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Case study

Tuberous sclerosis complex and hydrosyringomielia: Report of two cases

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ABSTRACT

Two patients with typical tuberous sclerosis complex (TSC) associated with cervical or dorsal–lumbar hydrosyringomielia are described for the first time. Syringomielic cavities are small in extension in both cases, leading to significant clinical symptoms as bilateral pes cavus and scoliosis in one patient only. So far, tuberous sclerosis had not been reported to involve primarily the spinal cord, and other factors directly linked to syringomiely are not present in both these patients.

1. Introduction

Tuberous sclerosis complex (TSC) is a genetically determined, variably expressed, multisystemic disorder that may affect many human organs with well-circumscribed, benign, non-invasive lesions. CNS abnormalities, mainly cortical tubers and subependimal nodules, are the hallmark of TSC and underline its most common and clinically serious manifestations.[1] The skin, retina, heart, kidney and lung are often involved as well.

Bone involvement and, in particular, vertebral lesions may be present,[2–4] even though they are often asymptomatic. Surprisingly, the spinal cord does not seem to be primarily involved in TSC, and to our knowledge no reports on this subject are so far available.

In the present paper, two patients with a confirmed TSC associated with hydrosyringomielia are described for the first time.

2. Case report 1

This 12-year-old female is the third child of a non-consanguineous healthy couple. Her mother and father were 32 and 33 years old, respectively, at the time of her birth. Familial history was negative. The pregnancy was complicated by a spontaneous abortion of a twin brother at 40 days of gestation, slow intrauterine growth and placental displacement at 6 months and half. Spontaneous delivery was at 29 weeks; birth weight was 1200 g. Postnatal cyanosis was reported and Apgar scores were 5 and 7 after 1′ and 5′, respectively.

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The girl developed respiratory distress during the first week of life and a heart interventricular defect was concurrently diagnosed. A catheterisation of the umbilical artery was then performed. Psychomotor development is referred to as normal. When she was 16 months old, she manifested a prolonged febrile seizure 5 days after assuming measles, rubella and mumps vaccine. At 5 years, weekly complex partial seizures started, partially controlled by valproic acid therapy.

A wake and sleep EEG recording showed independent slow and sharp waves over parietal and occipital areas. Due to persisting episodes of fixed gaze and unresponsiveness lasting less than 1 min, carbamazepine replaced valproic acid, leading to complete seizure control. A portal cavernoma was diagnosed at the age of 8 years.

At the age of 11 years, neurological examination revealed minor pyramidal symptoms, hand dyspraxia, absence of the right abdominal cutaneous reflex, bilateral pes cavus and genu valgus. A moderate clumsy and leaning forward gait was noted as well. The Rx study of the vertebral column showed a right convex dorso-lumbar scoliosis with increased dorsal kyphosis. Kidney and heart echocardiography as well as ophthalmologic examination were normal. Hepatic echoes confirmed a 2 cm large portal cavernoma. Motor and sensitive nerve conduction of the upper and lower limbs was in normal range. Mental level and school performances were also within normal limits.

MRI scans performed at this time showed multiple cortical and subcortical tubers over left frontal-basal, parietal and insular areas, as well as right frontal and temporal lobes. Small bilateral and hyper intense subependimal nodules, one of these very close to the right foramen of Monroe, were concurrently present together with a marked ex vacuo dilation of both lateral ventriculi with scalloped edges, configuring a periventricular leukomalacia (Fig. 1). A small hydrosyringomielic cavity between the fifth and

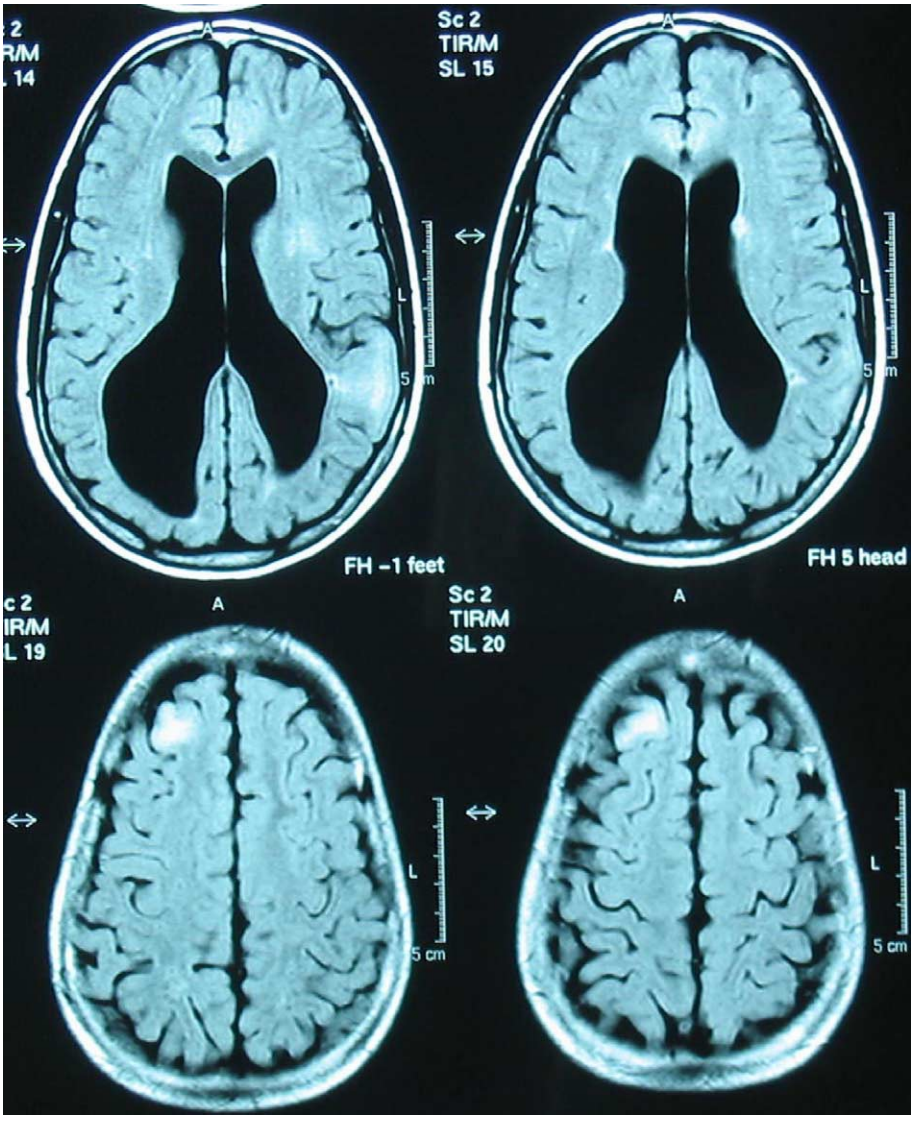

Fig. 1 – Case 1. FLAIR-weighted axial MRI brain images showing left parietal and right frontal cortical and subcortical tuberous and hyperintense subependimal nodules associated with a marked ex vacuo dilation of both lateral ventriculi with scalloped edges.

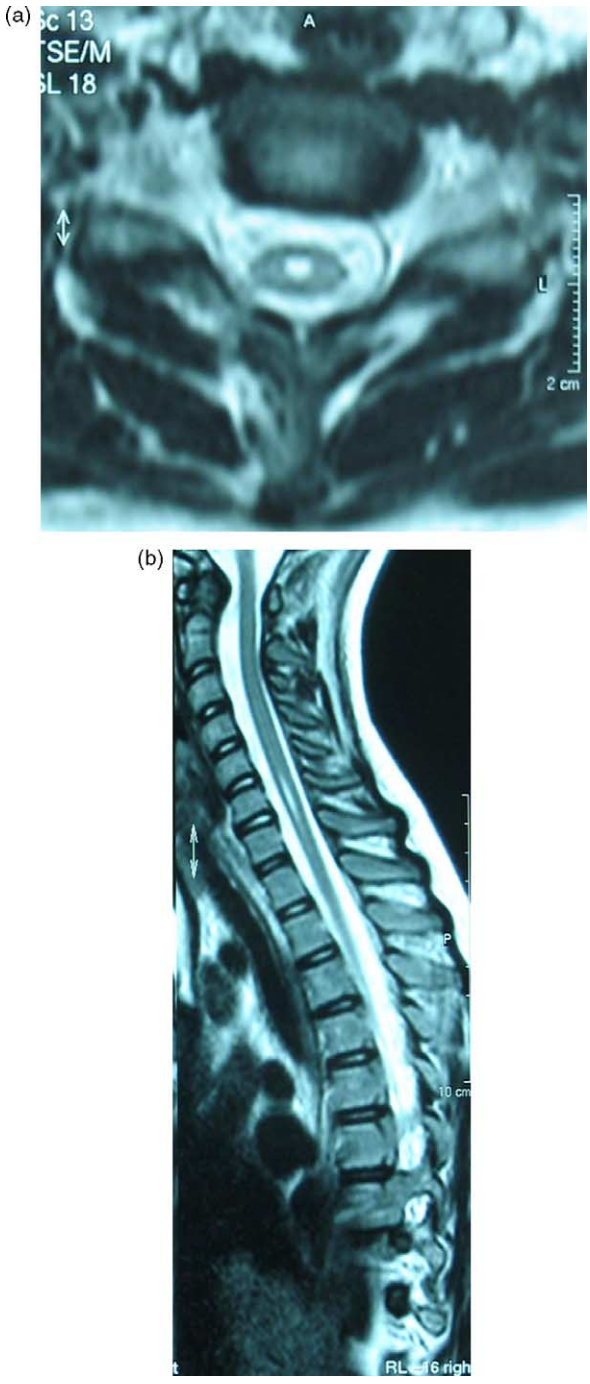

Fig. 2 – Case 1. T2-weighted axial (a) and sagittal (b) MRI scans of the spinal cord disclosing a small hydrosyringomielic cavity between the fifth and seventh cervical vertebrae.

seventh cervical vertebrae was revealed by MRI study (Fig. 2a and b).

Electroneuronography, carried out on median, peroneal and sural nerves, showed signs of axonal damage in abductor V muscle. These findings were compatible with an anterior horn cell disorder involving C8-T1 levels of the spinal cord.

3. Case report 2

This patient was the only child born to non-consanguineous parents; his father was affected by tuberous sclerosis complex and was concurrently carrier of a balanced translocation q11.23–q22.11.

He was born at term after an uneventful pregnancy and spontaneous, uncomplicated delivery. His birth weight was 3100 g; psychomotor development was normal. At the age of 7, because of a facial sebaceous adenoma associated with multiple cutaneous hypomelanotic macules, a brain MRI was performed, disclosing subependimal nodules localised in the left lateral ventricule close to the foramen of Monroe,

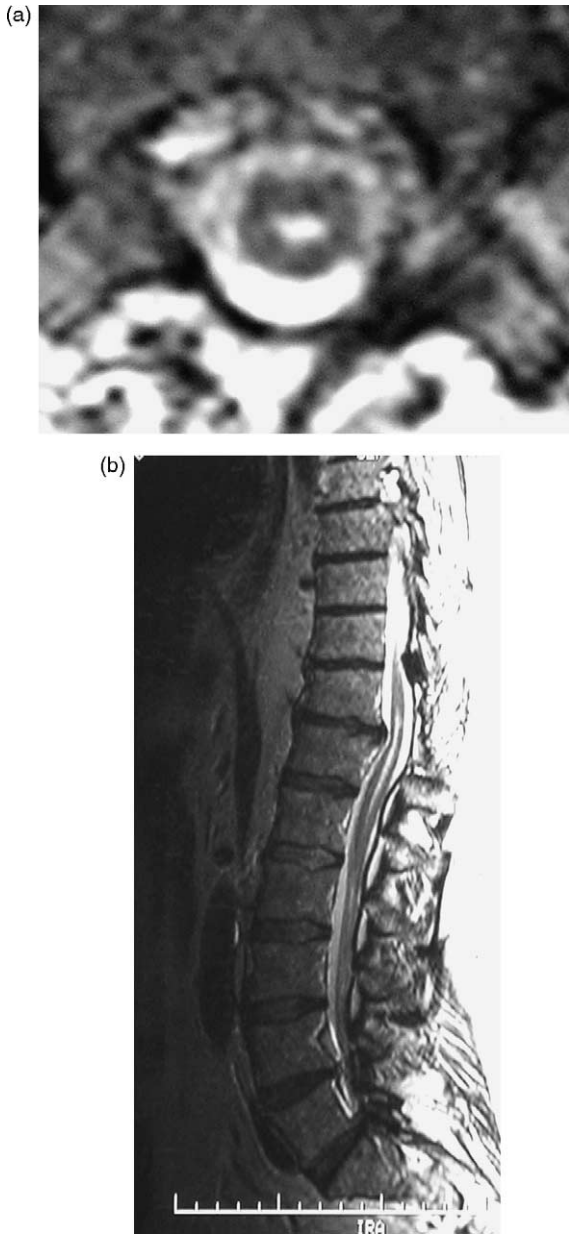

Fig. 3 – Case 2. T2-weighted axial (a) and sagittal (b) MRI scans of the spinal cord showing a syringomielic cavity between D11 and L1 concurrently with an intervertebral diskal hernia between D11 and D12.

and multiple tubers in the left frontal and parietal cortex and in the gyrus cinguli, thus confirming the diagnosis of tuberous sclerosis complex. At the age of 18, bilateral renal angiomiolypomatosis was diagnosed; later on, due to left hydronephrosis, the patient underwent left nephrectomy.

At 32 years, a spinal MRI, performed because of lumbar ache, showed an intervertebral diskal hernia between D11–D12 and below a syringomielic cavity between D11 and L1 (Fig. 3a and b). The evoked motor potentials at the lower limbs disclosed an impairment of the central motor pathways. Presently, mental level is within normal limits.

4. Discussion

In the present report, the combination of TSC and cervical or dorsal–lumbar spinal hydrosyringomielic cavity is, to our knowledge, described for the first time in two patients.

Syringomiely is defined as a tubular cavitation within the spinal cord. To date, it is suggested to refer to all intraspinal cavities of non-tumoral nature as hydrosyringomielia,[5] including hydromyelia which is a dilatation of the cord central canal lined with ependyma, and syringomielic cavity that is lined by glial cells.

Hydrosyringomielia is hardly related with TSC that generally seems to spare the spinal cord both in humans and in animal models for tuberous sclerosis such as the Eker rats in which there is a naturally occurring mutation in Tsc2 gene,[6] and in Tsc1 and Tsc2 knockout mice.[7,8]

Furthermore, factors directly linked to syringomiely such as Arnold-Chiari malformation type I and hydrocephalus,[5] or spinal trauma,[9] and postmeningitic spinal arachnoiditis[10] are not present in the clinical history of both our patients.

So far, the only involvement of the spinal cord in TSC is represented by spinal cord metastases of subependimal giant cell astrocytomas.[11] A vertebral body disorder is then possible in TSC in 6–34% of patients,[2,3] and is represented by small, asymptomatic sclerosis of the vertebrae, that only rarely may be expanding and extensive.[3] They generally appear since the age of 20, though in some cases early and severe symptoms as cyphoscoliosis and vertebral conjunction (D10–L2) are reported.[4]

The cohexistence of TSC brain tubers and subependimal nodules and acquired periventricular leukomalacia with dilation of both lateral ventricules, strictly linked to premature birth, is noteworthy in patient 1. The latter might have somewhat hidden the typical TSC signs for a considerable period, making the correct diagnosis difficult.

In the same patient, clinical signs such as bilateral pes cavus, mild muscle hypotrophy in the distal lower limbs, slight scoliosis and absence of homolateral abdominal reflexes are directly linked to the syringomielic cavity.

In patient 2, symptoms due to the hernial compression and vertebral pathology are predominant, while syringomiely seems to be substantially asymptomatic, just like it is in many cases.[12]

The small extent of the spinal cavity in our patients may explain the absence of significant motor or sensitive deficits. Indeed, neuropshysiological data showed only mild signs of chronic denervation, with loss of motor units in upper or lower limbs, respectively. Accordingly, motor deficits of the upper limbs were absent in about 40% of patients with syringomielic syndrome and weakness or atrophy in any of the four extremities was lacking in 22% of patients as well. Therefore, clinical features are variable with many atypical clinical manifestations.[12]

To the best of our knowledge, this is the first report of the co-occurrence of syringomielia and TSC. The possible pathogenesis of this phenomenon remains unclear, and we cannot exclude the chance of an incidental association. Nevertheless, when suggested by clinical findings, we recommend to consider the possibility of spinal abnormalities.

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