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MEET THE EXPERT

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Sentinel headache

Abstract Patients with subarachnoid haemorrhage (SAH) frequently describe the occurrence of an underestimated or even ignored severe headache in the days or weeks preceding the bleeding. If recognised early, this warning headache might lead to specific investigations and, if indicated, a surgical approach might avoid a dramatic haemorrhagic event. In a recent and exhaustive systematic review, the incidence of a sentinel headache (SH) was evaluated in a range of 10–43% of SAH patients. SH seems to be due to a minor bleeding from a leak of a berry aneurysm and usually occurs in the preceding two weeks. Such a period is similar to the one for rebleeding in SAH and supports the hypothesis of the warning leak. Nevertheless, a warning headache can precede a SAH in unruptured aneurysm even without a minor bleeding. Underestimation or misdiagnosis of SH depends on incorrect evaluation of the headache characteristics (unusual, severe, abrupt, thunderclap), overestimation of cranial CT sensitivity (false negative increasing over the elapsing time), failure to perform lumbar puncture (LP) in patients with negative CT, incorrect evaluation of CSF findings (xanthochromia may be absent in the first 12 h) and failure to differentiate traumatic tap from true SAH. Considering the diagnosis of SH in all cases of a severe, sudden-onset (thunderclap) headache, and performing all the appropriate diagnostic exams, including LP if necessary, could prevent subsequent massive bleeding and its invalidating or fatal consequences.

Key words Sentinel headache • Subarachnoid haemorrhage

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"The worst headache in my life": what it means, what could it hide, what we have to do?

Headache is the main complaint in 20% of outpatients consulting the neurologist [1] and about 1.2–4.5% of all adult patients presenting to an emergency department (ED) complaining of a headache [2, 3]. Of these, 4.3–6.4% are secondary headaches and 0.5% have a vascular pathogenesis [4]. Data from the "NEU" Project, concerning neurological burden of Neurology in the Emergency in Italy, showed that headache (23%) and cerebrovascular diseases (26%) were the main cause of neurological consultations in ED [5]. About 12–25% of all patients presenting to the ED with a sudden-onset severe headache, described as the "worst of their lives", have a subarachnoid haemorrhage (SAH) [6, 7]. In a large prospective observational study, among 455 patients presenting to ED for headache, 107 had a "worst headache" and 20 patients of this group (19.5%) had a SAH, diagnosed by cranial CT scan in 18 patients and by lumbar puncture (LP) in two with negative CT scan [7]. Although less than 1/1000 of patients presenting to ED has a SAH [1], early recognition is critical considering the high lethality of the disease and because early surgery of an identified aneurysm improves outcomes.

Patients with SAH frequently describe the occurrence of an underestimated or even ignored severe headache in the days or weeks preceding the bleeding. If recognised early, this warning headache might lead to specific investigations and, if indicated, a surgical approach can avoid a dramatic haemorrhagic event. Over 60 years ago, Richardson and Hyland [8] observed that SAH patients admitted to hospital frequently reported a misdiagnosed severe headache preceding the event. True incidence of this warning headache is difficult to evaluate. In a recent and exhaustive systematic review, the incidence of a sentinel headache (SH) was evaluated in a range of 10–43% of SAH patients [9]. The wide range of incidence could be due to a recall bias, but some studies comparing SH incidence in aneurysmal SAH *vs.* non aneurysmal SAH or stroke,

reported in those groups an incidence of just 4 and 5% respectively, when only severe previous characteristic headache was considered [10].

SH seems to be due to a minor bleeding from a leak of a berry aneurysm, firstly defined as "warning leak" by Gillingham in 1958 [11]. Usually SH occurs in the preceding two weeks, with a peak within 24 h and a minor peak in the 7–14 days before. Such a period is similar to the one for rebleeding in SAH and supports the hypothesis of the warning leak.

Nevertheless, a warning headache can precede a SAH in unruptured aneurysm even without a minor bleeding. This could be caused by stretching or dissection of the aneurysm wall.

As a misdiagnosis could produce serious consequences, physicians should pay attention to all worrisome headaches presenting the characteristic "red flags" suggesting a possible intracranial structural pathology, such as the sudden onset of a severe headache (thunderclap headache) typical of a SAH [12]. Symptoms and signs characteristic of SAH are severe sudden-onset headache (74%), frequently associated with nausea or vomiting (77%), loss of consciousness (53%), neurological signs including consciousness impairment (64%) and neck stiffness (35%) [13].

Cranial CT scan is the first choice investigation in suspected SAH but the sensitivity is related to the time elapsed from the bleeding, detecting blood in 95% within 24 hours, in 74% on the third day, in 50% after one week, in 30% after two weeks and absence of abnormal findings after three weeks. CSF examination with spectrophotometry, performed after 12 h, shows a higher sensitivity, with evidence of xanthochromia in 100% of SAH within 14 days, in 70% in the third week and in 40% in the fourth. Because of its risks, LP should be performed only after cranial CT [14]. Thin slices (5 mm) cranial CT should be performed, because small blood collections may not be evident with thicker slices (10 mm) [15]. Brain MRI showed nearly the same sensitivity in acute phase (94%) and higher sensitivity in subacute phase (100%) [16]. If strong clinical evidence of SAH is still present in the absence of abnormal findings in all the previously described exams, MR angiography or conventional angiography is suggested to exclude the presence of an unruptured cerebral aneurysm.

Usually the characteristic clinical features of SAH such as the presence of neurological signs and symptoms, consciousness impairment and neck stiffness are not present in SH. Underestimation or misdiagnosis of SH depends on incorrect evaluation of the headache characteristics (unusual, severe, abrupt, thunderclap), overestimation of cranial CT sensitivity (false negative increasing over the elapsing time), failure to perform LP in patients with negative CT, incorrect evaluation of CSF findings (xanthochromia may be absent in the first 12 h) and failure to differentiate traumatic tap from true SAH [17]. The wide spectrum of incidence range among different studies is probably related to the frequency of misdiagnosis rather than a recall bias. Physicians' competence and health care organisation allow a correct diagnosis [6, 9]. Educational programmes have been associated with a lower frequency of misdiagnosis [18]. Considering the diagnosis of SH in all cases of a severe, sudden-onset (thunderclap) headache, and performing all the appropriate diagnostic exams, including LP if necessary, could prevent subsequent massive bleeding and its invalidating or fatal consequences.

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