SHORT REPORT

Seasonal variability in spontaneous cervical artery dissection

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We examined the seasonal variability of spontaneous cervical artery dissection (sCAD) by analysing prospectively collected data from 352 patients with 380 sCAD (361 symptomatic sCAD; 305 carotid and 75 vertebral artery dissections) admitted to two university hospitals with a catchment area of 2 200 000 inhabitants between 1985 and 2004. Presenting symptoms and signs of the 380 sCAD were ischaemic stroke in 241 (63%), transient ischaemic attack in 40 (11%), retinal ischemia in seven (2%), and non-ischaemic in 73 (19%) cases; 19 (5%) were asymptomatic sCAD. A seasonal pattern, with higher frequency of sCAD in winter (31.3%; 95% confidence interval (CI): 26.5 to 36.4; $p=0.021$) compared to spring (25.5%; 95% CI: 21.1 to 30.3), summer (23.5%; 95% CI: 19.3 to 28.3), and autumn (19.7%; 95% CI: 15.7 to 24.1) was observed. Although the cause of seasonality in sCAD is unclear, the winter peaks of infection, hypertension, and aortic dissection suggest common underlying mechanisms.

There is considerable evidence indicating that the occurrence of stroke,¹ stroke mortality,² myocardial infarction,² and spontaneous dissection and rupture of the aorta³ shows seasonal variability, with increased frequency in winter. Spontaneous cervical artery dissection (sCAD) is a major cause of ischaemic stroke in young adults.⁴ We investigated the seasonal variability of sCAD as the impact of seasonal changes on its occurrence has not been properly studied in a large cohort of patients.

METHODS

All patients with sCAD admitted to the neurological departments of the University Hospitals Bern and Zürich, Switzerland from 1985 to May 2004 were prospectively included in the study. Although the investigated patients do not derive from a population based database, the two hospitals are 110 km distant from each other and are the only departments of neurology in the counties of Bern and Zürich with a population 2 200 000 inhabitants.

Cervical artery dissections were classified as spontaneous when occurring spontaneously or secondary to a minor trauma.⁵ Dissections occurring after an obvious head or neck trauma were classified as traumatic and excluded from the present study.^{6–7}

The seasonal pattern of sCAD was analysed using the date of symptom onset, which was split into quartiles based on seasonal trends. For asymptomatic sCAD, the date of symptom onset of the accompanying sCAD was used. Two patients with an isolated asymptomatic spontaneous internal carotid artery dissection (sICAD) were not included because the date of symptom onset could not be determined. The four seasons were defined as winter (21 December through 20 March), spring (21 March through 20 June), summer (21

June through 20 September), and autumn (21 September through 20 December).

Investigations

Baseline investigations

Risk factors for ischaemic stroke, connective disorders associated with sCAD, and a family history of sCAD were assessed as reported before.⁴ All patients underwent physical and neurological examinations, routine blood tests, a 12-lead electrocardiogram, ultrasound, and neuroradiological examinations. Patients with ischaemic stroke also underwent cranial computed tomography (CT) and/or magnetic resonance imaging (MRI).

Ultrasound studies

Ultrasound studies were performed with the same equipment (for extra- and transcranial colour duplex studies Acuson XP 10 or Sequoia (Mountain View, CA, USA); for transorbital Doppler studies EME or Multi-Dop X4 (DWL, Überlingen, Germany)) using recently published diagnostic criteria.⁴

Radiological investigation

sCAD was diagnosed by cervical MRI and cerebral magnetic resonance angiography (MRA), or intra-arterial digital subtraction angiography (DSA).^{4–8} MRI diagnosis of sICAD or spontaneous vertebral artery dissection (sVAD) was based on detection of a mural haematoma in the cervical internal carotid artery or vertebral artery, respectively. Diagnosis of sICAD on DSA was based on detection of an irregular stenosis (string sign), segmental stenosis beginning distal to the carotid bulb, or a pseudoaneurysm. Intimal flaps, double lumen, and dissecting aneurysms were considered to be specific, and irregular stenosis (string sign) was assumed to be suggestive for sVAD.⁸ Occlusive forms were confirmed by the presence of a mural haematoma on cervical MRI.

Angiograms and CT and MR images were reviewed by two experienced neurologists.

Statistics

Normally distributed data were expressed as means $\pm$ standard deviation. Descriptive statistical methods involving the determination of means, standard deviations, and frequencies were used to calculate patient characteristics. We tested the null hypothesis that the sCAD were equally distributed across the four seasons using χ^2 analysis.

RESULTS

A total of 352 consecutive patients presenting with 380 sCAD (305 sICAD and 75 sVAD) were identified. A total of 277

Abbreviations: CI, confidence interval; DSA, digital subtraction angiography; MRA, cerebral magnetic resonance angiography; MRI, magnetic resonance imaging; sCAD, spontaneous cervical artery dissection; sICAD, spontaneous internal carotid artery dissection; sVAD, spontaneous vertebral artery dissection

patients presented with 286 symptomatic sICAD (ten recurrences), which were accompanied by 16 asymptomatic sICAD and five sVAD. The remaining 75 patients showed 75 symptomatic sVAD (two patients had already suffered an sICAD), which were accompanied by three asymptomatic sICAD. The sCAD were symptomatic in 361 (95%; 286 sICAD and 75 sVAD) of 380 cases, and asymptomatic in 19 (5%; all sICAD) cases. The presenting symptoms and signs of sCAD were ischaemic stroke in 241 (63%) of 380 cases, transient ischaemic attack in 40 (11%) cases, retinal ischemia in seven (2%) cases, and non-ischaemic (headache, neck pain, Horner's syndrome, pulsatile tinnitus, and palsy of the caudal cranial nerves on the side of dissection in patients with sICAD; headache, neck pain, and cervico-radicular pain or senso-motor deficits in case of sVAD) in 73 (19%) cases. Patient characteristics are displayed in table 1.

As shown in fig 1, sCAD occurred more often in winter (31.3%; 95% confidence interval (CI): 26.5 to 36.4; $p = 0.021$) compared to spring (25.5%; 95% CI: 21.1 to 30.3), summer (23.5%; 95% CI: 19.3 to 28.3), and autumn (19.7%; 95% CI: 15.7 to 24.1). sICAD also occurred more often in winter than in the other seasons ($p = 0.033$), whereas sVAD showed a statistically insignificant trend towards increased occurrence in winter ($p = 0.153$) (fig 2). A peak during winter persisted when the years were grouped into four periods (1985–89, 1990–94, 1995–99, 2000–04), but this trend was not significant.

DISCUSSION

The present study demonstrates mild seasonal variation in the occurrence of sCAD and sICAD with a peak in winter. Seasonality was not found in patients with sVAD, but the lower number of patients in this group may have prevented the detection of significant results.

In contrast to the present study, Mayo Clinic patients were reported to show a peak frequency of sCAD in autumn.⁹ The lack of a winter peak in the US study may be explained by differences in patient selection. The Mayo Clinic patients were referred from the whole USA. Conversely, the present cases came from a defined Swiss area. Furthermore, the lower number of patients included in the US series might have prevented the detection of a winter peak.

Influenza epidemics have been associated with acute myocardial infarction, and influenza vaccination has been linked to reduced risks of stroke, recurrent myocardial infarction, and cardiac disease.¹⁰ Furthermore, a recent US study observed that the peak months of mortality from cerebrovascular and ischaemic heart disease are in winter, and coincided with peaks in pneumonia and influenza,² suggesting that these peaks are probably related to the incidence of influenza.² Two case-control studies have reported that infectious disease affecting especially the upper respiratory tract is an independent risk factor for sCAD,^{11, 12} although the reason for this association remains unclear. One

Figure 1 Seasonal distribution of 361 spontaneous cervical artery dissections.

Figure 2 Seasonal distribution of spontaneous dissection of the internal carotid ($n = 286$) and cervical vertebral ($n = 75$) arteries.

may speculate that an inflammatory process, possibly triggered by influenza virus infection, could damage the vessel wall by activating pro-inflammatory cytokines, free radicals, or proteases.¹¹ Mechanical factors such as violent coughing, sneezing, or vomiting associated with viral infection could be responsible for vessel dissection. However, such an association was not found in a case-control study.¹¹

A winter peak has also been reported for cardiovascular disease including aortic dissection.^{1, 3} Hypertension is the main vascular risk factor for aortic dissection, and blood pressure is well known to be higher in winter.^{3, 13} Elevated blood pressure values may thus trigger vessel rupture in sCAD as in spontaneous aortic dissection, especially in winter.

In summary, both influenza and hypertension might well explain the observed winter peak of sCAD and sICAD. However, the authors have no data of their own to underscore their hypotheses, and further studies are needed to clarify these issues.

This study was hospital based and is thus possibly biased towards patients with stroke, while sCAD resulting in none or other neurological symptoms might have evaded diagnostic investigation. Furthermore, patients with sCAD are typically young adults, and the presence of a stroke increases their chance of being referred to a stroke unit. On the other hand, a population based study for investigating seasonal variation in sCAD would be very expensive due to the low prevalence of this disease. In addition, population based studies would probably suffer from surveillance bias, because the intensity of diagnostic investigations is likely to be higher in hospital compared to population based series.

Table 1 Characteristics of 352 patients with spontaneous cervical artery dissection*

	n (%)
Men	206 (58.5)
Smokers	135 (38.3)
Current/former smokers	101/34 (28.7/9.6)
Hypertension	97 (27.5)
Diabetes mellitus	6 (1.7)
Total cholesterol >5 mmol/l	132 (37.5)
Coronary artery disease	5 (1.4)
Peripheral artery disease	2 (0.6)

Current/former smokers denotes cigarette smoking within the last 5 years/abstention from cigarette smoking for more than 5 years.

*Patients had a mean age $\pm$ SD of 45 ± 10 years.

The winter rates of sCAD could be due to the fact that many Swiss people engage in winter sporting activities such as skiing, ice skating, and ice hockey. However, these activities probably replace sports undertaken in other seasons, for example, hiking and mountain climbing. To the best of our knowledge, no study has examined whether the total amount of sporting activity, which is associated with increased risk of developing an sCAD, differs in winter from other seasons. Nowadays, many classic winter sports are also enjoyed in autumn and spring, while many sporting activities formerly not undertaken in winter are now carried out all year round. In conclusion, there is no evidence to support the hypothesis that winter sports had an impact on the winter peak of sCAD observed in this investigation.

We conclude that sCAD, similar to infection, hypertension, and aortic dissection, shows a seasonal pattern with a peak occurring in winter, suggesting common underlying pathophysiological mechanisms.

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