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Pearls and Oysters: De Novo Seizure and Stroke in the Elderly: The Issue of Chicken and Egg

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Abstract:

Seizures immediately preceding the occurrence of an ischemic or hemorrhagic stroke are a rare but well documented phenomenon, for which the term “heraldic seizure” has been proposed. Cerebrovascular disease is the most common cause of epileptic seizures in elderly patients, thus screening and management of vascular risk factors should be done systematically in cases of late-onset epilepsy. MRI may help to distinguish heraldic seizure from stroke-elicited seizure by showing abnormalities confined to the cortex that spare vascular territories, increased MRA flow in the ipsilateral cerebral arteries and enhancement of the leptomeninges on postcontrast MRI. Here we present a case report that illustrates the difficulty of making the diagnosis of a heraldic seizure at onset.

Pearls:

Seizure immediately preceding the occurrence of an ischemic or hemorrhagic stroke is a rare but well documented phenomenon, for which the term of heraldic seizure has been proposed.

MRI may help to distinguish heraldic seizure from stroke-elicited seizure, showing abnormalities confined to the cortex that spare vascular territories, increased MRA flow in the ipsilateral cerebral arteries and enhancement of the leptomeninges on postcontrast MRI.

Oy-sters:

Heraldic seizure may be difficult to distinguish from the more common situation where seizure is provoked by a stroke, especially when facing with a long lasting post-ictal deficit.

Considering cerebrovascular disease as the most common cause of epileptic seizures in elderly patients, screening and management of vascular risk factors should be done systematically.

Heraldic seizure could also precede, in rare cases, intraparenchymal hemorrhages.

We present the case of an 81-year-old woman with history of endometrial carcinosarcoma and essential thrombocythemia, without known modifiable cardiovascular risk factors. She presented to the emergency room with new onset, persistent since a few hours, right-hand motor clonic jerks, without ipsilateral face or leg involvement. The electroencephalogram (EEG) performed after the administration of two injections of 1 mg clonazepam followed by 15mg/kg IV fosphenytoin was normal, however the treatment reduced the focal motor status epilepticus for a few hours only. Brain CT-scan, laboratory tests and EKG were normal. A first Magnetic Resonance Imaging (MRI) scan performed two days after the onset while the patient still had clonic movements, revealed a left cortical precentral hyperintensity in Diffusion Weighted Imaging (DWI) and Fluid Attenuation Inversion Recovery (FLAIR) sequences, with reduced Apparent Diffusion Coefficient (ADC) and gadolinium enhancement (Figure 1). These findings were interpreted as post-ictal changes by a neuroradiologist. The introduction of 100mg twice daily lacosamide stopped the seizures in 72 hours. As expected, we observed a post-ictal right hand motor deficit. However, the paresis also involved the right side of the face (initially not involved during the seizures) and lasted more than 48 hours, so that a control MRI was performed. This exam showed multiple cerebral infarctions in the middle cerebral artery territory (Figure 2). A less than 50 % stenosis at the origin of the left internal carotid

artery with an atherosclerotic plaque was also found (Figure 2); echocardiography was normal. We introduced an antithrombotic treatment. EEG at hospital discharge showed left central spikes and we continued the antiepileptic treatment with lacosamide. At two months follow-up the patient had almost fully recovered and remained seizure free.

Discussion:

Cerebrovascular disease is known to be the most common cause of provoked seizure in the elderly^{1,2}, generally defined as patients over 60 years-old^{2,3}. The risk of seizure occurrence after a first stroke ranges from 5.7% during the first year to 11.5% within 5 years⁴. Interestingly, late-onset seizures without known cardiovascular disease also represent a risk factor for stroke^{5,6}. In this context, the specific term of “heraldic seizure” has been used to describe epileptic seizures immediately preceding cerebral infarction. This term now encompasses seizures of cerebrovascular origin occurring before any evidence of stroke, possibly triggered by silent ischemia⁷ and, in rare cases, also occurring before intraparenchymal hemorrhage⁸. The exact pathophysiology of heraldic seizures remains unclear, however there is increasing evidence that occult cerebrovascular disease could be the cause of epileptogenesis via disordered cerebral blood flow, inflammation and blood-brain barrier disruption, leading to neuronal hyperexcitability⁹. Thus, heraldic seizures should be considered as a warning symptom of cardiovascular disease in elderly patients. Consequently, a systematic screening for the presence of vascular risk factors should be performed following a de novo late onset seizure, and corresponding treatment considered. In our case, the most prominent cerebrovascular risk factor was the significant stenosis of the internal carotid artery.

This case also underlines the difficulty of diagnosing heraldic seizure and making a therapeutic decision. While the MRI imaging after heraldic seizure can be normal, similar findings in signal intensity in DWI, ADC and FLAIR sequences can be found both after a seizure and during early stroke. In our case, given the clinical presentation and the absence of known cardiovascular risk factors at the time of the first MRI, the images were interpreted as post status epilepticus alterations, even though cerebral ischemia was a valid differential diagnosis. In general, findings confined to the cortex and not respecting vascular territories, increased flow in the ipsilateral cerebral arteries on MRA (not shown in our case because unavailable, see Lansberg et al.¹⁰) and enhancement of the leptomeninges on postcontrast MRI should orient the clinician to an epileptic origin¹⁰. In addition, post-ictal neurological deficit is quite common in the context of focal motor status, but its long duration should lead to renewal of the cerebral imaging. Post-ictal deficit has been reported to last between 173 seconds and 22 minutes¹¹ while longer durations of up to 36 hours have been observed when a structural lesion of the brain existed¹². While there have been some studies examining early and late poststroke epilepsy prevention, to our knowledge there is no study regarding heraldic seizures and the risk of developing epilepsy. The rate of long-term post-stroke epilepsy is low as compared to the rate of early post-stroke seizures, so that the initiation and duration of antiepileptic drugs should be considered accordingly¹³. In our case, the initiation of anti-epileptic treatment appeared mandatory because of the severity of the clinical presentation at the onset, and the therapy continuation was justified by the persistence of interictal epileptiform discharges on the control EEG, which we considered as a sign of an active epileptogenic zone due to the ischemic lesion.

Figure 1- first MRI (48h after seizure's onset)

Axial MRI slice: Left cortical hand region precentral lesion (arrowheads). (A) Diffusion weighted imaging (DWI) hypersignal with (B) low apparent diffusion coefficient and corresponding (C) Fluid Attenuation Inversion Recovery (FLAIR) hypersignal with (D) T1 gadolinium enhancement.

Figure 2– Control MRI (48h after seizure stop)

Axial MRI slice: left cortical infarction in middle cerebral artery territory (arrowheads). (A) Diffusion weighted imaging (DWI) (B) Apparent diffusion coefficient (C) Fluid attenuation inversion recovery (FLAIR). (D) CT - angiography revealing an atherosclerotic plaque in the left internal carotid artery (arrowhead).

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