each cervical manipulation and obtain consent of the patient after providing detailed information.

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