S.K. Gill · M.M. Brown
F. Robertson · N. Losseff
Editors

Stroke Medicine

Case Studies from Queen Square

Springer

Stroke Medicine

S.K. Gill • M.M. Brown • F. Robertson
N. Losseff
Editors

Stroke Medicine

Case Studies from Queen Square

Springer

Editors
S.K. Gill
UCL Institute of Neurology Education Unit
National Hospital for Neurology
and Neurosurgery
London
UK

F. Robertson
Lysholm Department of Neuroradiology
National Hospital for Neurology
and Neurosurgery
London
UK

M.M. Brown
Brain Repair & Rehabilitation
UCL Institute of Neurology,
University College London
London
UK

N. Losseff
Department of Stroke
National Hospital for Neurology
and Neurosurgery
London
UK

ISBN 978-1-4471-6704-4 ISBN 978-1-4471-6705-1 (eBook)
DOI 10.1007/978-1-4471-6705-1

Library of Congress Control Number: 2015942706

Springer London Heidelberg New York Dordrecht

Printed on acid-free paper

Springer-Verlag London Ltd. is part of Springer Science+Business Media (www.springer.com)

For our patients.
-The Editors

Preface

> The details of the case are important: their analysis distinguishes the expert from the journeyman. CM Fisher [1]

Learning through case analysis is a technique that centuries old and used in almost all disciplines. This 'storytelling' method of teaching adds layers of richness and a depth that can not be found in the linear structure of a standard textbook. The value of this – and the reason why we have chosen it for this book – is that it allows the reader the ability to view the thought processes involved in clinical decision-making. These 'grey cases' are often referred upward through the hierarchies of a specialty and can end up in tertiary centres where the diagnostic processes may be inexplicit. The aim of the book is to allow insight into the process of diagnosis and provide the tools to cut through the complexity inherent in neurovascular medicine to formulate a diagnosis and treatment plan. These are real cases, and it is important to recognise that despite the considerable experience of the physician it is possible that a alternative direction or treatment is followed before an answer is found. The discussion that follows each case describes the reasoning behind case management and highlights how an element of becoming a better physician means being open to exploring alternative possibilities. These cases also demonstrate how collaborative analysis of cases with other specialists increases the odds of good decision-making and that this is a vital skill to foster, in addition to being one of the most enjoyable aspects of clinical practice.

We hope that reading this book will add to your general clinical education as well as increase your depth of knowledge and understanding of neurovascular medicine. We have chosen cases that you are likely to come across as stroke physicians of the future and hope to leave you better equipped to problem-solve. In addition we hope this will inspire you to talk about your cases with your colleagues to explore clinical conundrums and enable you to resolve questions which often have no single right answer.

The structure of each chapter means that you are 'talked through' the case presentation and investigations. This is then followed by a thorough analysis with key learning points to highlight underlying principles. Imaging is included to illustrate the cases and we have also included radiological learning points. This book is a suitable companion for anyone from medical students through to experienced physicians to develop their knowledge and understanding of neurovascular medicine.

London, UK Sumanjit K. Gill, BSc.hons, MBBS, MRCP
London, UK Martin M. Brown, MA, MD, FRCP
London, UK Fergus Robertson, MA, MD, MRCP, FRCR
London, UK Nicholas Losseff, MD, FRCP

Reference

1. Caplan L. Fishers rules. Arch Neurol. 1982;39:389–90.

Contents

Contributors

Matthew Adams, MB BChir, FRCR Lysholm Department of Neuroradiology, National Hospital for Neurology and Neurosurgery, London, UK

Deepa Arachchillage, MRCP, FRCPath Haemostasis Research Unit, Department of Haematology, University College London Hospitals NHS Foundation Trust and University College London, London, UK

Asaipillai Asokanathan, MRCP (UK), DGM (London) Department of Stroke, East and North Hertfordshire NHS Trust, Stevenage, UK

Anish Bahra, FRCP, MD Department of Neurology, Bartshealth, Whipps Cross Hospital, London, UK and Department of Neurology, National Hospital for Neurology and Neurosurgery, London, UK

Pervinder Bhogal, MBBS, MRCS, FRCR, PG Dip MedEd Atkinson Morley Department of Neuroradiology, St. Georges Hospital, London, UK

Lucy Blair, MBChB, BMedSci Hyper Acute Stroke Unit, University College Hospital, London, London, UK

David Bradley, MRCPI, PhD Stroke and Acute Brain Injury Unit, National Hospital for Neurology and Neurosurgery, London, UK

Martin M. Brown, MA, MD, FRCP Stroke Research Group, Department of Brain Repair & Rehabilitation, UCL Institute of Neurology, University College London, The National Hospital for Neurology and Neurosurgery, London, UK

Nicholas F. Brown, MBBS, MA, MRCP Department of Neurology, Royal Free Hospital, London, London, UK

James R. Brown, FRCS Department of Vascular Surgery, Southend University Hospital, Southend on sea, Essex, UK

Andreas Charidimou, MD, MSc Stroke Research Group, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, London, UK

Gerry Christofi, BSc, PhD, BM BCh, MRCP, MRCP Neurorehabilitation, National Hospital for Neurology and Neurosurgery, London, UK

Hannah Cohen, MD, FRCP, FRCPath Department of Haematology, University College London Hospitals NHS Foundation Trust and University College London, London, UK

David Collas, BSc, MBBS, FRCP Stroke Medicine, Watford General Hospital, Watford, UK

David Doig, MBChB, BScMedSci (Hons), MRCP Stroke Research Group, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, University College London and National Hospital for Neurology and Neurosurgery, London, UK

Daniel Epstein, MBCHB, MRCP Stroke Medicine, Barnet Hospital, Barnet Hertfordshire, UK

Rachel Farrell, MB BCh, MRCPI, PhD Neurorehabilitation, National Hospital for Neurology and Neurosurgery, UCLH, London, UK

Laura Flisher, BSs Hons, BSc Hons, HPC, CSP Therapies and Rehabilitation, National Hospital for Neurology and Neurosurgery, London, UK

Vijeya Ganesan, MRCPCH, MD Neurosciences Unit, UCL Institute of Child Health, London, UK

Sumanjit K. Gill, BSc Hons, MBBS, MRCP Education Unit, National Hospital for Neurology and Neurosurgery, UCL Institute of Neurology, London, UK

Lionel Ginsberg, BSc, MBBS, PhD, FRCP, FHEA Department of Neurology, Royal Free Hospital, London, UK

Joan P. Grieve, MD, FRCS (SN) Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, London, UK

Paul Guyler, MRCP Acute Stroke Medicine, Southend University Hospital, Southend on sea, Essex, UK

Jeremy C.S. Johnson, MBBS, BSc Department of Stroke, National Hospital for Neurology and Neurosurgery, London, UK

Fiona Kennedy, MB, Bch, BAO, MRCP (UK) Stroke Research Group, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, University College London and National Hospital for Neurology and Neurosurgery, London, UK

Ashvini Keshavan, MB, BChir Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, University College London and National Hospital for Neurology and Neurosurgery, London, UK

Ruth Law, MA, MBBS, MRCP Department of Medicine, University College London, London, UK

Alexander Leff, PhD, FRCP Institute of Cognitive Neuroscience and Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, University College London and National Hospital for Neurology and Neurosurgery, London, UK

Thaya Loganathan, MRCP Acute Stroke Medicine, Southend University Hospital, Southend on sea, Essex, UK

Nicholas Losseff, MD, FRCP Department of Stroke, The National Hospital for Neurology and Neurosurgery, London, UK

Robert I. Luder, BSc (Hons), FRCP (UK) Department of Stroke Medicine, North Middlesex University Hospital, Edmonton, London, UK

Ari Manuel, MBBS, MRCP, BSc, DipLATHE Oxford Sleep Unit, Oxford University Hospitals NHS Trust, Oxford, Oxfordshire, UK

Áine Merwick, MB, BMed Sc, MSc, PhD, MRCPI Department of Neurology, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

Kelvin Kuan Huei Ng, MBBS Stroke Neurology Department, Hamilton General Hospital, Hamilton, ON, Canada

Georgios Niotakis Paediatric Neurology, Great Ormond Street Hospital for Children, London, UK

Anthony O'Brien, MRCP Acute Stroke Medicine, Southend University Hospital, Southend on sea, Essex, UK

Rupert Oliver, PhD, MRCP Department of Neurology, Guy's and St. Thomas' Hospitals, St. Thomas' Hospital, London, UK

Richard Perry, BM, BCh, MA, PhD, MRCP (UK) Department of Neurology, National Hospital for Neurology & Neurosurgery, London, UK

Menelaos Pipis, MBBS, BSc (Hons), MRCP Department of Medicine, Northwick Park Hospital, Harrow, Middlesex, London, UK

Stefanie Christina Robert, MD, MRCP, FFICM Intensive Care Unit, Homerton University Hospital, London, UK

Anne Jutta Schmitt, Dr. Med. Univ. Department of Radiology, University College London Hospital, London, UK

Raja Farhat Shoaib, MRCPS Acute Stroke Medicine, Southend University Hospital, Southend on sea, Essex, UK

Robert Simister, MA, FRCP, PhD Comprehensive Stroke Service, National Hospital for Neurology and Neurosurgery, UCLH Trust, London, UK

Devesh Sinha, MRCP Acute Stroke Medicine, Southend University Hospital, Southend on sea, Essex, UK

Shaun Ude, MRCP Acute Stroke Medicine, Southend University Hospital, Southend on sea, Essex, UK

David J. Werring, BSc, MBBS, PhD, FRCP Stroke Research Group, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, London, UK

Victoria Wykes, MB, PhD, MRCS Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, London, UK

Chapter 1
A Rapidly Progressive Dementia

Andreas Charidimou and David J. Werring

Clinical History

A 76-year old man presented following a brief episode of collapse whilst on the train. He remembered feeling unwell, and then waking up on the train surrounded by people, having briefly lost consciousness. He reported no chest pain, nor any markers of seizure activity. Prior to this event he had suffered progressive cognitive decline over at least 6 months, with difficulties with memory, concentration and sustained attention. During his inpatient stay, the patient became more confused with worsening cognitive impairment, frequent disorientation in time and place, inappropriate behaviour and wandering.

He had a past medical history of hypertension, a right frontal intracerebral haemorrhage (ICH) associated with a fall 2 years before current presentation, and a previous ischaemic stroke causing left hemianopia.

Examination

The cranial nerves were normal apart from longstanding left homonymous hemianopia. Reflexes were symmetrical with flexor plantar responses and there was no limb weakness or sensory deficits. Neuropsychological assessment demonstrated impaired recognition memory, executive function, cognitive speed, attention, and nominal skills.

A. Charidimou, MD, MSc (✉) • D.J. Werring, BSc, MBBS, PhD, FRCP (✉)
Stroke Research Group, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, London, UK
e-mail: a.charidimou@ucl.ac.uk; d.werring@ucl.ac.uk

S.K. Gill et al. (eds.), *Stroke Medicine: Case Studies from Queen Square*,
DOI 10.1007/978-1-4471-6705-1_1

Investigations

A non-contrast CT of the brain demonstrated an established right temporal-occipital infarct and volume loss in the right frontal lobe. CT angiography showed no evidence of an arteriovenous malformation or other vascular abnormality. A brain MRI scan including T2*-weighted gradient-recalled echo (T2*-GRE) and susceptibility-weighted imaging (SWI) showed multiple strictly lobar cerebral microbleeds, predominantly in the occipital and temporal lobes, extensive superficial cortical haemosiderin staining, and a previous ICH in the right frontal lobe. There were also severe confluent and patchy white matter hyperintensities (leukoaraiosis) and an area of encephalomalacia consistent with a mature infarct in the right temporal-occipital lobe. Representative images are shown in Fig. 1.1.

Routine blood tests including biochemistry, renal, liver, and bone profiles, full blood count, and CRP were normal; the autoimmune screen was negative. Lumbar puncture was performed, and analysis revealed clear cerebrospinal fluid (CSF). Glucose was normal; the protein level was mildly elevated (0.73 g/L; normal range: 0.13–0.40 g/L) without pleocytosis (<1 white cell, <1 red cell; only occasional small mature lymphocytes and rare macrophages). CSF 14-3-3 protein was negative. Electroencephalogram (EEG) recording on two occasions showed generalized slowing of background rhythms but no epileptiform activity.

The patient remained extremely confused, with inappropriate behaviour, while his cognitive function continued to decline. A diagnosis of severe cerebral amyloid angiopathy (CAA) was suspected and the patient had a non-dominant (right) frontal brain biopsy to confirm the diagnosis and exclude any treatable pathology. Neuropathology confirmed severe CAA in the leptomeninges and cerebral cortex. Routine haematoxylin and eosin (H&E) stain showed circumferential thickening and

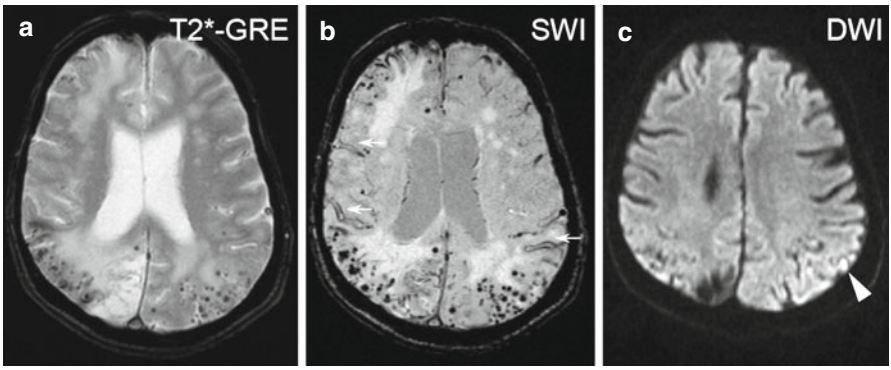

Fig. 1.1 (**a**) T2*-weighted gradient-recalled echo (*T2*-GRE*) MRI shows numerous lobar cerebral microbleeds particularly in posterior brain regions characteristic of cerebral amyloid angiopathy. (**b**) Susceptibility-weighted imaging (*SWI*) shows even more numerous cerebral microbleeds and extensive cortical superficial siderosis involving multiple cerebral sulci (*black serpiginous lines*; *arrowed*). Marked confluent and patchy white matter hyperintensities (leukoaraiosis) are also evident. (**c**) Diffusion weighted imaging (*DWI*) shows a small hyperintense lesion (*arrowhead*) consistent with an acute ischaemic lesion in the left parietal lobe ("microinfarct")

amorphous eosinophilic appearance of leptomeningeal, cortical and to lesser extent white matter blood vessels with conspicuous loss of smooth muscle cells. This was accompanied, particularly in the leptomeninges, by patchy cracking and "double-barrelling" of the vessel walls. Immunohistochemistry confirmed widespread amyloid-β deposition within the leptomeningeal and cortical blood vessels, including capillaries. There was no evidence of either prion protein or vasculitis (Fig. 1.2).

The patient was treated with antihypertensives and donepezil (a centrally acting reversible acetylcholinesterase inhibitor), but his cognition and behaviour continued to progressively deteriorate.

Discussion

Sporadic CAA is a common age-related cerebral small vessel disease, characterised by progressive deposition of amyloid-β in the wall of small cortical and leptomeningeal arteries [1]. Population-based autopsy studies show that the prevalence of CAA is 20–40% in non-demented, and 50–60% in demented elderly populations [2, 3]. Deposition of amyloid-β causes injury to the vessel wall, which in moderate to severe disease may rupture, causing cerebral microbleeds, cortical superficial siderosis or larger symptomatic ICH [4]. Amyloid-β deposits can also narrow or occlude vessel lumen, potentially causing cerebral ischaemia (cerebral infarction, "microinfarcts" or leukoaraiosis) [5]. The cause of CAA is not known. Conventional vascular risk factors do not seem to play a major causal role. Although some genetic risk factors (especially the apolipoprotein E e4 allele) are robustly associated with CAA, age remains the most powerful risk factor [4].

Although CAA is most often recognized by the occurrence of spontaneous lobar ICH in the elderly, it can also cause transient focal neurological deficits, disturbances of consciousness, and progressive cognitive decline [4, 6].

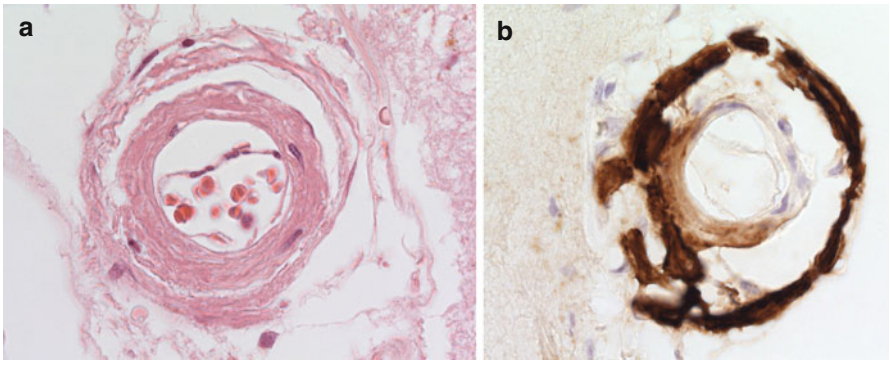

Fig. 1.2 (**a**) Haematoxylin and eosin (H&E) stain showing thickening and amorphous eosinophilic appearance of leptomeningeal small blood vessels with double barrelling of the vessel walls. (**b**) Immunohistochemistry showing severe amyloid-β deposition within a leptomeningeal vessel (*brown*), with double barrelling and patchy cracking

Symptomatic, spontaneous, lobar intracerebral haemorrhage in elderly patients is the most common clinical manifestation of CAA [4, 6]. The majority of intracerebral haemorrhages (>75%) in the elderly are spontaneous (non-traumatic), attributed to resulting from rupture of small arteries affected by two main processes: hypertensive arteriopathy (characterised by lipohyalinosis and fibrinoid necrosis of small lenticulostriate arterial perforators) or CAA (characterised by vascular amyloid-β deposits in the cortex and subcortical white matter). CAA accounts for up to 20% of spontaneous ICH in elderly subjects; CAA-related ICH are typically lobar, due to the distribution of the arterial pathology, and characterized by frequently early recurrence or synchronous multiple haemorrhages. By contrast, deep or infratentorial ICH (e.g. basal ganglia, thalamus and pons) are characteristic of hypertensive arteriopathy haemorrhage. There is also an association between CAA and anticoagulation or thrombolysis related ICH [7–9].

CAA is also associated with transient focal neurological episodes (sometime called "amyloid spells"), which can resemble transient ischaemic attacks, migraine auras or focal seizures [10–12]. Patients often complain of recurrent, brief (minutes), stereotyped attacks of paresthesias or numbness (spreading smoothly over contiguous body parts), visual symptoms (sometimes migraine aura-like), face or limb weakness or dysphasia. Although these symptoms may clinically suggest transient ischaemic attacks, increasing data suggest that "amyloid spells" in CAA are more often associated with intracranial bleeding (especially cortical superficial siderosis or focal convexity subarachnoid haemorrhage on T2*-GRE MRI) and a high early risk of symptomatic lobar ICH (24.5% [95% CI: 15.8–36.9%] at 8 weeks) [10]. Thus, antithrombotic drugs should generally be avoided in these patients due to the risk of serious future ICH [13].

There is increasing evidence that CAA is an important cause of cognitive impairment and dementia, although dissecting its independent impact is confounded by coexisting Alzheimer's disease and other age-related cerebrovascular pathologies [3]. Nearly all cases of Alzheimer's disease show CAA, while patients with CAA usually have some evidence of parenchymal amyloid. However, by contrast with Alzheimer's disease, the dementia associated with CAA typically progresses rapidly, usually with both large and small areas of haemorrhage and infarction, and prominent white matter abnormality (leukoaraiosis). Although it is difficult to attribute the rapid cognitive decline to any particular pathological component, the Religious Orders Study autopsy series found that moderate-to-severe CAA was associated with lower performance in specific cognitive domains after adjusting for Alzheimer's disease pathology and other potential confounders, notably perceptual speed and episodic memory [14].

A distinctly rare but clinically aggressive form of CAA is that of CAA-related inflammation (also termed cerebral amyloid angiitis, amyloid-β related angiitis and cerebral amyloid inflammatory vasculopathy) [15], characterized histopathologically by vascular or perivascular inflammatory infiltrates associated with amyloid-β laden vessels [16, 17]. CAA-related inflammation typically presents with acute cognitive decline, behavioural changes, seizures, headache, and focal neurologic deficits [15]. Neuroimaging typically reveals a potentially reversible leukoencephalopathy consisting of patchy or confluent, usually asymmetric white

matter changes, sometimes with mass effect and contrast-enhancement, lobar ICH and multiple strictly lobar cerebral microbleeds on T2*-GRE MRI sequences (Fig. 1.1) [15]. The syndrome may respond to corticosteroids or other immunomodulatory treatment. CAA-related inflammation is similar to that observed in patients with Alzheimer's disease who developed meningo-encephalitis after immunisation against human amyloid-β (ARIA: Amyloid-Related Imaging Abnormalities) [16–19], which may relate to rapid movement of amyloid from brain parenchyma into blood vessels [20, 21].

The "gold standard" for definitive diagnosis of CAA remains histopathological analysis, usually from haematoma evacuation or brain biopsy and, less commonly, brain autopsy [22]. However, the radiological demonstration of haemorrhagic manifestations of the disease in the brain (especially using T2*-GRE or SWI MRI) allow the *in vivo* clinical-radiological diagnosis of CAA. The diagnosis of CAA currently relies on the demonstration of multiple haemorrhagic lesions in strictly lobar brain areas – the "Boston criteria", including both cerebral micro-bleeds, as well as ICH, although pathological validation for microbleed-only patients is limited [22–24]. Cerebral microbleeds are small, dark, rounded areas detected on blood-sensitive MRI sequences that seem to reflect small areas of bleeding from fragile vessels affected by small vessel disease including CAA [25]. The detection of cortical superficial siderosis as in our patient, possibly reflecting repeated episodes of bleeding into the subarachnoid space and over the surface of the brain seems to another characteristic imaging feature of CAA [23].

In summary, our case represents a progressive dementia due to severe CAA, a common but under-recognized form of cerebral small vessel disease. Our case illustrates the characteristic clinical and neuroimaging spectrum of CAA and the important role of advanced brain MRI including blood-sensitive sequence for investigation and *in vivo* diagnosis. As populations age, CAA is likely to become an increasingly important cause of disability in stroke medicine. With the prospect of disease-modifying treatments to reduce vascular amyloid deposition [4], as well as effective treatment of all known risk factors (including hypertension), making the correct diagnosis of CAA will become increasingly important.

Key Clinical Learning Points

1. CAA is a common age-related cerebral small vessel disease
2. It is caused by amyloid-β deposition in small cortical and leptomeningeal arteries
3. CAA is commonly associated with lobar intracerebral haemorrhage in elderly patients
4. CAA can also present with transient focal neurological symptoms or progressive cognitive impairment and dementia
5. CAA-related inflammation is an uncommon but distinctly aggressive subtype of CAA, which typically presents with acute cognitive decline, behavioural change, seizures, headache, and focal neurologic deficits

Key Radiological Learning Points

1. CAA diagnosis relies on neuroimaging demonstration of multiple areas of strictly lobar cerebral haemorrhage (Boston criteria)
2. Characteristic imaging correlates on blood-sensitive MRI sequences (including T2*-GRE or SWI) include strictly lobar cerebral microbleeds, ICH and cortical superficial siderosis
3. Other imaging findings in CAA include white matter hyperintensities (leukoaraiosis) and small or large areas of cerebral infarction, including apparently clinically silent "microinfarcts"

References

1. Vinters HV. Cerebral amyloid angiopathy. A critical review. Stroke. 1987;18(2):311–24. Epub 1987/03/01.
2. Keage HA, Carare RO, Friedland RP, et al. Population studies of sporadic cerebral amyloid angiopathy and dementia: a systematic review. BMC Neurol. 2009;9:3. Epub 2009/01/16.
3. MRC CFAS. Pathological correlates of late-onset dementia in a multicentre, community-based population in England and Wales. Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS). Lancet. 2001;357(9251):169–75. Epub 2001/02/24.
4. Charidimou A, Gang Q, Werring DJ. Sporadic cerebral amyloid angiopathy revisited: recent insights into pathophysiology and clinical spectrum. J Neurol Neurosurg Psychiatry. 2012;83(2):124–37. Epub 2011/11/08.
5. Smith EE, Schneider JA, Wardlaw JM, et al. Cerebral microinfarcts: the invisible lesions. Lancet Neurol. 2012;11(3):272–82. Epub 2012/02/22.
6. Viswanathan A, Greenberg SM. Cerebral amyloid angiopathy in the elderly. Ann Neurol. 2011;70(6):871–80. Epub 2011/12/23.
7. Rosand J, Hylek EM, O'Donnell HC, et al. Warfarin-associated hemorrhage and cerebral amyloid angiopathy: a genetic and pathologic study. Neurology. 2000;55(7):947–51. Epub 2000/11/04.
8. Sloan MA, Price TR, Petito CK, et al. Clinical features and pathogenesis of intracerebral hemorrhage after rt-PA and heparin therapy for acute myocardial infarction: the Thrombolysis in Myocardial Infarction (TIMI) II Pilot and Randomized Clinical Trial combined experience. Neurology. 1995;45(4):649–58. Epub 1995/04/01.
9. McCarron MO, Nicoll JA. Cerebral amyloid angiopathy and thrombolysis-related intracerebral haemorrhage. Lancet Neurol. 2004;3(8):484–92. Epub 2004/07/21.
10. Charidimou A, Peeters A, Fox Z, et al. Spectrum of transient focal neurological episodes in cerebral amyloid angiopathy: multicentre magnetic resonance imaging cohort study and meta-analysis. Stroke. 2012;43(9):2324–30. Epub 2012/07/17.
11. Greenberg SM, Vonsattel JPG, Stakes JW, et al. The clinical spectrum of cerebral amyloid angiopathy: presentations without lobar hemorrhage. Neurology. 1993;43(10):2073–9.
12. Charidimou A, Law R, Werring DJ. Amyloid "spells" trouble. Lancet. 2012;380(9853):1620. Epub 2012/11/06.
13. Charidimou A, Baron JC, Werring DJ. Transient focal neurological episodes, cerebral amyloid angiopathy, and intracerebral hemorrhage risk: looking beyond TIAs. Int J Stroke. 2013;8(2):105–8. Epub 2013/01/23.

14. Arvanitakis Z, Leurgans SE, Wang Z, et al. Cerebral amyloid angiopathy pathology and cognitive domains in older persons. Ann Neurol. 2011;69(2):320–7. Epub 2011/03/10.
15. Chung KK, Anderson NE, Hutchinson D, et al. Cerebral amyloid angiopathy related inflammation: three case reports and a review. J Neurol Neurosurg Psychiatry. 2011;82(1): 20–6. Epub 2010/10/12.
16. Eng JA, Frosch MP, Choi K, et al. Clinical manifestations of cerebral amyloid angiopathy-related inflammation. Ann Neurol. 2004;55(2):250–6. Epub 2004/02/03.
17. Scolding NJ, Joseph F, Kirby PA, et al. Abeta-related angiitis: primary angiitis of the central nervous system associated with cerebral amyloid angiopathy. Brain. 2005;128(Pt 3):500–15. Epub 2005/01/22.
18. Sperling R, Salloway S, Brooks DJ, et al. Amyloid-related imaging abnormalities in patients with Alzheimer's disease treated with bapineuzumab: a retrospective analysis. Lancet Neurol. 2012;11(3):241–9. Epub 2012/02/07.
19. Sperling RA, Jack Jr CR, Black SE, et al. Amyloid-related imaging abnormalities in amyloid-modifying therapeutic trials: recommendations from the Alzheimer's Association Research Roundtable Workgroup. Alzheimers Dement. 2011;7(4):367–85. Epub 2011/07/26.
20. Nicoll JA, Wilkinson D, Holmes C, et al. Neuropathology of human Alzheimer disease after immunization with amyloid-beta peptide: a case report. Nat Med. 2003;9(4):448–52. Epub 2003/03/18.
21. Ferrer I, Boada Rovira M, Sanchez Guerra ML, et al. Neuropathology and pathogenesis of encephalitis following amyloid-beta immunization in Alzheimer's disease. Brain Pathol. 2004;14(1):11–20. Epub 2004/03/05.
22. Knudsen KA, Rosand J, Karluk D, Greenberg SM. Clinical diagnosis of cerebral amyloid angiopathy: validation of the Boston criteria. Neurology. 2001;56(4):537–9. Epub 2001/02/27.
23. Linn J, Halpin A, Demaerel P, et al. Prevalence of superficial siderosis in patients with cerebral amyloid angiopathy. Neurology. 2010;74(17):1346–50. Epub 2010/04/28.
24. van Rooden S, van der Grond J, van den Boom R, et al. Descriptive analysis of the Boston criteria applied to a Dutch-type cerebral amyloid angiopathy population. Stroke. 2009;40(9):3022–7. Epub 2009/06/27.
25. Greenberg SM, Vernooij MW, Cordonnier C, et al. Cerebral microbleeds: a guide to detection and interpretation. Lancet Neurol. 2009;8(2):165–74. Epub 2009/01/24.

Chapter 2
A Headache After Starting the Oral Contraceptive Pill

Matthew Adams

Clinical History

An 18-year-old right-handed female student collapsed at home and was transferred to the Accident and Emergency Department of the local hospital by ambulance. She described a 5-day history of severe, progressively worsening generalised headache and reported that just prior to her collapse she developed left lower limb weakness. She then noticed that she had blurred vision, worse on lateral gaze, and a left sided hemisensory disturbance. She gave a past medical history of two spontaneous miscarriages and had recently started taking the oral contraceptive pill.

Examination

She was alert and orientated. Her temperature was 37.2 °C, blood pressure 154/70 mmHg and her pulse was regular. There were no rashes or clinical evidence of meningism. Her pupils were equal and reactive, there was no conjunctival injection, visual fields were normal to confrontation and eye movements were normal. Fundoscopy revealed bilateral early papilloedema, worse on the right. She had a mild left pronator drift, mild weakness of shoulder abduction and hip flexion (MRC score 4) and an extensor plantar response on the left. Sensory assessment was normal, as was a general physical examination.

M. Adams, MB BChir, FRCR
Lysholm Department of Neuroradiology,
National Hospital for Neurology and Neurosurgery, London, UK
e-mail: matthew.adams@uclh.nhs.uk

S.K. Gill et al. (eds.), *Stroke Medicine: Case Studies from Queen Square*,
DOI 10.1007/978-1-4471-6705-1_2

Investigations

Blood samples sent on arrival in casualty showed normal full blood count, renal and liver profiles. D-Dimer was significantly elevated.

A plain CT brain demonstrated abnormal high attenuation within the straight sinus, vein of Galen and right internal cerebral vein, all of which were markedly expanded (Fig. 2.1). Low attenuation was seen throughout the lentiform nucleus, caudate head, capsular white matter and anterior thalamus on the right with moderate associated swelling. There was no evidence of subarachnoid blood and the ventricles were not enlarged. MRI revealed abnormal signal, swelling and petechial haemorrhage within the deep grey nuclei, capsular and periventricular frontal white matter and splenium of the corpus callosum on the right (Fig. 2.2). Occlusive thrombus within the straight sinus, vein of Galen and right internal cerebral vein was seen as abnormally high signal and expansion of the vessels on the T1-weighted imaging (Fig. 2.3), absence of the normal flow voids on the T2-weighted sequences and abnormally low signal and exaggeration of vessel calibre on susceptibility weighted imaging (SWI-blood sensitive sequence with features in common with T2*-weighted imaging). MR venography confirmed absent flow.

Ophthalmological assessment showed papilloedema but normal visual acuity and fields.

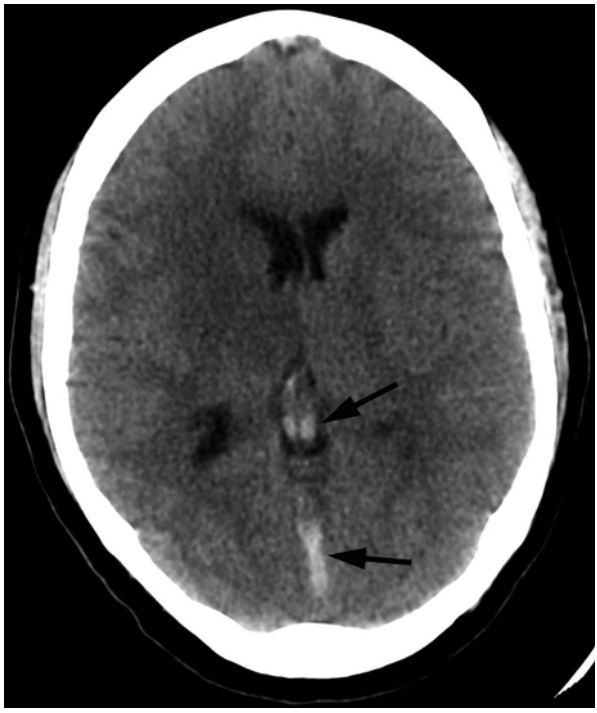

Fig. 2.1 CT showing high attenuation thrombus within distended internal cerebral veins and straight sinus (*arrows*) and low attenuation within the right lentiform nucleus, caudate head and thalamus on the right

A diagnosis was made of cerebral venous thrombosis involving the deep cerebral veins. Anticoagulation with low molecular weight heparin was commenced. She was discharged from hospital on oral anticoagulation and

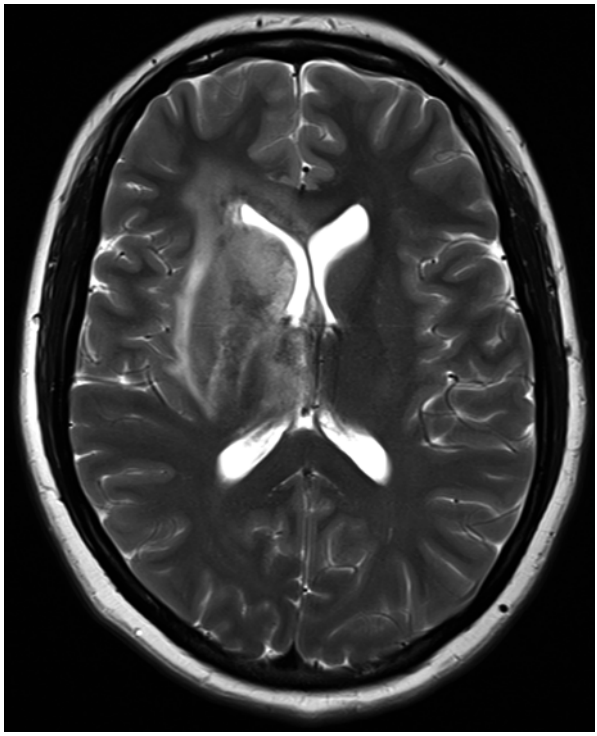

Fig. 2.2 T2-weighted axial image demonstrating swelling and abnormal signal throughout the lentiform nucleus, caudate head, thalamus, capsular white matter and genu of the corpus callosum on the right extending to the frontal periventricular white matter

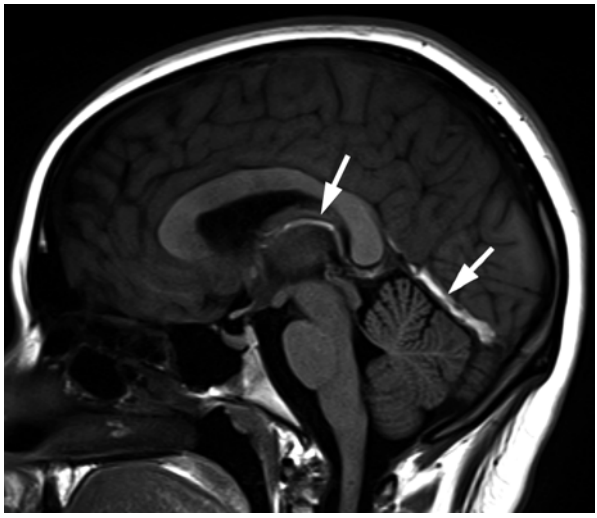

Fig. 2.3 T1-weighted sagittal image showing hyperintense thrombus within the straight sinus and internal cerebral vein (*arrow*)