# A 62-year-old man with progressive weakness in the extremities

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## Presentation of case

The patient was a 62-year-old construction site worker who had been in good health. On 18 March 1994, he was first seen at the Accident and Emergency Department (AED) of the hospital because of progressive weakness and increasing numbness of his right upper limb and both lower limbs. He was admitted into the medical ward with a diagnosis of stroke-in-evolution.

On admission, he gave a history of sudden onset of dizziness for one week. Two days before admission he noticed some numbness in the right side of his body and progressive weakness in the right upper arm and both legs. He could still walk, but with difficulty. He also noticed blurring of vision in both eyes and had moderate frontal headache.

He did not drink, but had smoked one packet of cigarettes daily for the past 40 years. He gave no history of hypertension, diabetes mellitus, heart disease, or tuberculosis. There was no known allergy and no history of medication.

On admission his temperature was 37°C; pulse was 60 beats per minute and regular; blood pressure was 130/80 mmHg. Heart sounds were normal and there were no murmurs. The chest was clear. Examination of the nervous system revealed an alert patient with a Glasgow Coma Scale (GCS) of 15/15. There was muscle weakness of the right side, pronator drift and some numbness. There were no cerebellar signs and he had a right hemiplegic gait.

The haematological and blood chemical values were as follows: haemoglobin was 10.1 g/L (13.2 to 16.7 g/L), the white cell count was 16.8 (4.0 to 10.8 x $10^9$/L) with 87% polymorphonuclear leucocytes, and the platelet count was 50 (140 to 380 x $10^9$/L). The red blood cell indices were: HCT 0.296 (0.39 to 0.50), MCV 94.1 (81 to 97 fL), MCHC 34.1 (32 to 35g/dL), MCH 32.1 (27 to 33 pg). The sodium was 127 (134 to 145 mmol/L), potassium 3.8 (3.5 to 5.1 mmol/L), urea 11.2 (3.4 to 8.9 mmol/L) and creatinine 105 (57 to 126 mmol/L).

X-ray films of the chest were normal. Urgent computerised tomographic (CT) scan of the brain revealed "widespread hypodensity over the left parietal/occipital lobe, ? vasogenic oedema with underlying neoplasm".

He was prescribed bed rest and given dexamethasone. His condition remained stable and it was recorded that his symptoms "improved on steroids". A CT scan performed with contrast enhancement showed an "enhanced lesion in the left parieto-occipital region, likely to be secondaries". The search for a primary tumour, including sputum cytology and chest X-ray studies, was unfruitful. The neurosurgeon was consulted and his opinion was "? secondaries to the brain, ? a glioblastoma, ? abscess".

On the ninth day following admission, the patient was transferred to another hospital while waiting for the results of magnetic resonance imaging (MRI) studies. These were performed on 6 April and revealed "a cystic tumour (solitary secondary or glioma) ... or a low grade abscess".

Two days later, he was again seen at the AED. This time, there was a history of vomiting "many times" and sudden onset of decreased response to verbal commands. He was unable to recognise faces. However, he could still walk. On examination, his temperature was found to be 37°C, pulse 70 beats per minute and regular. Blood pressure was 130/70 mmHg. The pupils were equal and reactive to light. Examination of the fundus revealed blurring of the optic disc. The diagnosis was left parieto-temporal tumour. He was given steroids. A CT scan revealed "one more lesion anterior and caudal to the previous tumour".

The patient's temperature suddenly rose to 39.1°C

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and the GCS became 10/15. Examination of the chest and heart revealed no abnormal signs. The lower abdomen was slightly distended. X-ray films of the chest showed "right lower zone haziness". The following day, he was mentally confused and the GCS was 13/15. There was decreased urine output. Two days later, the patient was taken to the operating theatre and a biopsy of the brain was performed.

## Differential diagnosis

Dr RLC Kay*: The first diagnosis that was given was "stroke-in-evolution". I think we have to exercise a bit of caution in making a diagnosis of stroke. It is so easy to make. Anyone who comes in with a hemiplegia you say it is a stroke. But if you look at the history more carefully, the patient had symptoms for over a week and it was a progressive symptom, starting with dizziness and later on a bit of difficulty in walking. It was a stepwise progression for a week. Stroke-in-evolution sounds very impressive but does not really mean very much. It is probably over-used too. It means progressive stroke and, by and large, all strokes progress depending on the time at which you see the patient. So there is nothing special about progressive strokes, but in the old days, people thought that they were something you could stop by giving the patient heparin and so on. Nowadays we do not think so. Also, progressive stroke that lasts over a week is very unlikely. You may allow a day or two. So the diagnosis of stroke cannot be substantiated and the CT scan does not show it either. The lesion is in the white matter and does not confine itself to a vascular territory. The location of occlusion of an artery in stroke can either be anterior or posterior. The anterior location would usually be the middle cerebral artery. The posterior part of the brain is supplied by the vertebral arteries. The present lesion covers both the middle cerebral artery territory and the posterior cerebral artery territory. The lesion is not confined to one vascular territory. We also notice that the patient had some headache, which is a little more in favour of either a haemorrhagic stroke or some space-occupying lesion. The examination showed that the patient was apyrexial with normal pulse and blood pressure, and everything else was normal apart from the fact that the patient had a hemiparesis. I have been asked to talk a little bit on the GCS. This scale was invented by Professor Bryan Jennett. It was invented by a neurosurgeon because neurosurgeons need to monitor the degree of consciousness of patients over a period of time. Many of these patients have head injuries and in the past people used terms such as semiconsciousness, stuporous or unresponsiveness. Everybody had a different meaning as to what they meant by semi-consciousness and it was a highly unsatisfactory situation. It was because of the difficulty of quantifying and measuring consciousness over a period of time that this scale came into being. It looks at three things: eyes, motor and verbal responses. So a completely conscious eye-opening patient would respond to a verbal command, would also talk to you, and when they talk to you, they would talk sense. This would give a GCS of 15. A not-so-conscious patient for example, might have their eyes closed but would open them to pain. If you cause pain to the extremities, the patient might withdraw an arm or a leg. When you talk to the patient they might talk back, perhaps in a mumble, or just some inappropriate words. The patient gets an appropriate GCS score. Notice the score does not go down to zero. Even a dead patient would have a score of three.

So the patient had a number of CT scans which showed vasogenic oedema and he was given dexamethasone. I shall leave it to Dr Critchley to talk about dexamethasone later on, except to say that not all oedemas respond to dexamethasone. Basically there are two types of cerebral oedema. One is vasogenic, which is due to leaky vessels. The other is cytotoxic, which is due to leaky cells. By and large, leaky vessels are more common than leaky cells. In this sort of situation we are dealing with a space-occupying lesion. Leaky cells occur in a cerebral infarct, for example. Patients with oedema after cerebral infarction will not respond to dexamethasome. This has been proven by clinical trials. This patient later on had magnetic resonance imaging (MRI). After the MRI the differential diagnosis came down to a solitary secondary, a glioblastoma, an abscess, or a resolving haematoma. It could not be a resolving haematoma because there was no haematoma there in the first place. So we are down to secondaries, glioblastoma and abscess. After the MRI the patient got worse. He was sent back from the convalescent hospital with vomiting and decreased response to verbal commands. He could not recognise faces and probably could not talk. So the patient had a left hemisphere lesion, right hemiparesis and now dysphasia. A patient who has a left hemisphere lesion does not talk to you. Do not say the patient is uncooperative or confused because he may be dysphasic. Even when he can talk, he may not understand what you want him to say. He can either have expressive or receptive dysphasia. However, he could still walk so he had not reached the stage of coma. We are told that his temperature was still 37°C and blood pressure was still normal. But there was bilateral blurred vision which

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could be due to bilateral papilloedema and repeat CT scan showed an even bigger lesion. We were dealing with a progressive situation despite steroids or because of steroids. We had a patient who seemed to have a tumour which was not controlled by steroids. Perhaps we were not dealing with a tumour, but with an abscess. If you say the patient had an abscess, why should the patient's temperature have been normal? Well, with patients who are receiving steroids, even if there was an elevated temperature, it would have been suppressed by the steroids. The normal temperature may have given us a false sense of security, but by the time he was readmitted, even the steroids could not suppress his elevated temperature. He became more comatose and seemed to have developed a systemic infection, with abdominal distension—for whatever reason. His chest X-ray films showed some haziness. Of course, the systemic infection may not have been related to the primary infection, but due to long term bed rest, giving rise to decubitus ulcer and pneumonia and so on. He continued to worsen and eventually had a biopsy done. Basically, I would favour an abscess in this situation. If it was an abscess it would have to be a rather indolent abscess and not of pyogenic origin such as a staphylococcal abscess. Patients with a staphylococcal abscess anywhere would be very ill, with a high fever and high leucocytosis. This abscess would have to have been a non-pyogenic abscess. Over the years, we have had some non-pyogenic brain abscesses in the hospital. Table 1 shows a list of some of the usual causes. I am not saying that any of these is the eventual diagnosis in this patient. The first example of these abscesses is one caused by *Streptococcus milleri*. This organism was not well recognised until recently. It belongs to the *Streptococcus viridans* group and is a low grade infectious organism. It is relatively common amongst cerebral abscesses. *Nocardia asteroides* is a bacterium which thinks it is a fungus. *Cryptococcus neoformans* in Hong Kong has been shown to be associated with immunosuppression in half of the cases and classically *Cryptococcus* spp. affect the nervous system by causing meningitis. Our patient didn't have meningitis clinically. It is possible, but unlikely, to have *Cryptococcus* spp. causing a brain abscess without causing meningitis. We have had a couple of cases of *Naegleria fowleri* infection here associated with swimming, particularly in the hot springs of China. *Toxoplasma gondii*, we have seen it here associated with HIV. If you suspect brain abscess in an HIV-positive patient, the number one differential diagnosis is toxoplasmosis. Cysticercosis is uncommon, at least in Hong Kong, but we have seen that too.

Dr E Liang[†]: In the CT scan of the brain without intravenous contrast at the level of the top of the lateral ventricle, there is a hypodense lesion occupying the left parietal and occipital lobe. Around the lesion is a rim of vasogenic oedema due to disruption of the blood-brain barrier by either a neoplastic process or an inflammatory process. There is also some mass effect as we can see the sulci on the contralateral side quite clearly, while over the side of the lesion the sulci are effaced (Fig 1). Further behind in the posterior aspect of the lesion there is a small nodule as well. After intravenous contrast, there can be seen a ring enhancement around the lesion, which is thin and not sharp. The central density is probably that of a proteinaceous fluid or necrotic tissue. The differential diagnosis was of a ring-enhancing lesion in the brain. First of all, it could be a primary tumour such as a glioblastoma with a necrotic centre. Among other CNS tumours, lymphoma is a possibility but rarely does it give this type of radiological appearance. Certainly in this man's age group one has always to consider a solitary metastasis. Other than neoplastic conditions, we have to consider inflammatory conditions such as cerebral abscess, or a tuberculoma. Still others include a haematoma or infarction, or more rarely, an arterio-venous malformation. In the absence of any clinical evidence of inflammation, I would rate solitary metastasis as the number one differential diagnosis. An infective process such as an abscess or tuberculoma has to be excluded. Magnetic resonance scan imaging performed 11 days later showed that the vasogenic oedema was much less

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**Table 1. Uncommon causes of brain abscess**

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|---|---|
| *Streptococcus milleri* | Dental origin |
| *Nocardia asteroides* | Gram-positive filamentous bacteria affecting the lungs |
| *Cryptococcus neoformans* | Fifty percent of cases associated with HIV |
| *Naegleria fowleri* | Fresh water swimming |
| *Toxoplasma gondii* | High association with HIV |
| *Cysticercus cellulosae* | Ingestion of faecal contamination |

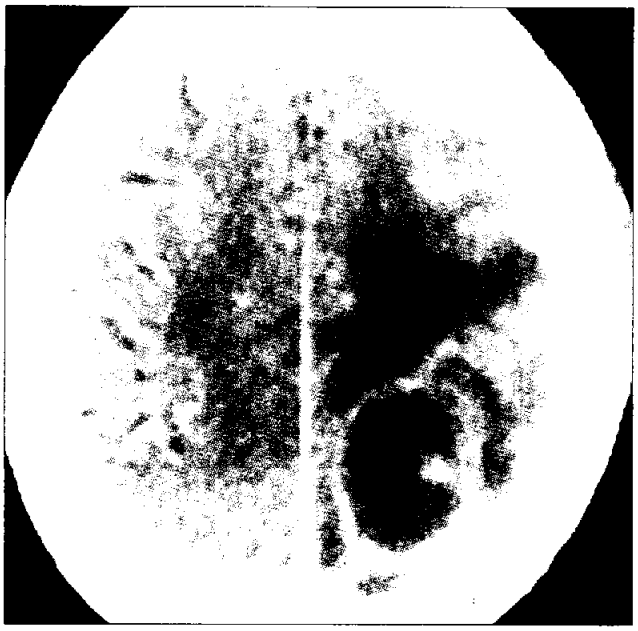

*Fig 1. Contrast-enhanced CT showing a ring-enhancing lesion with a nodule situated in the right posterior parietal lobe. Vasogenic white matter oedema is seen anterior to the lesion.*

than before, probably because of the effect of steroids. However, the lesion now had a lobulated appearance, developing a satellite lesion (Fig 2). With contrast (gadolinium), there was a rim enhancement. After the MRI, the differential diagnoses were still a necrotic tumour from a metastasis, a primary brain tumour, a brain abscess, or tuberculoma.[1]

Prof J Lee[‡]: Could this be an infarct?

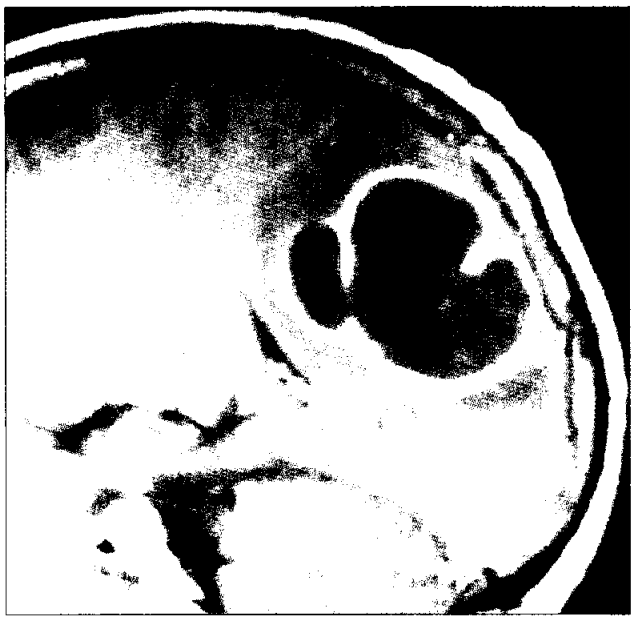

*Fig 2. Gadolinium enhanced MRI (T1 weighted, parasagittal) showing the development of a satellite abscess anterior to the original lesion in the right posterior parietal lobe*

Dr Liang: This is not likely. An infarct typically involves both the grey and white matter and here only the white matter is involved.

Dr KYC Goh[§]: I would just like to ask the radiologist why, from the MRI, you thought it could be a solitary metastasis or a glioblastoma, because the picture is such a well-enhanced rim lesion. That would make you think of a cystic tumour or an abscess rather than a metastasis.

Dr Liang: For tumours of the brain in this age group, secondaries are more common.

**Clinical diagnosis:**
*Brain tumour or abscess*

**Dr Kay's diagnosis:**
*Brain abscess*

Dr Goh: We performed an occipital craniostomy on 14 April. Using an ultrasound probe we located the exact site of the lesion. We inserted a cannula in order to aspirate some tissue. Instead of tissue, we aspirated 100 ml of greenish pus. Immediately after the procedure the patient improved considerably. His fever came down. We also inserted a Hickman line at the same time to give him antibiotics.

Prof Lee: Cytological studies were also done. Dr Chang, please.

Dr A Chang[‖] : We received 2 ml of fluid. There were many polymorphonuclear leukocytes and fibrin. This is consistent with material aspirated from an abscess.

Prof Lee: After the aspiration biopsy of the brain the patient progressively had reduction of urine flow and went into renal failure. There was no infection in the ear, nose or throat regions. On day 43 after he was first seen, he was in multiorgan failure and died. An autopsy was performed.

## Pathological discussion

Dr WY Chan[¶]: At autopsy we found a well-built 62-year-old man. There was a surgical wound on the left side of his head and a few patches of ecchymosis on his arm. In the gastrointestinal tract we found a small ulcer 2 cm in diameter in the mid-oesophagus, and there

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*Fig 3. Appearance of the right kidney at autopsy. Throughout the surface and cut section, there were multiple yellow-white nodules measuring 0.1 to 0.3 cm in diameter.*

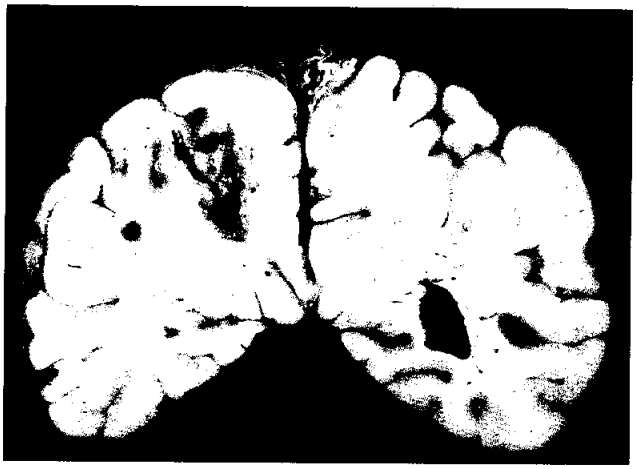

*Fig 5. Coronal section of the brain showing a partially collapsed cavity in the right lobe of the posterior parietal area*

was marked oesophagitis and gastritis. The liver was normal, weighing 1388 g. The heart was grossly unremarkable, but microscopically, we found several microabscesses with some fungal organisms in the interventricular septum. The lungs were very heavy: the left side weighed 920 g and the right 1165 g. They were markedly oedematous with focal areas of haemorrhage and consolidation. There were thrombi in some large and small blood vessels. Microscopically, there was oedema and acute inflammation. The urinary bladder showed inflammation. In the right ureter there were two yellowish nodules in the mucosal lining. In the kidneys there were multiple yellowish nodules measuring from 0.1 to 0.3 cm. Some of them were soft and necrotic (Fig 3). Microscopically, multiple abscesses replaced much of the kidney parenchyma. Grocott stain revealed septated fungal hyphae with budding (Fig 4). Sections of the brain revealed a cystic lesion of 3 cm diameter in the left parietal lobe (Fig 5). The meninges contained yellowish nodules. The histology confirmed brain abscess with inflammatory cells and foam cells (Fig 6). In the wall of the abscess, fungi were present. In summary, the final anatomical diagnoses were: disseminated candidiasis involving kidney, brain, heart, and ureter (the abscess in the brain also contained fungi); disseminated intravascular coagulation; and pulmonary thromboembolism, pulmonary oedema, and haemorrhage.

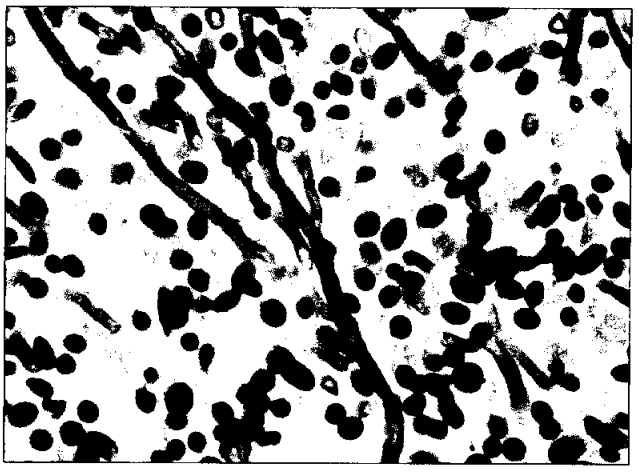

*Fig 4. Photomicrograph of a nodule in the kidney showing septated fungal hyphae (x 860)*

Dr DJ Lyon**: The microbiology from this patient essentially falls into two parts. The first is the presenting brain abscess. We received some pus from the operative procedure from which we grew three organisms: two were anaerobes (*Peptococcus* spp. and *Eubacterium* spp.) and an aerobic gram-negative bacillus. Two weeks later we grew *Candida albicans* from the blood culture and several days later, from postmortem kidney and blood. I would like to say a few words about the pathogenesis of brain abscess. It is important to consider the route of spread of infection to the brain. The commonest source is spread from a contiguous focus of sepsis—usually infection of the ear or the sinuses. In this case, the infection spread directly through the bone to the brain tissue. Also common is haematogenous spread from a focus elsewhere in the body such as from the lung in a patient with lung abscess or bronchiectasis. Some abscesses are secondary to trauma, while in others the means of spread of infection is unknown and these are classified as cryptogenic. The most important organisms are *Streptococcus milleri*, gram-negative bacilli such as coliforms and *Pseudomonas* spp., and anaerobes. Most brain abscesses are polymicrobial—the exception being when the cause is *Staphylococcus aureus*, which is usually the only organism isolated. Staphylococcal abscesses

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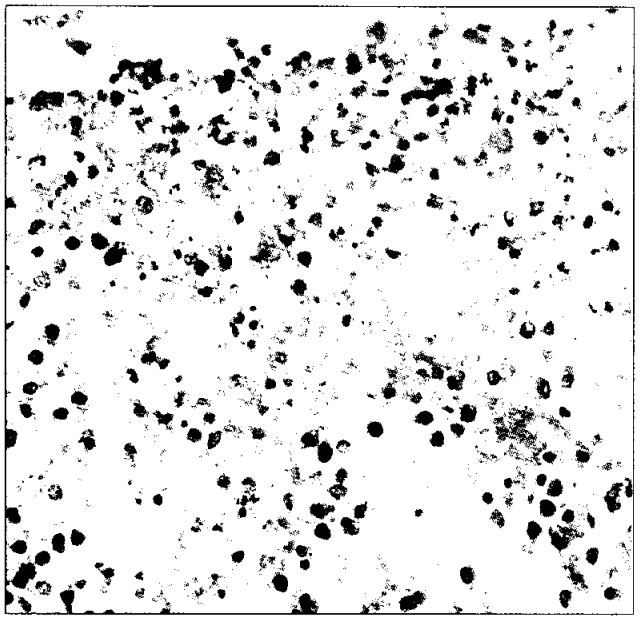

*Fig 6. Photomicrograph of the abscess in the brain (x 200)*

are often secondary to trauma. Abscesses caused by fungi are usually seen in immunocompromised patients. In this patient we did not grow *C albicans* from the original pus sample received, but it was present at that site in the postmortem samples. It is likely that the disseminated candidal infection developed during therapy for the brain abscess. Risk factors for the development of candidaemia include colonisation at multiple sites, long duration of antibiotic therapy, multiple antibiotics, use of Hickman catheters, haemodialysis, prolonged neutropaenia and corticosteroid administration. Several of these risk factors were present in this patient (prolonged and multiple antibiotics and steroids). Since the attributable mortality of candidaemia is approximately 30%, it is important to consider this possibility in patients with these risk factors.

Dr J Critchley[††]: Dexamethasone is a standard treatment for brain tumour-related cerebral oedema. The usual regimen is to give an intravenous bolus of dexamethasone (10 to 20 mg) and then to give the patient 16 mg of dexamethasone daily for one week. There has been much debate on the value of corticosteroids to treat cerebral oedema since the early published studies in the 1970s.[2,3] By the 1980s the concensus was that the oedema associated with brain tumours responds better to dexamethasone than that due to head injury. The onset of response is about eight to 48 hours and the maximum clinical effect is from three to seven days, after which it diminishes. However, the value of corticosteroids for other causes of cerebral oedema remains controversial. High dose corticosteroids have been shown to be of benefit following head trauma up to a daily dose of 100 mg of dexamethasone. Three early studies have shown that high dose therapy is more effective than low dose therapy or placebo, based on the rates of survival and clinical recovery with less long term disability in survivors. The advantages of the high dose over the low dose regimen are reduced for brain tumours. More recent texts and studies support use of the standard (low dose) dexamethasone regimen for tumour-related cerebral oedema. However, the value of dexamethasone in head injury and stroke remains questionable and appears to increase the incidence of infection.[4,5]

We have to consider why this 62-year-old male with a left parieto-occipital lesion was given steroids. The history was progressive over seven days and you will have noticed that on admission, the blood film revealed a raised white blood cell count suggestive of infection. That should have raised the possibility of an abcess, but the patient was given low dose dexamethasone—without antibiotics—for three weeks. During this time, the patient deteriorated further. Despite this, at four weeks, further corticosteroids were given. However, a key factor which I am sure confused the clinicians, was that in the clinical notes there was a record of the CT scan showing an "enhanced lesion likely to be secondaries". If I had read that, I also might have thought that this indicated multiple secondaries.

To conclude, I would like to stress that when we give a patient high doses of dexamethasone, we must be aware of the relevant side effects of corticosteroids, such as enhancement of peptic ulceration, diabetes and infection. That is why patients are usually also given $H_2$-receptor antagonists with dexamethasone therapy. We give corticosteroids for their antiinflammatory and immunosuppressive actions. They reduce oedema and swelling, but the price one pays is that the immune response and its manifestations are also reduced and the likelihood of the spread of any infection is enhanced. Unfortunately, in this case, it is quite possible that the deterioration in the patient's condition was promoted by the corticosteroid therapy.

Prof Lee: There is one biochemical aspect that is of interest, and that is the low blood sodium.

Dr Y Lolin[‡‡]: When I heard that this was a neurological patient, the first thing I thought was that there was salt loss. It is a very common condition due to neuroendocrine disturbances of the control of sodium retention by the kidney and inappropriate ADH secre-

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tion. However, before you say somebody has cerebral salt loss, you have to exclude other causes. In hospital patients who have hyponatraemia, the commonest cause is from urinary tract infection (UTI); also patients who have just been catheterised and even those with cystitis. If there is any infection invading the ureter, this will induce salt loss. In this patient, when I was told of his low sodium I thought it was a cerebral cause. But having seen the kidneys, I think it was salt loss due to UTI.

Dr HK Ng[§§]: I support Dr Lyons' hypothesis that candidiasis occurred at a secondary stage of the disease. When we examined the brain abscess, we were conscious of the possibility of fungal organisms. At the time of aspiration biopsy of the brain abscess there were no fungal organisms. The source of infection in this case was the acute pyelonephritis that Dr Chan has shown in the kidney. I think it was the cause of the sepsis. If we learn anything from this case, I advise we go back to the patient's medical records and look at the results of the urinalysis.

**Anatomical diagnosis:**
*Brain abscess; acute pyelonephritis; disseminated candidiasis*

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