One hundred and thirty-six brain tuberculomas in a single patient

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Although large case series continue to be reported from developing countries,[1] multiple brain tuberculomas are unusual and rare, even in immunocompromised patients.[2] The maximum reported number of tuberculoma in one patient has been 100.[3] Herein, we report a single patient with 136 brain tuberculomas.

A 76-year-old married, non-smoker, retired army driver, Saudi male, was admitted to King Abdul-Aziz Specialist Hospital, Taif, Kingdom of Saudi Arabia after referral from a local hospital with a 2 month history of low grade fever with evening rise, night sweats, anorexia, weight loss of 8 kgs, and gradually worsening confusional state leading to fecal and urinary incontinence, which had not improved by treatment from local doctors. He had no history of head injury, headache, neck stiffness, vomiting, jaundice or joint pains. He was treated as a case of pulmonary tuberculosis 40 years back for one year with unknown drugs, and had been a diabetic for the last 4 years on glibenclamide with poor diabetic control due to dietary noncompliance. He had not been outside Saudi Arabia in the recent past, but had occasionally consumed raw milk. There was no family history of tuberculosis, and he had not used any immunosuppressive drugs recently. On examination, he was well-hydrated, conscious but confused, disoriented in time, place and person, was uncooperative with combative behavior. He had no pallor, cyanosis, jaundice or lymphadenopathy, and no signs of meningeal irritation. Pupils were normal, and there was no diabetic retinopathy. Pulse was 80/min regular, blood pressure 120/60 mm Hg, temperature 37.7°C, and a respiration rate of 24/min. The rest of the clinical examination, including neurological evaluation, was unremarkable. With a background of past tuberculosis and recent diabetes with poor control, he was investigated with a provisional clinical diagnosis of tuberculous encephalitis. His investigations included an erythrocyte sedimentation rate (ESR) of 60 mm/1st hr, white blood cell count of 16.5 x10^9, hemoglobin of 13.5 gms/L, platelet count of 756 x 10^9, random blood glucose of 13.1 mmol/L, serum protein of 66 gms/L, serum albumin 23 gms/L, sodium (Na) 119 mmol/L, potassium (K) 3.9 mmol/L, creatinine 58.3 umol/L, urea 5.9 mmol/L, plasma osmolality 255 m.osmol/L, urine osmolality 247 m.osmol/L, urine K 20.4 m.mol/L, urine Na 71 m.mol/L. Urine examination showed glucose+++ with no ketonuria, pyuria or proteinuria. Chest x-ray and ECG were normal. An emergency plain CT brain showed normal brain parenchyma for age with a hypodensity in the left frontal region with no brain edema. A lumbar puncture was carried out, which revealed raised opening pressure with straw-colored cerebrospinal fluid (CSF). The CSF examination revealed total leucocyte count of 45 cells, with 94% lymphocytes and 6% polymorphs. The CSF glucose was 7.5 mmol/L, and protein 7.9 gms/L. Gram and acid-fast bacilli staining of the CSF sediment were negative. Urine, blood, and throat as well as the CSF cultures were negative. Blood film for malarial parasites and brucella antibody titers were negative. Thyroid function and serum cortisol were normal with negative HIV serology. A tuberculin test could not be carried out. In view of the history and supportive laboratory findings, he was diagnosed as a case of encephalitis due to brain tuberculosis with associated diabetes mellitus, Syndrome of Inappropriate Anti Diuretic Hormone (SIADH) secretion and reactive thrombocythemia. He was started on isoniazid, rifampicin, pyrazinamide, and ethambutol based on his weight (70 kgs) and subcutaneous insulin along with pyridoxine. This was combined with intravenous dexamethasone. He was given high salt diet with initial water restriction with improvement in hyponatremia. As the investigation of choice to rule out CNS tuberculomas, an MRI of the brain with contrast was arranged on the 13th admission day. The MR images revealed numerous ring enhancing rounded focal lesions of variable sizes (2-12 mm) randomly distributed in the brain involving cerebrum, cerebellum and brain stem suggestive of tuberculomas (**Figure 1**). The count of tuberculomas was carried out

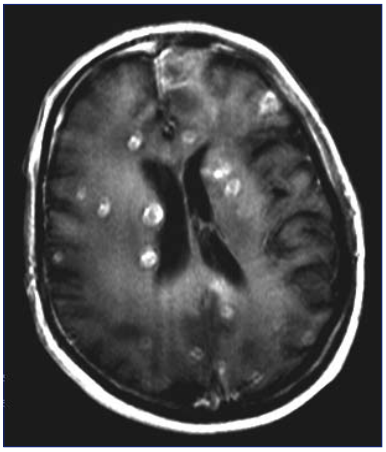

Figure 1 - An MRI contrast enhanced T1 weighted image showing multiple ring enhancing tuberculomas in both frontal and parietal lobes.

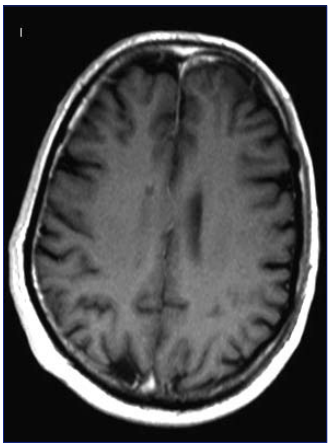

Figure 2 - An MRI contrast enhanced T1 weighted image showing interval resolution of most of the tuberculomas except one in the left frontal lobe after 4 months of antituberculous treatment.

by 2 experienced radiologists independently while evaluating only axial and coronal planes. A total of 136 tuberculomas were counted. This could be an under-estimate because there was motion blur in axial cuts while the coronal cuts were not completely recorded. Furthermore, tuberculomas in the same location in sequential cuts were not included in the count and this could also have underestimated the true count considering the fact that MRI slices were 5 mm while some of the tuberculomas were only 2 mm in diameter. As the patient had no symptoms related to lower limbs, MRI study of spinal cord was not carried out. With the above treatment, his mental status and fever improved within one week and he was discharged from hospital after 20 days on antituberculous therapy (ATT), subcutaneous insulin, oral prednisolone, and pyridoxine. He was followed up in the out-patient department (OPD) regularly with improvement in ESR, Na and weight. His steroids were tapered and stopped within 6 weeks, while pyrazinamide and ethambutol were discontinued after 3 months. A follow up MRI with contrast carried out after 4 months of treatment showed interval resolution of most of the tuberculomas except the larger ones indicating good radiological response to ATT (**Figure 2**). On regular OPD follow up after completion of 12 months of ATT, he was clinically normal and had no disease related complications or treatment related side effects.

Enhancing intracranial lesions with evidence of systemic tuberculosis as well as intracranial lesions responding to ATT have been routinely labeled as tuberculomas in different reports.[4,5] Intracranial tuberculomas can be asymptomatic or symptomatic. Small tuberculomas may not be associated with any features attributable to their presence, for example, seizures and focal neurological deficit as occurred in our patient. Our patient responded very well to ATT as evidenced by clinical improvement as well as interval resolution of most of the tuberculomas, except the 2 bigger ones at MRI study carried out after 4 months of therapy. We could not do an MRI study of the spinal cord, but it might be possible that asymptomatic spinal cord tuberculomas could have been associated with brain tuberculomas. Why our patient had multiple tuberculomas cannot be completely explained. It has been reported that HIV-infected patients have fewer tuberculomas as compared to non-HIV infected patients. These findings add to the hypothesis that tuberculomas are formed because of a robust immunological response to tuberculous infection.[3] As our patient had a past history of treated pulmonary tuberculosis and was HIV-negative, this could have been the possible explanation. However, presence of uncontrolled diabetes mellitus could have also contributed to extensive local spread in the brain.

In conclusion, brain tuberculomas can be missed by routine radiological imaging unless looked for by contrast CT or MR studies. Our case represents a high number of brain tuberculomas, with a good clinical and radiological response to ATT.

Received 5th April 2006. Accepted for publication in final form 21st June 2006.

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