Syringomyelia Developing as an Acute Complication of Tuberculous Meningitis

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ABSTRACT: ***Background:*** Tuberculosis of the nervous system has protean manifestations. Syringomyelia, though an uncommon complication of it, is usually of late onset. ***Methods:*** We report two patients with tuberculosis meningitis who developed syringomyelia acutely. The diagnosis was supported by neuroimaging and findings at laminectomy. ***Results:*** The two patients developed syringomyelia between 11 days and 6 weeks of the onset of tuberculous meningitis. They both had cord swelling and softening. ***Conclusions:*** Acute-onset syringomyelia should be suspected in any patient being treated for tuberculosis meningitis who subsequently develops limb weakness and/or sphincteric dysfunction. Inflammatory edema and cord ischemia appeared to be the underlying mechanisms in these early onset cases rather than arachnoiditis which is important in late-onset cases.

RÉSUMÉ: Syringomyélie comme complication aiguë d'une méningite tuberculeuse. ***Introduction:*** La tuberculose du système nerveux a des manifestations variées. La syringomyélie, bien qu'elle en soit une complication rare, est habituellement tardive. ***Méthodes:*** Nous rapportons les cas de deux patients, atteints de méningite tuberculeuse, qui ont présenté une syringomyélie aiguë. Le diagnostic a été étayé par l'imagerie et les constatations faites au moment de la laminectomie. ***Résultats:*** Les deux patients ont développé une syringomyélie entre 11 jours et 6 semaines du début de leur maladie diagnostiquée comme une méningite tuberculeuse. Ils avaient tous deux des manifestations d'oedème et de ramollissement de la moelle. ***Conclusions:*** La syringomyélie d'installation aiguë devrait être soupçonnée chez tous les patients qui sont traités pour une méningite tuberculeuse et qui développent subséquemment de la faiblesse des membres et/ou une dysfonction sphinctérienne. L'oedème inflammatoire et l'ischémie de la moelle semblaient être les mécanismes sous-jacents chez ces cas à début précoce plutôt qu'une arachnoïdite qui est une entité importante chez les cas tardifs.

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Tuberculosis remains a major public health problem worldwide. Efforts at control and eradication in many countries have been thwarted by overcrowding, poverty, homelessness, drug resistance and infection by the human immuno-deficiency virus (HIV).[1] The clinical presentation of tuberculosis of the nervous system may be atypical in some cases and the results of investigations may be confusing and could lead to a delay in diagnosis and institution of appropriate therapy.[2-4,6] The sequelae of tuberculous meningitis (TBM) include: persistent vegetative state, hemiparesis, cerebellar dysfunction and spinal syrinx.[2] Between 10 and 79% of subjects with TBM develop these various complications and about 7% of them die from the disease.[2,3] Therefore, TBM is a major cause of morbidity and mortality.

Syringomyelia is usually a late complication of tuberculous meningitis and the manifestation may not occur until after two decades of the acute infection.[5-7] However, there have been few reports on the development of syringomyelia as an acute complication. We recently encountered two patients with TBM who developed syringomyelia during the acute phase of their illness. The cases are presented in this communication.

Case Reports

Patient 1

A 35-year-old Saudi male was admitted with a 4-weeks history of low grade intermittent fever, cough, and generalized, throbbing headache. He vomited on one occasion. Three weeks later, he noticed difficulty with neck turning and pain. He smoked 20 cigarettes per day for the past 5 years. There was no substance abuse and he had no other past medical history.

On examination, he was asthenic, pale and febrile. He was confused and lethargic. His speech was slurred and he had neck stiffness with a positive Kernig's sign. He had no other neurologic deficit and the optic discs were normal. He had bilateral basal crackles on chest examination and tachycardia.

His brain CT scan was normal and he subsequently had lumbar puncture. The cerebrospinal fluid (CSF) was clear but with raised protein (0.96 g/L) and lymphocytic pleocytosis of 80 cells/mm^3. The sugar was 1.9 mmol/L while the corresponding blood sugar was 5 mmol/L.

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Gram and Zeihl-Neelsen stains of his CSF were negative. However, CSF culture was positive for M. tuberculosis. Brucella, VDRL, HIV, and vasculitis screen were negative. A chest X-ray showed basal consolidation but with no cavitary lesion. Sputum was positive for acid fast bacilli and cytology was negative for malignant cells.

The patient was started on rifampicin, isoniazid, pyrazinamide and ethambutol. Ten days later, he developed a sudden onset of flaccid paraplegia and he had sensory level at T_8. Urgent metrizamide myelography revealed a complete block at T_6 level. During emergency laminectomy a swollen, soft cord was found with meningeal inflammation. Meningeal biopsy showed granulomatous changes, caseation necrosis and giant cells consistent with TBM. Dexamethasone was added to the previous medications. MRI of the spinal cord done 2 weeks later showed a syrinx extending from T_5-T_{10} with associated cord swelling. (Figures 1A&B). The patient continued his medication and was discharged after 4 weeks. He has since been lost to follow-up.

Patient 2

A 32-year-old Indonesian lady presented with a 10-day history of febrile illness, non-colicky, central abdominal pain and vomiting. A day after the onset of symptoms, she developed irrational ideas and an altered level of consciousness.

Physical examination at entry revealed a drowsy, febrile, confused lady with evidence of meningeal irritation but no lateralizing signs. There was periumbilical tenderness without palpable masses on abdominal examination. The other systems were normal. Her initial hemogram showed leucocytosis (12,700/mm^3, with 93% neutrophils) and hemoglobin of 9.9 g/100 mls. Urinalysis yielded 3 white blood cells/hpf and few bacteria. Arterial blood gas analysis (at room air) was normal. Brain CT scan was normal and lumbar puncture yielded blood-stained CSF with lymphocytic pleocytosis (80/mm^3), RBC 380/mm^3, protein 0.3 g/L and sugar 2.0 mmol/L. She was commenced empirically on anti-tuberculous therapy (i.e., rifampicin, isoniazid, pyrazinamide, ethambutol with dexamethasone and ceftriaxone.

The following day she became alert and oriented but realized that she was unable to move her lower limbs with bilateral loss of sensation up to the anterior superior iliac spine. Only muscle flickering was discernible on examination of the lower limbs with hypotonia and hyporeflexia. There was also sensory loss up to L_1. CT myelogram showed spinal cord swelling with constriction between T_{10} and L_1. In addition, her serum electrolytes (in mmol/L) were deranged: Na 116, K 3.3, Cl 82, HCO_3 21, urea 2.4 and creatinine 49. Her urinary Na+ was 40 mmol/L and the serum osmolarity was 241 mOsmol. Her fluid intake was restricted to 600 mls per day and this was sufficient to correct the electrolyte and osmolality abnormalities within 5 days. The subsequent serum electrolytes and urea values were normal: Na 135, K 3.5, Cl 100, urea 4.6, creatinine 58. Her chest CT scan showed miliary mottling and fine needle aspiration of a nodule yielded numerous acid fast bacilli. Bronchial lavage cytology revealed numerous alveolar macrophages with benign bronchial cells. Posterior tibial nerve somatosensory evoked studies showed normal compound action potentials at the popliteal fossa but absent proximal potentials. However, her median nerve SSEPs studies were normal and thus suggested the possibility of a lesion at the thoracolumbar level. The following tests were negative: brucella serology, Widal's test, HIV, vasculitis screen, porphyria, VDRL.

An MRI showed a thoracic syrinx (Figure 2A-D) in the lower dorsal spine extending from T_{10}- L_1 level with focal cord swelling corresponding to that region. The syrinx was better demonstrated in the post enhanced T_1 weighted sagittal scan (Figure 2B).

She showed some improvement during her 3 months stay in the hospital. Her motor power improved to grade 3 but she remained incontinent. Repeat CSF examination was normal. She continued her anti-tuberculous therapy on discharge.

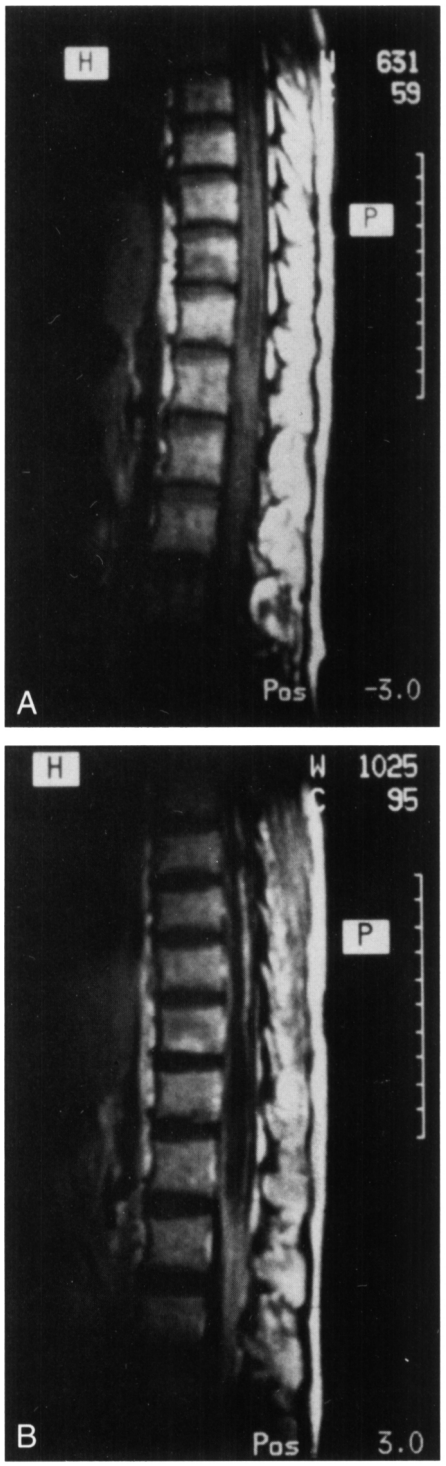

Figure 1: *(**A**) Sagittal T_1 weighted scan (SE 595/20) shows focal cystic area extending along the mid-dorsal spine (T_5-T_{10}) with associated cord swelling. (**B**) Axial proton density image with gadolinium enhancement at the mid-dorsal spine (T_7), shows low signal intensity area within the cord which indicates the presence of syrinx.*

Discussion

Syringomyelia is an uncommon and usually late complication of TBM. It was documented in only one out of 58 patients studied over a 30-year period by Kent and others.[3] In a recent review of the causes and conditions associated with the development of the cystic spinal cord, infective conditions accounted for only about 1% of the cases.[9] The vast majority of the cases are either associated with hind-brain herniation or secondary to birth injury.[9-11] The proposed mechanisms for the abnormal dilatation of the central canal include gliosis, ischaemia and inflammatory oedema.[10-11] Arachnoiditis secondary to TB could either result in

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***Figure 2:** (A) Sagittal T_1 weighted image of the mid-dorsal spine showing low signal intensity area with the cord with some expansion of the cord at the same level. The lesion is better delineated in the post-enhanced MR.*

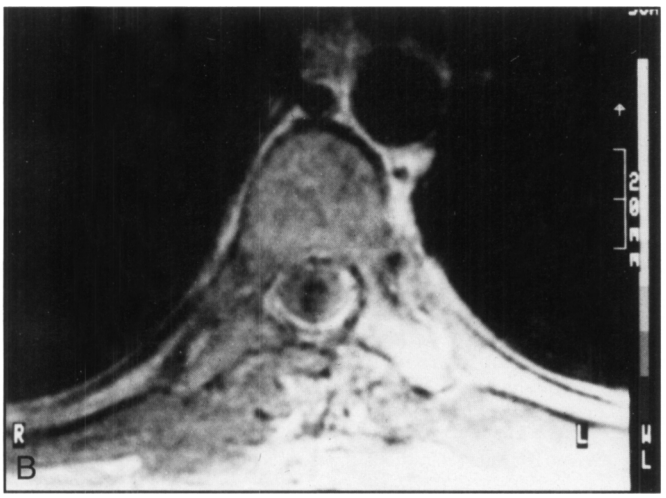

***Figure 2:** (B) the axial T_1 weighted scan.*

mechanical obstruction[9-12] or be associated with arachnoid cyst formation which contributes to cord damage.[10-13]

Acute onset of syringomyelia associated with TBM is less often reported. Fehlings and Bernstein reported the case of a 23-year-old Vietnamese male diagnosed with TBM who developed rapidly progressive myelopathy with evidence of granulomatous arachnoiditis and syringomyelia.[8] Schapira and others also documented the case of a 41-year-old male patient with pulmonary TB who developed acute paraplegia 2 days after stopping antituberculous therapy. MRI in that patient showed a large intramedullary cavity extending from T_2 to the conus medularis.[14]

Our cases of acute-onset syringomyelia complicating TBM

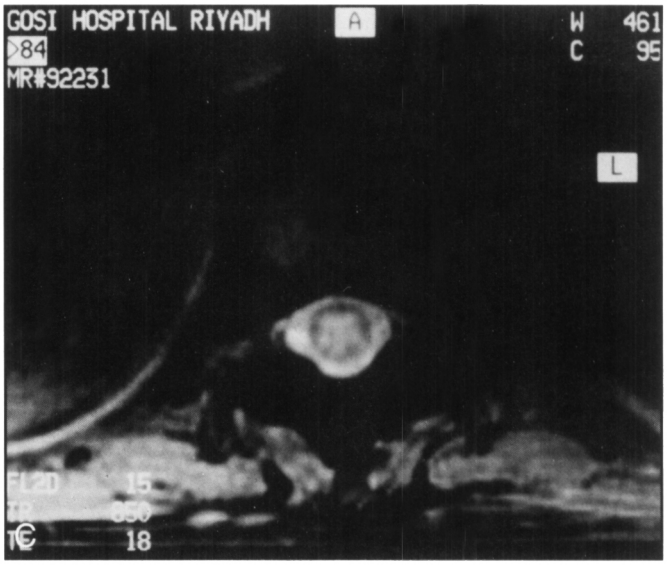

***Figure 2:** (C) shows the expansion of the cord and the large cystic area within it exhibiting relatively high signal intensity due to statis of fluid within the syrinx. Sagittal weighted image.*

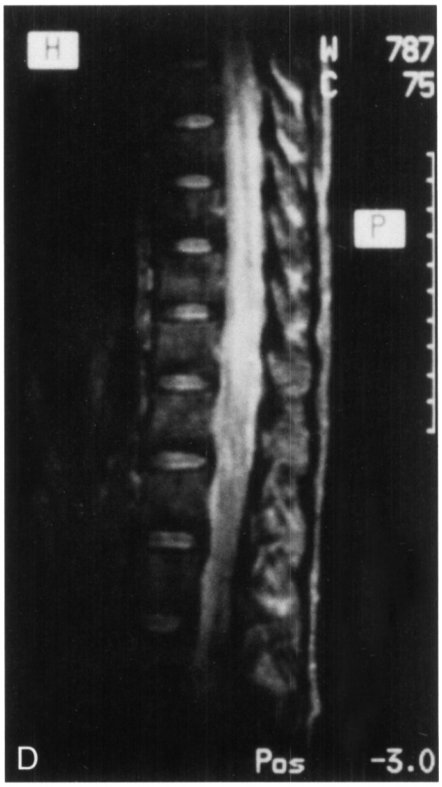

***Figure 2:** (D) showing the expansion of the cord with high signal intensity which is likely to be due to the syrinx.*

add to the sparse literature on this condition. Our first patient had evidence of myelomalacia at laminectomy which we ascribed to a combination of acute inflammatory edema and ischemia of the cord like Fehlings and Bernstein postulated in their case.[8] Our second patient developed the syndrome of inappropriate antidiuretic hormone secretion (SIADH) during the

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acute illness which is not uncommon in patients with TBM.[15,16] The condition responded to fluid restriction only. Although SIADH could be associated with edema, syrinx formation is not a reported complication. Diagnosis was facilitated by MRI without which the two cases would have been labelled as myelitis due to TB. Misdiagnosis or delayed diagnosis would therefore occur if MRI was not used and in this conjunction, both the T_1 and the first echo T_2 weighted images (proton density) are essential for differentiating the syrinx from myelomalacia. Earlier reports relied on either air or contrast dye myelography and autopsy verification.[3,7,9,11]

One could argue that the finding of syrinx was accidental in these cases in the absence of arachnoiditis and possibly that the patient had their cavities before they developed febrile illness but the evidence of acute meningeal disease at laminectomy and MRI findings were against this. None of our cases had evidence of hindbrain herniation, birth defects, Arnold-Chiari malformation, arachnoid cysts or evidence of hydrocephalus, as these were carefully looked for. The patients were also clinically well before developing the febrile illness. The location of the syrinx, evidence of cord pathology related to these locations would appear to support our impression that these patients presented with acute syringomyelia related to the recent tuberculous infection.

Neither of our patients had any specific therapy for the syringomyelia apart from anti tuberculous drugs and steroids. Untreated syringomyelia is compatible with long survival without progression in 35-50% of cases.[11] The best indication for surgical management either in the form myelotomy and syringotomy or shunt procedure is acute progression of neurologic disability,[11] which was not the situation with our cases. Workers in India have reported on the beneficial use of intrathecal hyaluronidase in the management of tuberculous spinal arachnoiditis.[13] Its mode of action being enzymatic hydrolysis of glucosaminidic bonds of hyaluronic acid to resolve arachnoidal adhesions. This could have been a useful adjunct to therapy in our patients if they had not developed their syrinx by the time the diagnosis was made.

In conclusion, these 2 cases complement the reports of early-onset syringomyelia associated with TBM. The presumed pathogenetic mechanisms include inflammatory edema and cord ischemia related to meningeal disease. It would therefore be worthwhile considering syringomyelia as a possible cause of new neurological signs in patients being managed for TBM. MRI of the spine and brainstem should be done early in such cases so as to increase the chance of making such a diagnosis.

Acknowledgement

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