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Case Report

Intracerebral Abscess as a Delayed Sequela of Ischemic Stroke: Case Report and Brief Review of the Literature

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Abstract

Intracerebral abscess formation as a late sequela to ischemic stroke is a rare entity. Intracerebral abscess is a life-threatening affliction with a significant mortality rate necessitating prompt diagnosis and treatment. We present the case of a 67-year-old female with cerebral ischemic infarction complicated forty weeks later by an intracerebral abscess. The diagnosis was only reached after repeat MR imaging with gadolinium and consequent stereotaxic craniotomy and excision of the lesion. We briefly review the literature pertaining to this unusual manifestation and discuss the imaging characteristics of, and treatment options for, cerebral abscess.

ABBREVIATIONS

ACA: Anterior Cerebral Artery; ADC: Apparent Diffusion Coefficient; AF: Atrial Fibrillation; CAD: Coronary Artery Disease; CSF: Cerebro Spinal Fluid; CT: Computed Tomography; CTA: Computed Tomographic Angiography; COW: Circle Of Willis; DWI: Diffusion-Weighted Imaging; EEG: Electroencephalography; FLAIR: Fluid-Attenuated Inversion Recovery; GAD: Gadolinium; GCS: Glasgow Coma Scale; HTN: Hypertension; ICA: Internal Carotid Artery; MCA: Middle Cerebral Artery; MRI: Magnetic Resonance Imaging; NIDDM: Non-Insulin Dependent Diabetes Mellitus; NIHSS: National Institute Of Health Stroke Scale; PCA: Posterior Cerebral Artery; TIA: Transient Ischemic Attack

INTRODUCTION

Ischemic stroke constitutes a major cause of disability worldwide and is one of the most common causes of death [1]. Patients with ischemic infarction are vulnerable to severe complications due to the severity of their disease and comorbidities [2,3]. Secondary complications after stroke include venous thromboembolism, ischemic heart disease and infection, particularly pneumonia and urosepsis. However, transformation of a non-septic cerebral infarct into an intracerebral abscess is rare. Intracerebral abscess is a life-threatening affliction with a mortality rate of 15% [4], necessitating prompt diagnosis and treatment. It can be caused by: spread from a contiguous focus of infection; haematogenous dissemination from a distant locus; cranial trauma; or be induced iatrogenically [5]. Areas of cerebral ischemia, infarction, haemorrhage and contusion can provide an opportunity for inoculation or bacteremic seeding of organisms, resulting in abscess formation [5]. There is a relative paucity of literature regarding abscess formation following acute cerebral infarction. We report a case of intracerebral abscess as a late sequela to ischemic stroke and review the literature pertaining to this rare complication.

CASE PRESENTATION

A 67-year-old female, with a past medical history of hypertension, type 2 diabetes mellitus and depression, presented to the emergency department with abrupt onset aphasia, a dense right hemiparesis and impaired consciousness. On admission she was found to be hypertensive at 210/93 mm Hg with all other vitals unremarkable. Neurological examination revealed a patient of GCS 12 (E4V2M6) with a dense right hemiparesis, hyper-reflexia and positive Babinski's sign. Routine laboratory investigations were unremarkable. The National Institute of Health Stroke Scale (NIHSS) score was 23. Non-contrast cranial CT demonstrated an area of hypodensity involving the left frontal lobe (Figure 1A). CT angiography from the arch of the aorta to the Circle of Willis (CTA COW) identified an occlusion at the origin of the left internal carotid artery (ICA), with markedly reduced opacification of the left middle cerebral artery (MCA) and its branches (Figure 1B). The patient was diagnosed with a left hemispheric MCA stroke secondary to a left ICA occlusion

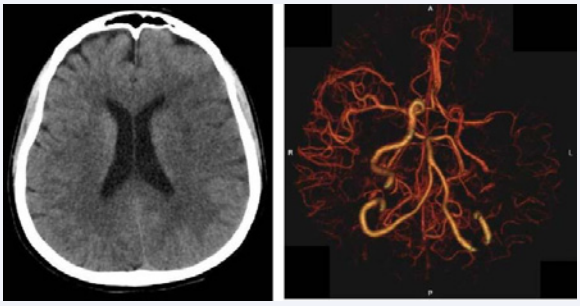

Figure 1 (A) Axial non-contrast CT brain at time of first admission demonstrating an area of hypodensity in the left cerebral hemisphere consistent with an acute left MCA territory infarct. (B) 3D reconstructions of the CTA COW demonstrating markedly reduced opacification of the left MCA and its branches due to occlusion at the origin of the left ICA artery.

and commenced on antiplatelet therapy with aspirin. She was not thrombolysed because the time of onset of stroke was unknown. She was subsequently transferred to a neurorehabilitation facility where, after a two-month inpatient stay, she was discharged home with residual deficits of expressive dysphasia, complete paralysis of right upper limb and moderately severe weakness of right lower limb. She remained dependent on care services for most daily activities.

Ten months later, the patient represented to the emergency department following an unwitnessed collapse followed by transient worsening of her dysphasia with a new receptive component. On admission her NIHSS score was 11 and GCS 13 (E4V3M6) with the afore-mentioned residual neurological deficits. Routine laboratory investigations were again unremarkable. Cranial CT with CTA COW did not demonstrate any new infarction or vascular pathology. Electroencephalography (EEG) showed focal slowing over the left hemisphere and intermittent left temporal epileptiform activity. The patient was diagnosed with post-stroke seizure, commenced on levetiracetam and transferred to neurorehabilitation for further treatment. After one month, she was noted to become increasingly confused and inattentive with poor comprehension, an inability to follow basic commands, disinhibition and impulsive behaviour. With the exception of deranged liver function tests, her laboratory investigations, including full blood work-up and inflammatory markers, remained normal. Repeat EEG showed focal slowing but no epileptiform activity. Her cognitive and functional decline warranted further investigation with an MRI brain, however, due to patient agitation, only limited sequences were initially obtainable. This imaging demonstrated a lobulated T1 hyperintense, T2 and FLAIR hypointense lesion within the old left MCA territory infarct (Figure 2). These images were discussed at the departmental neuroradiology meeting, where the differential of intracerebral abscess was raised, but additional imaging was considered necessary to confirm this possibility. Further imaging sequences were eventually obtained, delineating an irregular lesion within the area of left encephalomalacia with a thin rim of peripheral enhancement on post-contrast T1 images (Figure 3A) and homogenous diffusion restriction (Figure 3B). An intracerebral cerebral abscess was strongly suspected and the patient underwent a stereotactic craniotomy and excision of the left frontal mass, yielding a pale grey, non-suppurative lesion. Histopathology demonstrated well-circumscribed areas of infarctive necrosis surrounded by an infiltrate of macrophages and lymphocytes. *Staphylococcus warneri* was isolated from cultures of the specimen confirming the diagnosis of an intracerebral abscess. Neither precipitating event nor source of infection could be identified. Post-operatively, systemic antibiotic treatment with vancomycin, meropenem and flucloxacillin was administered for eight weeks, with complete radiological resolution of the abscess. Despite these measures however, only marginal functional improvement occurred and the patient was discharged to the care of a nursing home.

METHODS

Intracerebral abscess formation as a sequela to ischemic stroke is a rare entity. A literature search through the Pub-Med and Medline databases using the Boolean search terms [ischemic stroke] AND [complications] AND [intracerebral abscess] identified only fourteen papers (Table (1), modified with permission from [7]). For two of these, those by Ammon et al. [11], and Ichimi et al. [12], only the abstract was available in English. Of the remaining twelve studies published between 1993 and 2016, seven were case reports alone [6,8,10,13,14,17,19], three were case reports with literature reviews [7,9,16] and one was a letter to the editor [15]. For purposes of consistency in this review of intracerebral abscess as a complication of ischemic stroke, one of the patients reported by Chen et al. [14], was excluded as the patient presented with haemorrhagic stroke. In the report of Kraemer et al. [18], intracerebral abscess formation

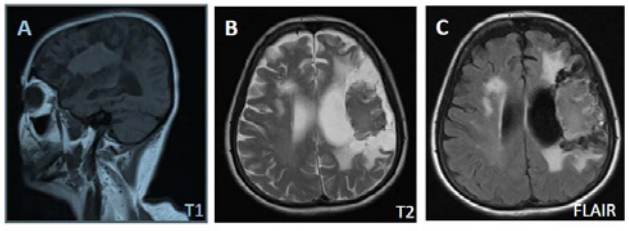

Figure 2 Initial MRI brain demonstrating the old left MCA territory infarct involving the left frontal and parietal lobes associated with encephalomalacia. In the central aspect of this area, there is a lobulated T1 hyperintense (A), T2 (B) and FLAIR (C) hypointense lesion.

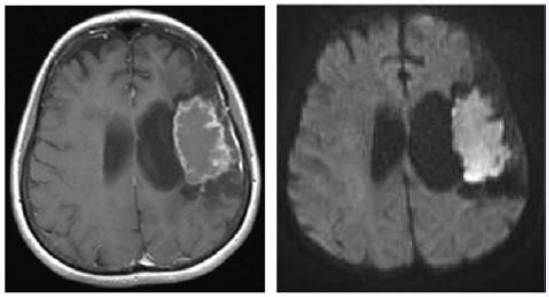

Figure 3 Further MR imaging of the brain demonstrates an irregular lesion within the area of left encephalomalacia which, on post-contrast T1 sequences, shows a thin rim of peripheral enhancement (A) and homogenous diffusion-restriction on DWI sequencing (B).

Table 1: Clinical features of previously reported cases from the literature and our current case (Table modified from reference 7 with permission). Those studies discussed here are highlighted in bold.

Reference	Age	Gender	Past Medical History	Infarct Location*	Interval from stroke to abscess detection (weeks)	Source of infection/ origin	Pathogen	8Treatment	Outcome
Amonn et al, 1984 [11]	68	M	Not specified	Right MCA territory	46	Bronchiectasis	Staphylococcus aureus	Death prior to treatment	Death
Ichimi et al, 1989 [12]	73	M	Not specified	Left MCA territory	11	Not known	Proteus vulgaris	Antibiotics (not specified)	Lost to follow-up
Arentoft et al, 1993 [13]	59	F	Chronic interstitial nephritis	Right MCA territory	12 days	Not known	Salmonella typhimurium	Ampicillin, gentamicin	Death
Chen et al., 1995 [14]	70	M	Not specified	Right MCA territory	5	Aspiration pneumonia	Not known	Surgery penicillin, ceftriaxone, metronidazole	Death
	56	F	HTN	Left putaminal haemorrhagic infarction	9	Septicaemia	Klebsiella pneumonia	Surgery cefotaxime	Recovered
Davenport et al., (letter) 1995 [15]	16	F	Nil	Left ACA territory	4	Septicaemia	Escherichia coli Enterococcus faecalis	Surgery Antibiotics (not specified)	Recovered
Shintani et al., 1996 [16]	40	M	Nil	Right PCA territory	9	Not known	Streptococcus species	Surgery cefotaxime	Recovered Residual homonymous hemianopia
Beloosesky et al., 2002 [10]	68	M	HTN NIDDM IHD Alcoholism	Left MCA territory	16	Urine	Proteus mirabilis	Surgery imipenem, gentamicin	Death
Miyazaki et al., 2004 [17]	77	M	AF HTN TIA	Left MCA territory	58	Pneumonia	Staphylococcus aureus	Surgery cefotaxime	Recovered
Kaplan et al., 2005 [9]	52	F	Not specified	Left frontotemporal and hypothalamic	8	Lung: pleural effusion	Staphylococcus aureus	Antibiotics (not specified)	Recovered
	60	M	Not specified	Right thalamic	7	Lung: interstitial fibrosis	Not known	Surgery Antibiotics (not specified)	Recovered
	40	M	Not specified	Lateral right insular lobe haemorrhagic infarction	9	Not known	Staphylococcus aureus	Surgery Antibiotics (not specified)	Recovered
Xue et al., 2005 [8]	56	F	HTN	Right temporal/occipital lobe	9	Not known	Staphylococcus aureus	Surgery Antibiotics (not specified)	Death
Emmez et al., 2007 [7]	64	M	HTN Knee prosthesis	Left PCA territory	6	Not known	Not known	imipenem	Recovered
Kraemer et Al., 2008 [18]	33	F	Not specified	Left MCA territory	7	Pneumonia	Group C Streptococcus Species	Surgery Antibiotics (not specified)	Recovered Residual right-sided hemiparesis
Yamanaka et al., 2011 [19]	75	M	Not specified	Left MCA territory	13	Not known	Staphylococcus epidermis	Surgery meropenem	Recovered
Wang et al., 2015 [6]	58	M	CAD HTN Hyperlipidemia	Right MCA territory	6	Not known	Not known	Surgery Antibiotics (not specified)	Recovered (died 6 months after surgery due to unrelated cause)

	42	F	Not specified	Left MCA territory	15	Not known	Pantoea agglomerans Bacillus macerans	Surgery	Recovered
Present case, 2016	67	F	HTN NIDDM Depression	Left MCA territory	40	Not known	Staphylococcus warneri	Surgery flucloxacillin, meropenem, vancomycin	Recovered Residual expressive aphasia and right hemiparesis

Abbreviations
ACA: Anterior Cerebral Artery; AF: Atrial Fibrillation; CAD: Coronary Artery Disease; HTN: Hypertension; MCA: Middle Cerebral Artery; NIDDM: Non-Insulin Dependent Diabetes Mellitus; PCA: Posterior Cerebral Artery; TIA: Transient Ischemic Attack
*All ischemic unless otherwise specified.

occurred following haemorrhagic transformation of the ischemic stroke and subsequent decompressive hemicraniectomy and was also omitted. In addition, the reports by Wang et al. [6], and Yamanaka et al. [19], have also been excluded in our review, since the complication of intracerebral abscess only manifested after invasive interventions for the ischemic stroke (decompressive hemicraniectomy and intra-arterial thrombolytic treatment respectively). Finally, the letter to the editor by Davenport et al. [15], is a response to the previously published report of Chen et al. [14], and is also thereby excluded. Taken together, there are only eight papers [7,8,9,10,13,14,16,17] describing 9 patients, and now our present case, that report intracerebral abscess formation at the site of preceding ischemic stroke. The demographics and clinical features of these 10 patients are highlighted in bold text in (Table 1).

RESULTS

The mean age of the 9 patients in these eight studies was 57.3, ranging from 40 to 77, with six males and three females. In five of the patients, hypertension was the only vascular risk factor. In one report [9], past medical history was not specified and in another [16], there was no significant history. Anterior circulation strokes involving the MCA territory (three left- and one right sided) were most common. The duration between stroke and diagnosis of intracerebral abscess varied significantly, ranging from twelve days to fifty-eight weeks. Although in some instances, the causative pathogen was not isolated, the most common were of the *Staphylococcus* species, as in the present case. No precipitating event or source of infection could be identified in four of the 9 patients previously reported, as was the case with our patient. In four of the other 5, the site of infection was felt to be pulmonary. Four of the 9 patients previously reported died.

DISCUSSION

The pathogenesis of intracerebral abscess formation within previously infarcted brain parenchyma can be explained in the context of tissue changes that occur in ischemia. There are four major routes by which bacterial or viral infection can gain access to the brain parenchyma [7,21,22]:

1. spread from a contiguous focus, for example middle ear, mastoid cell, paranasal sinuses;
2. haematogenous spread from a distant focus;
3. trauma;
4. via cranial or upper cervical nerves, for example, rabies or herpes.

The vascular event, in this case, infarction, results in local disruption of the blood-brain barrier which usually functions as a "protective shield" against microorganisms. In cerebral infarction, post-ischemic inflammation and necrosis of the blood vessel wall facilitate the passage of microorganisms. This makes this region vulnerable to microbial seeding in the event of bacteraemia secondary to infection elsewhere, leading to cerebral abscess formation [14,18,20]. It is interesting to note, however, that in our present case, no primary focus of infection was identifiable and the exact cause of abscess formation for this patient remains unknown.

There is no pathognomonic syndrome of intracerebral abscess, and as such, the diagnosis of this entity can be challenging for the clinician. Headache, fever and impaired consciousness are the most prevalent symptoms, although this triad is found in less than one third of patients with intracerebral abscess [22,23]. Interestingly, our patient had none of these symptoms, instead presenting with sub-acute cognitive and functional decline. Focal neurological deficits are similarly highly variable, and the scenario is even more complex in patients with residual neurology from their preceding ischemic stroke, such as in this case.

Radiologically, cerebral abscesses are characterized according to the stages of cerebritis and capsule formation [23,24]. These changes are demonstrable with cranial CT with contrast, however, cranial MRI is more sensitive in characterizing abscesses. The typical imaging appearances of an intracerebral abscess using these 2 imaging modalities are summarized in Table (2). The treating clinician also needs to be aware of other conditions which can cause lesions that can mimic the "classic" ring-enhancing appearance of an abscess. These include metastases, high grade glioma and evolving haemorrhage [24,26]. In our patient, only cranial CT and CTA COW were performed initially when she represented, which may have delayed diagnosis.

The treatment of intracerebral abscess usually involves timely surgical drainage, either by stereotactic aspiration or open surgical resection, combined with appropriate antimicrobial therapy for six to eight weeks [4]. Definitive antibiotic selection is dependent upon the pathogen grown in culture [4]. Empiric, broad spectrum antimicrobial therapy, is however, a reasonable option, if neurosurgical intervention is to be delayed for any significant time. Such empirical regimens include: cefotaxime or ceftriaxone, plus metronidazole; or, alternatively, meropenem

Table 2: Radiographic features of intracerebral abscess on CT and MRI.

Imaging Modality	Radiographic features
CT [23, 24]	- Ring of iso- or hyperdense tissue
	- Central low attenuation (fluid/pus)
	- Surrounding low density (vasogenic oedema)
	- Ring enhancement on post-contrast imaging
MRI [25, 26]	- T1 hyperintensity (to CSF) with ring enhancement with gadolinium
	(GAD)
	- T2/FLAIR hypointensity
	- High DWI signal/low ADC signal representing restricted diffusion

(plus vancomycin, if Staphylococcus aureus is suspected [4]). In certain patient groups with suspected cerebral abscess, such as organ transplantation or HIV infection, additional agents such as antifungals and antituberculous drugs should be used as well [4]. *Staphylococcus* species are the most commonly reported in the literature [27], as in our patient.

CONCLUSION

In summary, ischemic stroke can facilitate abscess formation within the infarcted area. Given its location within the area of the preceding infarction, the abscess may not manifest with specific symptoms nor even with additional neurological deficits. This can lead to diagnostic difficulties and delay effective treatment. Thus, our case report serves to increase awareness of intracerebral abscess formation as a sequela to ischemic stroke, in the hope that it may lead to better recognition and management of such, albeit rare, stroke patients.

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