Co-morbid Guillain-Barré syndrome and acute disseminated encephalomyelitis

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ABSTRACT

متلازمة جولين باريه والالتهاب الحاد المتعدد بالدماغ والحبل الشوكى هما مرضين مختلفين يصيبان المادة البيضاء في الدماغ ولكن يشتركان فى السبب المناعي الذاتي والحدوث بعد التهاب فيروسى أو تطعيم. ويعتبر حدوث هذان المرضان سوياً نادراً ولم يتم وصفه إلا في حالات قليلة جداً. ونقدم في هذا التقرير حالة طفلة تبلغ من العمر عشرة أعوام أصيبت بشلل رباعي حاد مع انعدام في الإستجابة العصبية للعضلات واحتباس بالبول. وقد بينت عينة السائل الدماغي ارتفاع متعدد فى عدد الخلايا ونسبة البروتين. وقد احتاجت إلى وضعها على جهازالتنفس الصناعى ولم تتحسن حالتها رغم اعطائها علاج مضادات المناعة عن طريق الوريد بل تطورت حالتها لاحقاً لتصاب بروئية بصرية مزدوجة وقلة بالوعى. وقد بينت أشعة الرنين المغناطيسى للدماغ تغيرات متعددة بالمادة البيضاء دلت على وجود التهاب حاد متعدد بالدماغ والحبل الشوكى. وبناءً على تطور ووصف الحالة والتأكد من التشخيص فقد تم تشخيصها بمتلازمة جولين باريه مع التهاب حاد متعدد بالدماغ والحبل الشوكى. وقد تحسنت الحالة بعد اعطاء علاج الميثيل بريدنيسولون عن طريق الوريد. لذا نستنتج أن حدوث متلازمة جولين باريه مع الالتهاب الحاد المتعدد بالدماغ والحبل الشوكى هي حالة نادرة وشديدة من المهم تشخيصها لتقديم العلاج المناسب بسرعة ومن ثم تحسن الحالة وشفائها.

Guillain-Barré syndrome (GBS) and acute disseminated encephalomyelitis (ADEM) are clinically distinct demyelinating disorders that share an autoimmune pathogenesis and prior history of viral infection or vaccination. Concurrent GBS and ADEM are uncommon with few reported cases. Our patient is a 10-year-old girl who presented with acute quadriparesis, areflexia, and urinary retention. Lumber puncture revealed mild pleocytosis and elevated protein. She required mechanical ventilation and failed to improve after intravenous immunoglobulins. She subsequently developed double vision and disturbed level of consciousness. Brain MRI revealed multiple white matter lesions suggestive of ADEM. Based on the temporal association and exclusion of alternative etiologies, we made a diagnosis of GBS and ADEM. She improved remarkably after intravenous methylprednisolone. We conclude that co-morbid GBS and ADEM is an uncommon entity presenting with severe neurological morbidity. Prompt recognition and treatment can hasten the recovery and therefore improve the neurological outcome.

Neurosciences 2013; Vol. 18 (2): 166-168

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Received 13th September 2012. Accepted 3rd January 2013.

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Guillain-Barré syndrome (GBS) and acute disseminated encephalomyelitis (ADEM) are acute post-infectious, inflammatory, demyelinating neurological disorders.[1,2] Guillain-Barré syndrome affects the peripheral nervous system, while ADEM affects the CNS. Molecular mimicry and cross-reactive immune response is considered to play a crucial part in the pathogenesis of GBS.[1,2] The ADEM pathogenesis is thought to be a result of a T cell mediated autoimmune response to myelin basic protein, which is triggered by an infection or vaccination. Although GBS and ADEM are clinically distinct, they share several features including an autoimmune pathogenesis, myelin injury, and prior history of viral infections or vaccination. However, concurrent GBS and ADEM affecting both the peripheral and CNS simultaneously is an uncommon situation, and only few cases have been reported.[3-5] Our

Disclosure. The authors declare no conflicting interests, support or funding from any drug company.

objective is to present a 10-year-old girl who presented with features of GBS associated with later development of ADEM. The few reported cases and related pediatric literature will be reviewed.

Case Report. A previously healthy 10-year-old girl presented to the emergency room of King Abdulaziz University Hospital in Jeddah, Saudi Arabia, with a 2-day history of generalized weakness, low-grade fever, and urinary retention. Ten days earlier, she had a mild upper respiratory tract infection (URTI). Her medical, family, and social histories were unremarkable. On examination, her vital signs were stable and she was conscious with no meningeal signs. Neurologically, she had severe quadriparesis that was worse in the lower limbs with inability to sit or stand. Her reflexes were absent with negative Babinski. No sensory abnormalities were noted. Her pupils were equal and reactive to light. Her urinary bladder was palpable, and the remaining systems were unremarkable. Initial investigations included a normal complete blood count, liver, and renal profiles. Her erythrocyte sedimentation rate was 50 mm/hr and C-reactive protein was 5.3 mg/L. She was started on broad-spectrum antibiotics and Acyclovir (Teva Pharmaceutical, USA). Initial non-contrast brain CT scan was normal. Lumber puncture (LP) revealed mild pleocytosis (14 cells/cubic mm), mainly lymphocytes, with elevated protein and negative gram stain. The next day her weakness worsened quickly with respiratory distress and double vision. On examination, she was confused with nystagmus and generalized paralysis. She was placed on mechanical ventilation and started on intravenous immunoglobulins IVIG (Biotest Pharmaceuticals, New York, NY, USA) of a total dose of 2 gram/kg. On follow up examination, she was noted to have facial diplegia, bulbar palsy, and features of right-sided sixth nerve palsy with normal fundal examination. Over the next few days, she remained confused and her weakness showed no significant improvement. Brain and spinal MRI showed multiple white matter lesions with high signal intensity involving the brain and brainstem, suggestive of ADEM (**Figures 1 & 2**). Viral studies came back negative including human immunodeficiency viral testing. Repeated LP was attempted and failed. Intravenous methylprednisolone (Sandoz, Annapolis, MD, USA) was started on day 6 of admission at a dose of 15 mg/kg/day for 3 consecutive days. She improved rather quickly and was extubated within the next week. She was shifted to the pediatric ward 3 weeks after initial presentation with slowly improving muscle power. She received extensive physiotherapy and was discharged home ambulating after spending a total of 5 weeks in hospital.

Discussion. We present an unusual case with GBS and subsequent features of ADEM. The presenting history was classic for GBS with preceding URTI and severe lower motor neuron weakness that progressed to involve the respiratory and bulbar muscles. Guillain-Barré syndrome is an acute demyelinating polyradiculoneuropathy that is characterized by progressive ascending muscle weakness and areflexia. Immune-mediated mechanisms due to molecular mimicry are considered to be responsible for the pathogenesis of GBS. Our patient failed to improve

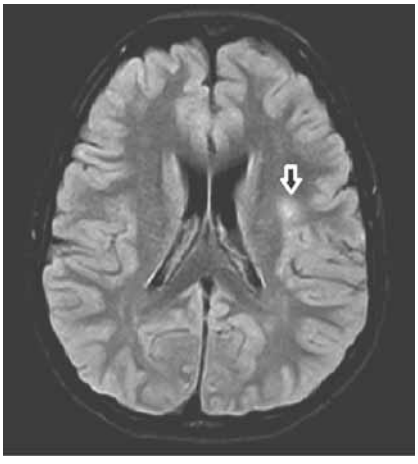

Figure 1 - Brain MRI showing a white matter lesion with high signal intensity on T2 Flair.

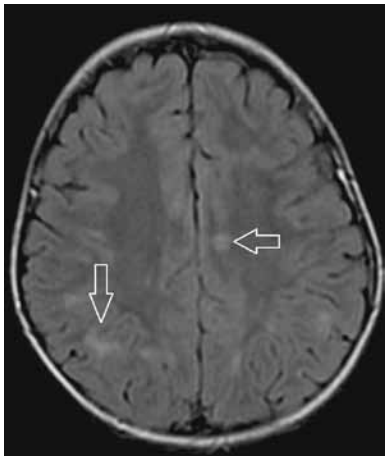

Figure 2 - Another MRI cut showing multiple white matter lesions with high signal intensity suggestive of acute disseminated encephalomyelitis.

on IVIG and subsequently developed disturbed level of consciousness and double vision suggesting an encephalitic picture. The findings on LP and MRI were suggestive of ADEM. Acute disseminated encephalomyelitis (ADEM) is a monophasic syndrome occurring in the context of an infection, immunization, or vaccination. It typically follows a prodromal phase of 1-4 weeks followed by the development of multiple white matter lesions in the brain, brainstem, and or spinal cord. Acute urinary retention is common in ADEM as seen in our patient. Successful use of high-dose steroids has been widely reported to provide marked improvement of the symptoms, which was also the case in our patient.[6] Acute disseminated encephalomyelitis usually has a favorable long term neurological outcome; however, recent literature suggests that a significant proportion of patients with ADEM will later develop multiple sclerosis. Follow up experience from developing countries does not support this view, and therefore further long term research is necessary to better describe this entity and its prognosis.

Simultaneous GBS and ADEM have been rarely reported in the pediatric literature. Patients may start by manifesting GBS, with brain MRI showing features of ADEM, while others may start with features of ADEM and then develop GBS during their hospitalization. Occasionally, patients may demonstrate transverse myelitis that evolves into GBS and associated with demyelination on brain MRI.[7] Combined ADEM and acute motor axonal neuropathy has been rarely reported.[8] The response of these cases to high dose IVIG and steroid treatment has been variable. In our patient, no clinical response was noted after IVIG therapy and rapid improvement of the neurological symptoms was only noted after pulse steroids. It is possible that the response is the result of the cumulative effects of both treatments as they were given in sequence.

The pathogenesis of both GBS and ADEM is thought to be due to autoimmunity to myelin protein antigens; however, several authors proposed that they may represent a continuous clinical spectrum resulting from an antibody-mediated post-infectious syndrome.[9] This concept suggests a single autoimmune disease involving both the peripheral and CNS. Based on this hypothesis, the simultaneous occurrence of GBS and ADEM suggests that the responsible pathogen share an antigen of both peripheral and central myelin. Others authors suggested that the immune response against a component of the myelin of the CNS may carry cross-antigenicity with the peripheral system. A significant increase in activated and helper inducer T-cells was observed in both GBS and ADEM suggesting a common pathogenic mechanism. This combined clinical entity represents a generic acute immunological nervous disease with various clinical presentations.

We conclude that co-morbid GBS and ADEM is an uncommon entity generally presenting with severe neurological morbidity; however, prompt recognition and treatment can significantly hasten the recovery and therefore may improve the neurological outcome. Further research of this unusual association and its pathogenesis is necessary to help understand its clinical course and prognosis.

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