Aeromedical Implications of Cerebral Cavernomas

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BACKGROUND: Cavernomas, cavernous angiomas, or cerebral cavernous malformations are clusters of endothelium-lined blood vessels usually found in the brain. With the increasing use of radiological imaging, these are being detected incidentally in asymptomatic aircrew. The UK Civil Aviation Authority (CAA) experience of cavernomas is described and the aeromedical concerns, that is, the risk of epilepsy, hemorrhage, and the development of a neurological deficit, are considered.

METHODS: A search of the CAA database between 1990 and 2020 was performed for the term 'cavernoma'. The gender, age at diagnosis, class of certification held, clinical presentation, location, and size of the lesion were noted. A PubMed literature review for papers with complications of cavernoma was performed.

RESULTS: Six cases of cavernoma have been declared to the CAA: five professional pilots and one private pilot. Five were men and one was a woman. The age range was between 38 and 60 yr, with a mean of 48 yr. Two cases presented with clinical symptoms and four were asymptomatic. Complication rates for seizure and hemorrhage were extracted from the published literature together with the significance of other factors such as cavernoma size, family history, multiplicity, and the development of new lesions.

DISCUSSION: A policy for the medical certification of aircrew with cavernomas that have presented with clinical symptoms and those that are detected incidentally is proposed.

KEYWORDS: cavernomas, cavernous malformations, fitness to fly, incapacitation risk.

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The widespread use of brain scanning (CT and MRI) for many symptoms have revealed a large number of asymptomatic lesions, including meningiomas and cavernomas. There is a risk of epilepsy with both of these conditions and an additional risk of hemorrhage with a cavernoma. The medical certification of a pilot with such an incidental finding presents a problem. Since cavernomas have this double risk, it is this incidental finding which is discussed here.

Cavernomas, also known as cavernous angiomas or cerebral cavernous malformations, are clusters of thin walled, endothelial lined sinusoidal blood vessels that usually occur in the brain, but may also occur in the spinal cord. In contrast to arteriovenous malformations, cavernomas do not have a high-pressure arterial supply or major venous drainage and only have small feeding and draining vessels with low pressure blood flow. There is normally no neural tissue within cavernomas.

The incidence of cavernomas is quoted as between 0.15 to 0.56 per 100,000 per year.[13] The prevalence is thought to be between 0.1% and 0.9%;[4,27] however, the true prevalence is unknown since lesions may remain asymptomatic and 20–50% of cavernomas are first identified incidentally.[8] Cavernomas present with a slight predominance in males and a mean age of 30 to 40 yr.[12,27] Of patients with cavernomas, 20% have a familial form which is inherited in an autosomal dominant pattern associated with one of three identified groups of genetic abnormalities.[8,10,12,27] The familial form usually results in multiple cavernomas, whereas the sporadic form is often solitary. About 25% of cavernomas are associated with a developmental venous anomaly (DVA).[2]

METHODS

A search of the Civil Aviation Authority (CAA) computer database that holds records of all initial applicants and medical

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certificate holders between 1990 and 2020 was performed using the diagnostic term 'cavernoma'. This diagnosis had been reported by the pilot to the CAA Medical Department or to a CAA Aeromedical Examiner. The medical notes were reviewed to obtain data on gender, age at diagnosis, medical certification held, the clinical presentation, and the location and size of the lesion.

A PubMed literature search was performed using the term 'cavernoma'. We limited our review to publications in English containing data on adults. We selected those papers that included information on the complications of cavernoma, including hemorrhage and seizure.

RESULTS

A regulatory database has the problem that if certification is withdrawn, there are no follow-up reports, so that any subsequent complications are unknown to the CAA. There were six cases of cavernoma found in the CAA medical database over the last 30 yr. Five were professional pilots and one was a private pilot applicant.

Five were men and one was a woman, with an age range of 38 to 60 yr and a mean of 48 yr. None presented with a seizure. Two cases presented with clinical symptoms, both due to pontine hemorrhage with focal neurological deficit; one had paresthesia of the right hand and face with gait instability, while the other had diplopia. The cavernoma was an asymptomatic incidental finding in the other four cases. Only one regained medical certification. (**Table I**)

DISCUSSION

Most publications relate to patients who have presented with symptoms resulting from a complication of a cavernoma, with far fewer papers reporting the follow-up of incidentally found asymptomatic cavernomas, which makes accurate assessment of the risks less reliable than the risks after presentation with an event. Since many cavernomas remain asymptomatic, estimates of the risks of an event from data derived from the incidental finding of an asymptomatic lesion must overestimate the true risk, but this cannot be quantified and the risks quoted here refer to published data.

The aeromedical concerns with brain cavernomas are the risk of epilepsy, the risk of hemorrhage, and the risk of developing a neurological deficit. The CAA only permits certification if the risk of a medical incapacitation is no greater than 1% per annum for professional multicrew operations. Where there is more than one risk of incapacitation, as is the case with some cerebral cavernomas, the cumulative risk must not exceed 1% per annum.

There are two situations to consider when a cavernoma is encountered in aircrew. A cavernoma may have presented with symptoms such as a seizure, hemorrhage, or a focal neurological deficit; or it may be an incidental finding if a brain scan has been performed for an unrelated reason.

If a cavernoma presents with a seizure, the 5-yr risk of seizure recurrence is 94%,[15] giving an annual recurrence risk of 19% per annum, assuming that the risk is constant over the 5 yr. There is no published data that shows if this risk changes with time. However, it is extremely unlikely that the risk would ever reach 1% per annum and, therefore, a pilot should be considered long term unfit. Even if the lesion is removed after the initial presentation with a seizure, up to 35% of patients will still have seizures after 3 yr. Assuming a constant rate in the first 3 yr, this would give a seizure recurrence risk of almost 12% per annum, which would also preclude certification.[9]

If the clinical presentation of a cavernoma is the result of a hemorrhage, the 5-yr risk of a recurrence is 18–30%.[6,14] This risk declines with time from 20% in the first year to 5% in the fifth year.[6] In a meta-analysis of 25 studies,[24] the rebleed rate in 2 yr for non-brainstem lesions was 6.3% and for brainstem lesions was 32%, and the mean time to the rebleed was 10.5 mo. In view of these two meta-analyses, certification is not possible after a bleed. There is also an increased risk of hemorrhage if there is a DVA associated with the cavernoma.[1,16]

If there is focal neurological deficit due to hemorrhage or an expanding lesion which is more common in brainstem lesions, medical certification will depend on the functional nature of the deficit and its importance for the flying task. If lesion resection is undertaken, up to 8% have a persistent neurological deficit, so certification will depend on the surgical result.[23] However, focal neurological deficit is often due to hemorrhage and, therefore, the associated rebleed risk must also be considered.

Of cavernomas, 20–50% are identified as an incidental asymptomatic finding.[8] The incapacitation risks associated with the incidental finding of a cavernoma depend on the risk of an initial clinical presentation of the same three complications.

In a meta-analysis of 22 publications of the intracerebral hemorrhage risk, 1620 subjects had relevant data, with over

Table I. UK CAA Cavernoma Experience.

			PRESENTATION			
SEX	LOCATION	SIZE MM	SEIZURE	ICH	FND	CERTIFICATION
M	R Parietal cortical	Not known	--	--	--	N
M	R occipital subcortical	17	--	--	--	Y
M	R Tempo-occipital cortical	10	--	--	--	N
M	L temporal cortical	10	--	--	--	N
F	Pontine	25	--	+	+	N
M	Pontine	8	--	+	+	N

ICH: intracranial hemorrhage; FND: focal neurological deficit.

5000 patient years of follow-up.[14] The 5-yr risk of intracerebral hemorrhage for brainstem lesions was 8%, but this figure was much less at 3.8% for non-brainstem lesions. In another meta-analysis, the annual risk of hemorrhage for non-brainstem lesions was 0.3%, but was 2.8% for brainstem lesions.[24] Using the 1% rule, brainstem lesions would not be acceptable for certification, but non-brainstem lesions might be acceptable if there were no other coexisting risk factors, such as an associated DVA, which has an increased risk of intracerebral hemorrhage,[1,16] or a risk of epilepsy.

Since cavernomas do not contain any neural tissue, they are not of themselves epileptogenic, but may induce seizures by their effect on surrounding brain parenchyma, probably by small leaks of blood products which form the hemosiderin ring.[7] The risk of epilepsy depends on the location of the cavernoma: in a study of 109 cavernoma patients, 49 of 81 (60%) with involvement of the cerebral cortex had epilepsy, particularly if the mesiotemporal cortex was involved; but none of the 17 subjects with subcortical lesions had epilepsy. Therefore, if there is no cortical involvement, there is no risk of epilepsy,[20] which accords with other subcortical lesions.

There are several other factors to consider for certification. The existence of multiple cavernomas will increase the likelihood of developing a complication, as the risk depends on the same three risk factors for each lesion. Multiple lesions may be seen in 30% of patients and may be familial in 9%.[3] Familial cases are more likely to have multiple cavernomas and are also more likely to develop new lesions and, therefore, more likely to develop a complication. A study of 21 asymptomatic patients diagnosed with familial cavernomas followed up for an average of 2.2 yr reported symptomatic hemorrhage rates of 6.5% per patient-year and asymptomatic hemorrhage rates seen on MRI of 13% per patient-year.[26.]

There is a risk of a cavernoma changing in size over time. A prospective volumetric analysis of 107 cavernomas over a mean period of 3.7 yr found that 43% increased in size, 35% decreased in size, and 22% remained the same.[11] As such variable changes cannot be forecast, there is a need for regular follow-up scans for ongoing certification. The size of the lesion by itself does not seem to affect the risk of hemorrhage; however, increasing size may be a factor.

Several studies have quantified the incidence of de novo lesion development, ranging from 0.1 to 0.6 new lesions per patient year.[17,19] This is more common in the familial form of the disease than in the sporadic form, but this does occur in both. About 30% of familial patients develop new cavernomas, whereas only about 4% of sporadic patients develop new lesions over a mean period of 2 yr.[18,22]

There is much debate as to whether a hemosiderin ring on imaging should be classified as a hemorrhage. Of cavernomas, 80–90% have a surrounding hemosiderin ring. An expert group reviewed this and concluded that the mere existence of a hemosiderin halo should not be considered to constitute hemorrhage and defined hemorrhage as the acute or subacute onset of symptoms referable to a cavernoma with radiological, surgical, or pathological evidence of recent hemorrhage.[5] This definition was postulated to try to achieve uniformity in published series. However, MRI evidence of a hemorrhage within the cavernoma or outside the hemosiderin rim may be asymptomatic. Since almost all cavernomas have a hemosiderin ring, the risk data we have used takes this into account. It is unknown whether there is a difference in hemorrhage rates between those with a hemosiderin ring and those without, but the hemosiderin ring may contribute to the development of epilepsy if the lesion affects the cortex.

A policy for medical certification is considered. Factors which would preclude certification are all pilots or applicants with cavernomas who have presented with symptoms, typically headache, hemorrhage, a seizure, or focal neurological deficit. For those with an incidental finding of cavernoma, brainstem lesions would not be acceptable due to the risk of hemorrhage and involvement of brainstem functions. Lesions with any involvement of the cerebral cortex would be disqualifying due to the risk of epilepsy. Additional factors which may also preclude certification are the presence of multiple lesions due to the additive risks of more than one lesion and the presence of a DVA, which is associated with an increased risk of hemorrhage. The certification of familial cases depends on whether there are multiple lesions with their cumulative risks. Factors which may permit certification would be the incidental finding of a single asymptomatic cavernoma, that is not located in the brainstem, and is strictly subcortical and without an associated DVA. It is proposed that this would allow professional pilot certification with a copilot restriction and unrestricted private pilot certification. The total risk must not exceed 1% per year. In view of the risk of expansion and the development of new lesions, there is a need for regular follow-up scans for ongoing certification with both sporadic and familial cases; it is suggested that this is undertaken every 6 mo for the first 3 yr and then annually.

Other worldwide regulatory aviation authorities have different policies. Australia's Civil Aviation and Safety Authority has no published policy. The Federal Aviation Administration has no published policy, but has reported a case of an asymptomatic pilot with a strong family history who was found to have three cavernomas and was denied certification.[21] Transport Canada's policy is that applicants with cavernomas that are deep, with no evidence of previous hemorrhage, may be considered fit; all others should be considered unfit.[25]

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