Journal of Molecular Biomarkers & Diagnosis
ISSN: 2155-9929

Carlo et al., J Mol Biomark Diagn 2017, 8:2
DOI: 10.4172/2155-9929.1000325

Case Report Open Access

Thalamic "Personality" and Triptans…Prescient of A Stroke?

Canepa Carlo[1]*, Griffiths Pahet[2], and Brett James[3]

[1]James Paget University Hospital, Stroke and Neurology, UK
[2]University Hospital, Stroke/Care of the Elderly Wyllie, Hilary, UK
[3]James Paget University Hospitals NHS Foundation Trust, Stroke, UK

Abstract

27-year-old female patient with history of migraine with sensory aura. Approximately four months previous to her admission, her migraines were increasing in frequency; due to this, she increased her dose of sumatriptan. One month previous to her admission, she presented an acute episode of the "worst migraine attack in her life", without any associated focal neurology. Despite reducing in intensity, the headache persisted from that day onwards. After approximately one week, she developed neurobehavioral changes, which progressively worsened. Her CT on admission showed a hypo density in the right anterior thalamus; an MRI done three days later demonstrated a chronic (>3 weeks old) right thalamic stroke. The "worst migraine of her life" correlates well with the occurrence of the right thalamic stroke. The previously increased dose of sumatriptan seems to have precipitated the event and, the neurobehavioral changes fit nicely with the anterior damage to the thalamus.

Keywords: Neuroimaging; Neurology; Stroke; Neurology

Background

Stoke in young adults can be challenging to diagnose, especially in the absence of typical focal symptoms. This case illustrates an unusual neurobehavioral presentation of stroke associated with thalamic infarct in a patient with classic migraine with aura. Non-resolving neurology in a patient with a migraine should always prompt further evaluation.

Case Presentation

27-year-old, right-handed female patient who at the age of 23 was diagnosed with a right epithelial cell ovarian tumour for which she underwent a right salpingo-oophorectomy without complications. Two years later she was diagnosed again with another epithelial cell tumour, this time in the left ovary and this led to a left salpingo-oophorectomy and a hysterectomy.

Since the age of fifteen, the patient suffered also from headaches of various characteristics. During her adolescence, her headaches were very much related with her menstrual period and were short-lived, localized to both frontal lobes and associated with neither vomiting nor photophobia. However, throughout the following years, she would develop migraine-like symptoms (with sensory auras, characterized by facial and tongue Paresthesias associated with disguesia and abnormal olfaction), which progressively worsened, leading to numerous analgesic trials without obtaining proper control. Each episode presented throbbing pain localized over the right frontal-temporal lobe, lasting between one and 3 hours and commonly associated with nauseas, vomiting and photophobia.

Approximately one month before her admission to our hospital, she claimed to present one distinctive episode of "the worst headache she ever had" (preceded with a prolonged sensorial aura, of approximately 2-3 hours), which lasted almost 24 hours and was associated with several episodes of vomiting, extreme sensitivity to light and sound, disorientation, dizziness and blurred vision. Unfortunately, she did not seek any medical attention. During the following days, although the severity of her headache greatly reduced, it did not completely subside. Furthermore, she continued to have dizziness and occasional episodes of blurred vision and vomiting.

Eventually, after 3 days of persistent symptoms, she was evaluated by her GP who advised her to continue to take sumatriptan for her migraines (which she had been previously taking). She admitted to taking "inadequately" (sometimes excessively) sumatripan during the previous three to four months before the severe migraine occurred. When asked about this inadequate administration, she admitted to taking two or three tablets per day and definitely more than 10 tablets per month. Essentially, on her own account, she decided to take sumatriptan as a "prophylactic" treatment rather than a "rescue" one.

Interestingly, approximately one week after her severe migraine episode, the patient (her husband and her parents), described a rather "sudden and abrupt change in personality", completely different from her usual easy-going nature. She became increasingly intolerant to minimal changes in her daily routine and noticed that any minor comment coming from her husband or family immediately triggered an angry response, "snapping" back at them aggressively. More so, she stated to have as she mentioned, a "terrible memory" (she stated that since the onset of the severe migraine, her memory for new events, names, dates and daily occurrences had deteriorated tremendously and this was also creating more emotional distress). During the following weeks, she became disinterested in others, unconcerned with important dates and events and markedly more "slow" to do everything. Furthermore, she began to have difficulty enumerating simple items, organizing thoughts and constantly forgetting the time and the basic facts.

Approximately one month after the "severe" episode of headache she was admitted. Her physical examination was unremarkable: no limb weakness was noted, no sensory deficiency or cranial nerve palsy; cerebellar function was normal, balance intact and her reflexes were preserved in all four limbs. However, she did appear to be very upset

***Corresponding author:** Canepa Carlo, James Paget University Hospital, Stroke and Neurology, UK, Tel:+ 01493 452452; E-mail: Carlo.Canepa@jpaget.nhs.uk

Received March 10, 2017; **Accepted** March 23, 2017; **Published** March 25, 2017

Citation: Carlo C, Pahet G, James B (2017) Thalamic "Personality" and Triptans…Prescient of A Stroke? J Mol Biomark Diagn 8: 325. doi: 10.4172/2155-9929.1000325

about many minor details, intolerant to subtle comments (mainly from her family), depressed at times and generally, emotionally labile. And this was completely different to her usual personality. This was the only abnormal change she presented; she had no focal neurology.

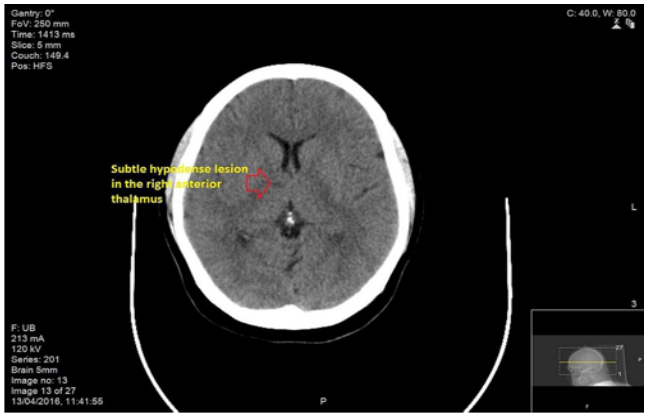

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Figure 1 (CT Head): Subtle hypo dense lesion visualized in the right anterior thalamic region. No signs of bleeding or midline shift.

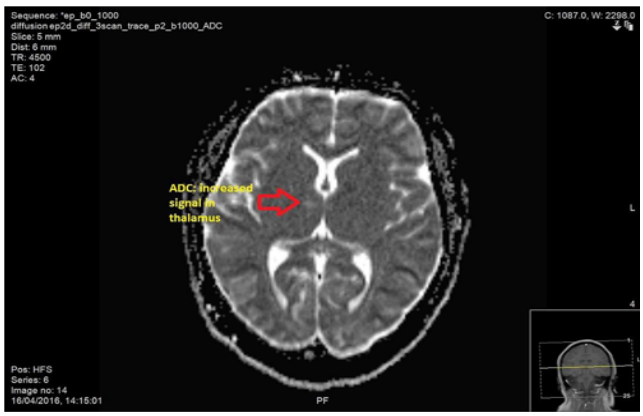

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Figure 2 (DWI-MRI): Absence of increased signal in the right thalamic region (in the anterior nucleus).

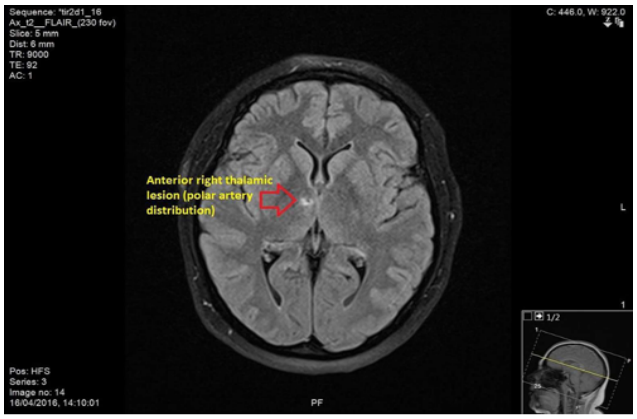

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Figure 3 (ADC-MRI): Increased signal in the right thalamic region (in the anterior nucleus).

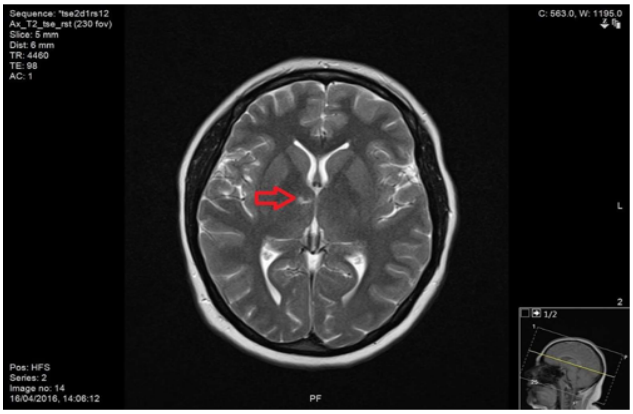

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Figure 4 (T2-FLAIR): Right anterior thalamic region lesion, in the area supplied by the right polar artery.

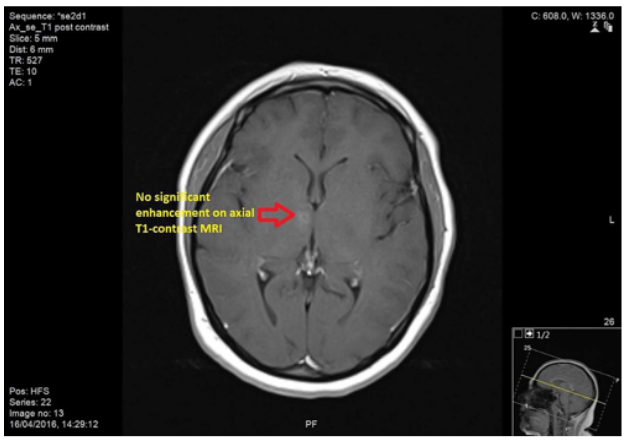

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Figure 5 (T2 Axial): Increased signal in the right anterior thalamus.

A non-contrast CT Head was done (Figure 1), which showed a subtle hypo density in the right anterior thalamic region. This came as a surprise, as she only had a persistent headache without focal neurology. Nevertheless, she was treated as a likely sub-acute stroke and fully investigated. A 24-hour tape, echocardiogram, CT-angiogram, blood investigations (including antibodies for autoimmune diseases, coagulation disorders, paraneoplastic syndromes, etc.) were requested; all results were normal. A CT chest, abdomen, pelvis (CT-CAP) was requested to rule out possible malignancy (new onset or metastatic); this was also normal. Also, a gynaecological evaluation did not reveal any problem. Treatment with aspirin 300 mg once a day was started.

Soon after, she had an MRI Head, which revealed a chronic stroke (at least more than 3 weeks, corresponding to the onset date of her "worse" headache). The DWI did not show any increased signal in the right thalamic region (Figure 2), however, the ADC map (Figure 3) showed an increase signal in the right anterior thalamic region. Furthermore, T2-FLAIR (Figure 4) and axial-T2 image (Figure 5) showed a well-defined, circular shaped intensity in the same region (corresponding to the polar artery territory). Finally, on the axial-T1-post contrast (Figure 6), coronal post contrast (Figure 7) and sagittal MRI sequence (Figure 8), there was no significant enhancement, ruling out any neoplastic aetiology. These MRI findings represented a stroke

of at least 3 weeks of age, roughly corresponding to the onset of her "worse" headache one month ago.

Interestingly, all the behavioural changes that she presented started sub acutely after that episode, suggesting that the precise location of the stroke, i.e. the right anterior thalamic region (supplied by the right polar artery) was directly linked with the neurobehavioral disturbance displayed thereafter. More so, it was proposed that the underlying aetiology for her stroke was probably migraine (with aura)-induced, aggravated by an inadequate administration of sumatriptan.

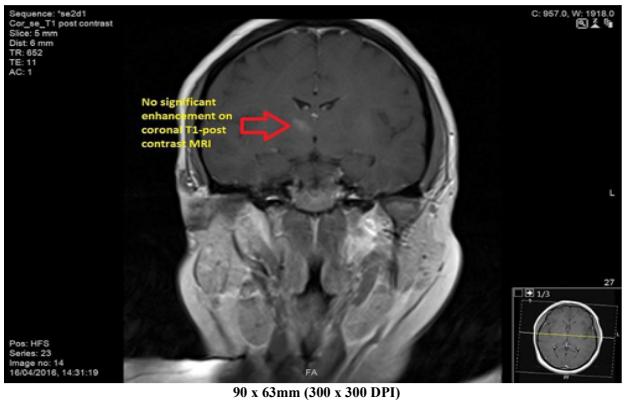

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Figure 6 (T1-Axial post contrast): Very poor post enhancement uptake in the right anterior thalamus (suggestive of a non- neoplastic lesion; more suggestive of an ischemic lesion).

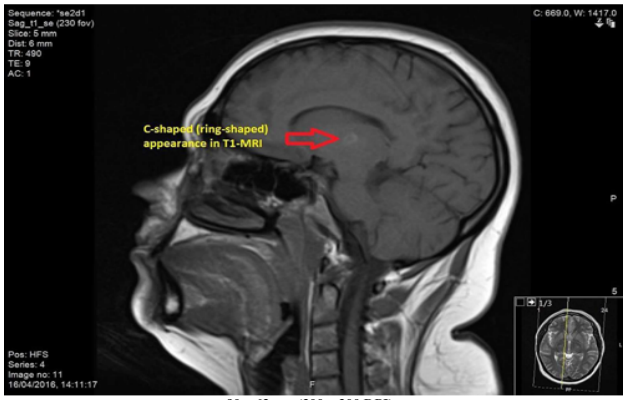

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Figure 7 (T1-Coronal Post contrast): Very poor post enhancement uptake in the right anterior thalamus (suggestive of a non- neoplastic lesion; more suggestive of an ischemic lesion).

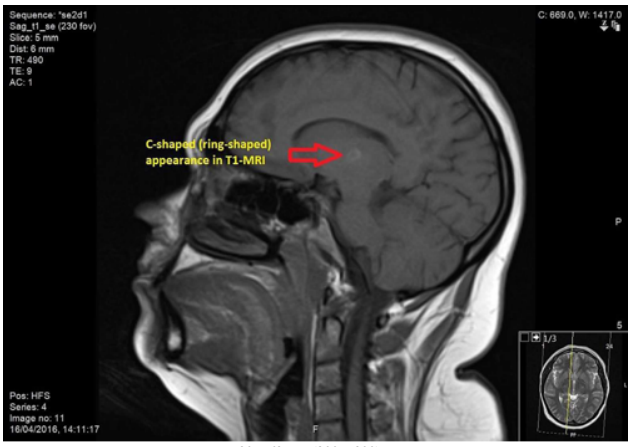

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Figure 8 (Sagittal MRI): C-shaped (ring-like lesion) in the anterior aspect of the thalamus.

We advised on discontinuing any triptan-based treatment in the future and we provided alternate analgesic treatments for her headache. The behavioural changes were managed with citalopram and cognitive therapy (long term). She is currently on clopidogrel and simvastatin for secondary prevention of stroke and continues to be followed up in clinic on a regular basis. She will also have continuous occupational therapist assessments and formal memory assessments in the community.

Investigations

1. CT head and CT chest-abdomen and pelvis
2. MRI head
3. 24-hour tape
4. CT-angiogram of carotid arteries and vertebro-basilar arteries
5. Transthoracic echocardiogram
6. Blood tests including coagulation/thrombophilia screen; antibodies for vasculitis, infectious diseases and paraneoplastic syndromes

Differential Diagnosis

1. Cervical artery dissection
2. Patent foramen ovale (PFA) or other cardiac pathology allowing micro emboli
3. CADASIL
4. Autoimmune vasculitis (possibly PACNS)
5. Metastatic disease/primary neoplasm
6. Hypercoagulability
7. Infectious disease or granulomatous process

Treatment

The patient received aspirin 300 mg once/day for two weeks, followed by clopidogrel 75 mg once/day, simvastatin 40 mg once/day and citalopram 10 mg once/day. She was advised to discontinue taking all types of Triptans for her migraines and was also prescribed gabapentin 200 mg TDS for headaches (which improved her symptoms considerably). If the behavioural symptoms do not improve, we will refer her for cognitive behavioural therapy in a specialized centre. Furthermore, she will continue to have outpatient follow up in our outpatient stroke clinic.

Outcome and Follow-Up

The patient has been seen as an outpatient in our stroke clinic and also, by members of our multidisciplinary team. She is doing well; her behavioural changes are still present, however, they are not getting any worse and she is learning how to manage them appropriately; her memory is unfortunately quite poor. She is compliant with the medications prescribed.

Discussion

The vascular supply to the thalamus stems mainly from the posterior circulation and it consists mainly of four main arteries: (1) thalamo-geniculate arteries, (2) polar artery (tubero-thalamic, anterior internal optic or pre-mammillary pedicle), (3) paramedian arteries (thalamo-subthalamic arteries) and (4) posterior coroidal arteries.

As we can see in the MRI, this patient had a small stroke in the anterior nucleus of the right thalamus, which is supplied by the polar artery. This artery arises from the posterior communicating arteries and it supplies the antero-medial and anterolateral regions of the thalamus (including the reticular nucleus, mamillo-thalamic tract, part of the ventral lateral nucleus, the dorsal-medial nucleus and anterior thalamic pole). Isolated polar artery infarctions-as in our patient-occur in about 15% of all thalamic strokes and usually are due to embolism.

The main clinical findings in patients with infarcts here are neuro-psychological abnormalities. Abulia, apathy and slovenly-as classically seen in frontal lobe syndromes-are seen in polar artery strokes. The major abnormality in most reports is apathy and abulia. There is usually inertia with decreased spontaneity, decreased amount and volume of speech and decreased spontaneous activity. More so, answers are usually slow and delayed; spoken and written replies are terse and tend not to be elaborated on; patients can have difficulty making lists or organizing pictures temporarily; executive functions such as choice of response, inhibition of response, choice of actions among alternatives, selection, sequencing and organizing acts and activities, changing strategies to meet new exigencies, and planning are usually impaired. Furthermore, loss of self-activation (apathy) is often present and is commonly accompanied by amnesia, with inability to make new memories, resulting from interruption of the mamillo-thalamic tract.

Our patient displayed many of the previously described symptoms. Primarily, her neuro-psychological syndrome was centered on anterograde amnesia (presumably secondary to mamillo-thalamic tract involvement), apathy, abulia, decreased spontaneous activity and occasionally, violent outbursts, emotional lability and unfounded defiant attitude towards her family. All these changes were absolutely atypical for the normal, kind and gentle personality the patient (and her family) described to previously have.

The MRI, in this case, proves the chronology of the event as it helps us associate the onset of her neurobehavioral with a particular time (this proved very useful as the patient did not have any focal neurology). DWI is an ideal sequence for imaging patients with acute stroke; the sensitivity of DWI for acute ischemic stroke ranges from 73% (3 hours after the event) to 92% (>12 hours of the event) [1]. The combination of high ADC signal with low DWI signal indicates that the stroke is not acute (0-7 days) or sub-acute (1-3 weeks); rather, that it's chronic (more than 3 weeks old). In acute strokes, there is marked hyper intensity in DWI and hypo intensity on ADC; in sub-acute strokes, there is ADC pseudo-normalization, which occurs, in the second week (7-15 days) while DWI remains hyper intense due to T2 shine-through. In chronic strokes-as in the case of our patient-the DWI signal is low or absent (Figure 2) and the ADC map signal is high (Figure 3). Therefore, our patient only presented neurobehavioral manifestations and the MRI findings were crucial to determining this.

Now, with regards to migraines, Triptans and stroke, we can mention the following important points. First of all, migraine and stroke have been linked by numerous individual studies [2] and three meta-analyses [3]. Overall, there is consistent evidence that individuals with migraine are approximately 2 times more likely to develop an ischemic stroke [4] and in most studies this association is limited to patients with migraine with aura and stronger among younger women, particularly if they smoke or/and use oral contraceptives [5]. Because migraine is very a prevalent disease with approximately 20% of the general population being affected at least part of their lives, it is not surprising that many patients with a stroke have a history of migraine.

Clinically, the International Headache Society has established the criteria for a migraine-related stroke. They require that a patient with a history of migraine with aura has a, for that patient, typical aura, persisting for >60 minutes and with neuroimaging signs of an infarct in a relevant area and provided that the stroke is not attributed to another disorder. Applying these criteria makes a migraine-related infarct a very rare event [6].

Learning Points

1. Migraines with aura are associated with an increased risk of ischemic stroke

2. Triptans can increase the risk of stroke associated with its vasoconstrictive effect.

3. Strokes in young patients are always challenging due to the atypical risk factors and presentations they usually have. In this case, the lack of weakness, sensory loss, cranial nerve palsy or cerebellar signs perhaps delayed her admission. However, we must remember that strokes can also present solely with cognitive and neurobehavioral changes, such as in this case. If we have a young patient with sudden onset of abnormal behaviour in the context of migraines with aura, we suggest stroke to be one of the most important differential diagnosis to consider.

4. MRI scans in young patients with stroke are absolutely vital. As we can see in this case, it provided us with an accurate chronology of the events, tracing the stroke back to the episode of the "worst headache in her life" and providing us with evidence to support stroke-induced neurobehavioral changes (related with anterior thalamic damage).

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