

## CASE REPORTS

## A case of cerebral haemorrhage—can *Ginkgo biloba* be implicated?

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### Abstract

**The case of a 56 year old man who suffered a spontaneous intracerebral haemorrhage after regular self medication with the herbal preparation, *Ginkgo biloba* leaf extract is described, and the possible association is discussed.**

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### Case report

A male taxi driver was found confused at the wheel of his car after a parking mishap in the taxi rank, unable to stand and complaining of severe pain behind his right eye and temple. On admission to hospital, he was noted to have developed a left hemiparesis, left hemianopia, and left sided neglect. An emergency computed tomogram revealed a right parietal haematoma with considerable oedema and midline shift. There was no evidence of recent alcohol ingestion. A full blood count, erythrocyte sedimentation rate, prothrombin time, fibrinogen concentration, serum urea and electrolytes, and autoimmune screen results were normal. Serum cholesterol was subsequently reported as slightly raised. A cerebral angiogram did not reveal any vascular abnormality. He was a non-smoker with no history of hypertension, diabetes, or vascular problems and there was no relevant family history.

On transfer to the neurorehabilitation unit seven days later, he had severe left sided neglect, left cortical sensory disturbance, a left hemianopia, and profound topographical disturbance. His wife mentioned to a nurse that he had been in the habit of taking *Ginkgo biloba* leaf extract 40 mg three times a day for the previous 18 months. He had taken it as a general tonic having read about it in the tabloid press. He took no other herbal or proprietary medication on a regular basis. In response to his wife's comment, we sought the assistance of our drug information service for evidence of a possible connection between ginkgo extract and the patient's condition.

### Discussion

*Ginkgo biloba* is the botanical name for the Maidenhair tree (also called the fossil tree or the Kew tree). It is an eastern Asiatic tree, a gymnosperm, related to trees such as the pines and spruces, though unlike the latter two, ginkgo is broad leaved. It is not known with certainty if the tree grows in the wild, but is a popular tree for planting in parks and along

streets as it is relatively pest free and thrives in cities. While the pulp of its fruit can result in unpleasant allergic reactions if eaten, the nut within the fruit is a sweet kernel that is edible when cooked. The seeds, when consumed in large amounts, contain sufficient amounts of toxin that can result in convulsions, unconsciousness, and even death (gin-nan food poisoning). The leaves form the basis of an increasingly popular herbal preparation, either alone or in combination with other herbal extracts.

*Ginkgo biloba* extract is widely advertised in the media and on the internet as a panacea for a wide range of conditions that would appear to have a dysvascular aetiology. These comprise dementia, peripheral vascular disease, memory impairment, erectile dysfunction, premenstrual syndrome, asthma, senile macular degeneration, tinnitus, and vertigo. These conditions, as one might expect, affect large swathes of the middle and older aged population to a greater or lesser extent, thus resulting in a large and ready market for the product.

The extract is thought to exert its effects through its influence on the prostaglandin metabolism, antagonism of platelet activating factor and scavenging of free radicals, which result in vasodilatation, reduced blood viscosity, suppression of inflammatory cascades, increased tissue tolerance to ischaemia, and inhibition of peroxidation of lipid membranes.<sup>1</sup>

However, there have been some recent reports of its possible association with cerebral and extracerebral haemorrhage. Rowin and Lewis, in 1996, postulated that a case of bilateral subdural haematoma had resulted in part from the chronic use of *Ginkgo biloba* extract.<sup>2</sup> A prolonged bleeding time was demonstrated which resolved on discontinuing the extract. In 1997, there were separate reports of a subdural haematoma by Gilbert,<sup>3</sup> and a hyphema by Rosenblatt and Mindel,<sup>4</sup> both clinical events being temporally related to ingestion of the extract. The following year, a case of unexplained subarachnoid haemorrhage, associated with a prolonged bleeding time after *Ginkgo biloba* extract ingestion during the preceding six months, was described by Vale,<sup>5</sup> and Matthews<sup>6</sup> reported a case of parietal lobe haemorrhage in a woman who had been stable for a long period of time on warfarin but had started to take the extract two months before the event.

Odawara *et al*, in criticism of Rowin and Lewis's case report, pointed out the poor

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reproducibility of bleeding time and also questioned its relative significance to that of unrecalled trivial head trauma in cases of subdural haematoma.<sup>7</sup> In reply, Rowin and Lewis suggested that unrecalled trivial head trauma could work in conjunction with a disturbed bleeding status rather than the two operating as distinct risk factors.

Ours is the latest in the reported series, a case of parietal haemorrhage with no previous medical or drug history other than the use of *Ginkgo biloba* extract in the preceding 18 months.

Herbal remedies are widely thought of as benign, precisely the premise for exempting them from the stringent scientific scrutiny of benefits and adverse effects, and the rigorous pharmacological purity and standardisation imposed on allopathic medications. There is increasing evidence of significant interactions with prescribed medications as recently shown with St John's Wort.<sup>8</sup> Other serious side effects such as renal failure with aristocholia<sup>9</sup> and hepatotoxicity with proprietary herbal mixtures<sup>10</sup> merit serious consideration. Yet all herbal medications are available freely over the counter and with little recognition of their possible adverse effects.

The literature on studies pertaining to the benefits and side effects of *Ginkgo biloba* extract is both equivocal and less than scientifically rigorous.<sup>11</sup> We are conscious that the connection with haemorrhage is anecdotal, but there is enough prevailing evidence to serve as an invitation to all doctors who confront spontaneous haemorrhage in hospitals to be aware of pertinent herbal remedies such as *Ginkgo biloba* and to record them in the drug history. It is also entirely appropriate, and desirable, that the Committee on Safety of Medicine's yellow card

### Key points

- The herbal preparation *Ginkgo biloba* leaf extract is promoted as a remedy for a wide range of conditions (for example, dementia, erectile dysfunction, tinnitus)
- There are grounds to suspect an association with intracranial haemorrhage as described in this case
- Awareness of these suspicions should encourage proper documentation of all herbal remedies used when patients present to medical staff

be duly dispatched, as was done in our case. That would be the first step in gauging the true association between *Ginkgo biloba* extract and haemorrhage.

Meanwhile, our patient remains with a left inferior quadrantanopia, a devastating handicap for a taxi driver.

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