A Case of Pediatric Neuromyelitis Optica Spectrum Disorder (First Case Reported in Kingdom of Bahrain)

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Neuromyelitis optica spectrum disorder (NMOSD) is a rare inflammatory disorder of the central nervous system that usually occurs in adult females. The disease usually presents with inflammation of the optic nerve with or without spinal cord involvement, but extra CNS manifestations are well documented.

As more and more new cases are reported in the pediatric, we present this teenage girl that though her presentation was atypical, the diagnosis of NMSOD was confirmed in view of the radiological and laboratory findings. She sustained initial phase and a relapse and was managed later by immune modulating agents and she showed a remarkable response.

Here we present this case as the first reported case of NMOSD in the pediatric population in Kingdom of Bahrain and we address some differences between adult and pediatric presentation of the disease.

CASE

A 12-years-old Bahraini female not known case of any medical illness presented to the emergency department in Salmaniya medical complex with hypoactivity, back rash and abdominal tenderness. The patient was in her usual state of health till 2 weeks prior to presentation when she developed subjective fever one day after going to a public swimming pool. The patient went to private clinic where she was diagnosed to have a urinary tract infection and was prescribed Augmentin. The condition didn't improve, and she developed increased fatigability, reduced feeding, vomiting and abdominal pain over the next 2 weeks with eruption of extensive skin lesion with itching and vesicles over the back of the neck. On arrival to Salmaniya medical complex she was lethargic with hypotension and bradycardia. She was noted to have a vesicular rash with golden crusty lesions, erythematous base, irregular edges on the distribution of left C1 to C7 dermatomes and the left corner of the mouth. There was also a palpable left posterior auricular lymph node around 2 X 2 cm. On further examination mild generalized abdominal tenderness was noted. Otherwise, rest of clinical examination was unremarkable. The patient was stabilized with multiple normal saline boluses and was started on ceftriaxone. Collections were done and showed normal CBC, LFT, ESR and urine Routine, while U/E revealed hyponatremia with Na of 127. Urine Culture was collected which later was found to be growing pan sensitive E. coli.

The patient was seen by dermatology and was given impression of herpetic zoster infection, Steven Johnson syndrome and possibility of vasculitis. The patient was seen by rheumatology team who requested Anti microsomal antibodies, ANA titer, CRP, VDRL, Anti U1RNP, anticardiolipin antibodies, C3, C4 and all came to be normal. Viral study including EBV and CMV were done and showed past infection while it was Equivocal for HSV1, so she was managed with acyclovir. Few days later the patient developed blurring of vision, with color desaturation mainly over the left eye. There was no diplopia, no headache, no gait problems, no other complains, but there was some nonspecific altered behavior from the base line.

Ophthalmic assessment was done and fundoscopy revealed bilateral blurring of disc margins mainly on the left, so neurology team were consulted. On neurology review the examination revealed a fully conscious, alert and oriented girl, with full extraocular movements, Pupils were equal, round, and reactive to light. There was no facial asymmetry, there was no pronator drift, no ataxia, but there was spastic catch in the right lower limb, non-sustained clonus in the left feet and brisk deep tendon reflexes in all extremities. Romberg sign was negative.

MRI brain was requested and showed symmetrical high T2 and FLAIR intensities in the periventricular white matter adjacent to the third ventricle, medial thalami and the mammillary bodies. Patchy high FLAIR signal intensities in the optic tracts, chiasma and nerves. Faint FLAIR high signal intensities in the white matter adjacent to the aqueduct of sylvius and around the central canal in the craniocervical junction with no restriction of diffusion or enhancement (Figure 1). Also patches of high T2 signal intensities with enhancement were seen in the cervical spinal

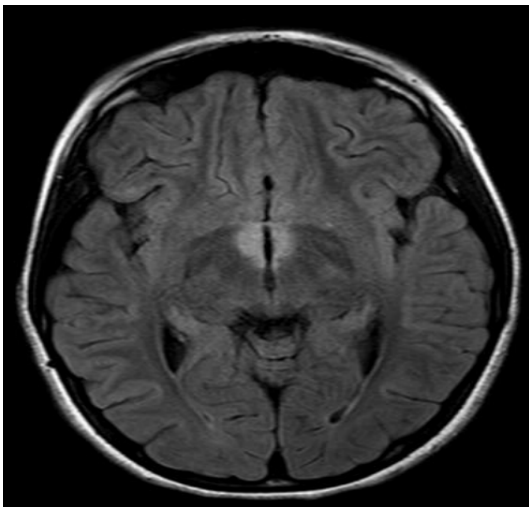

Figure 1: First presentation MRI brain showing FLAIR signal intensities in the periventricular white matter adjacent to the third ventricle, medial thalami and the mammillary bodies

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cord, mostly involving the posterior aspect of the cord opposite C2, C3, C6 and C7 vertebral bodies with cord swelling (Figure 2).

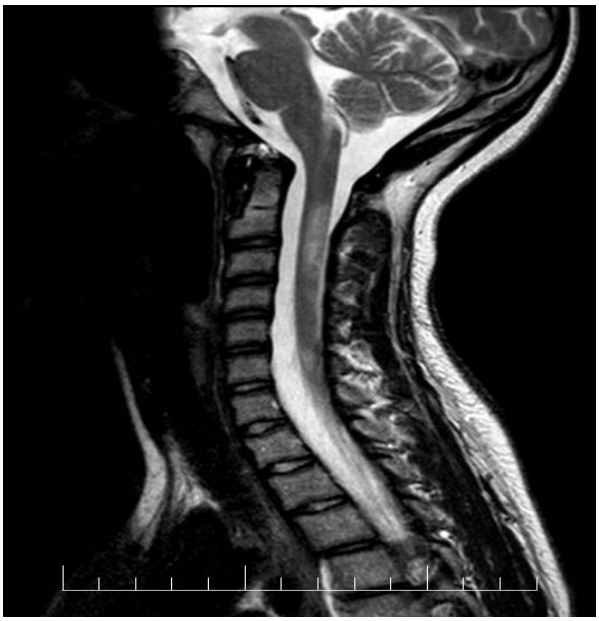

Figure 2: First presentation Spine MRI showing patches of high T2 signal intensities with enhancement involving the posterior aspect of the cord opposite C2, C3, C6 and C7 vertebral bodies with cord swelling

In the view of the clinical and radiological findings an impression of neuromyelitis optica was kept with ADEM, and Wernick's encephalopathy as a less likely differential. Lumbar puncture was done and sent for cell count, chemistry, AQP4 antibodies, viral PCR. The results showed CSF leukocytosis with lymphocyte predominance, normal biochemistry and negative culture. Serology came to be negative for oligoclonal bands and positive for AQP4 while viral PCR was negative. The patient was started on Pulse methylprednisolone for 5 days and was kept on Thiamine.

Meanwhile the vision improved, and she was able to appreciate colors and read sentences. Her behavior was back to normal according to relatives and even the herpetic rash in the back resolved. Ceftriaxone and acyclovir were continued for 14 days total and the patient was discharged on tapering prednisolone over 6 weeks and a follow up in neurology clinic.

3 months later patient presented to accident and emergency with acute visual loss in the left eye as she was unable to even perceive light, there was associated pain on moving the left eye too. There were no other associated complaints, no weakness, no numbness. On examination the patient was conscious, alert, oriented with no apparent restriction of extraocular movements despite complaining of pain on moving the globe. There was no other cranial nerves involvement. Power, tone and reflexes were all normal in both upper and lower limbs.

The patient was admitted, and emergency MRI brain was done which revealed optic neuritis with high T2 and FLAIR signal intensities in left optic nerve involving the posterior part of the intraorbital and intracanalicular part of the nerve. It was highly swollen with heterogenous high T2 signal intensity and mild enhancement following administration of intravenous contrast medium. Almost complete resolution of the previous high T2 signal intensities in the thalamic floor and periventricular white matter around the 3rd ventricle (Figure 3).

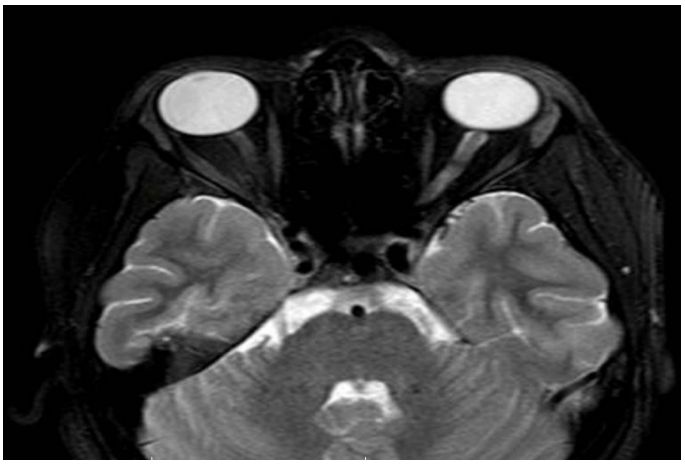

Figure 3: Second presentation orbit MRI showing swollen left optic nerve with high heterogenous T2 signal intensities involving the intraorbital and intracanalicular part of the nerve

In the view of the clinical and radiological picture patient was started on pulse methylprednisolone for 5 days followed by tapering prednisolone. The patient showed improvement as she was able to recognize faces but still unable to read, so a central venous line was inserted, and 5 sessions of plasmapheresis were done over 10 days extracting 50 ml/kg in each session. By the end of the course her vision improved much, and she was able to recognize large letters and had some color perception. The patient was discharged with a follow up elective admission in 2 weeks for Rituximab infusion as per protocol in which Rituximab 1 gram infusion was given in 500 ml Normal saline at a rate of 50 mg/hour and was increased every 30 minutes by 50 mg/hour till maximum 400 mg/hour. The patient had another session of rituximab infusion 10 months later.

The patient had another MRI done after receiving the second rituximab infusion that showed complete resolution of the left optic nerve involvement and significant reduction in the high T2 and FLAIR signal intensities in the periventricular white matter. The patient's vision showed remarkable improvement by that time and was fully recovered by the end of the year. There were no significant neurological sequelae except for some mild numbness in the right foot. By that time patient reached 14 years of age so she was referred for adult neurology for further follow up.

CONCLUSION

NMOSD is a spectrum of inflammatory diseases of central nervous system that usually occurs in the third decade of life with a female to male ratio of 10:1. But more cases are reported to occur in the pediatric population with variable presentation which necessitate further revision of the diagnostic criteria and management to meet the findings and response in the pediatric age group.

The disease incidence in pediatric population is unknown but, in some studies, it was estimated to be 0.03/100.000[1], It usually presents in a relapsing pattern with bilateral or unilateral optic neuritis with or without long segment (>3 segments) transverse myelitis. The presented case showed the typical optic and cord involvement mentioned in the literature. Also, other extra CNS systemic autoimmune manifestations like hypotension and bradycardia can be the initial presentation which is the case in our patient with neurological findings evolving later in the course of the disease.

The disease is presumed to be sporadic though that familial cases were reported among adult population. NMOSD was found to be associated with other autoimmune diseases such as SLE, Ulcerative colitis and myasthenia gravis. Our patient was screened for autoimmune disorders but was unremarkable. NMOSD was also found to be as a part of paraneoplastic presentation.

Our patient was diagnosed by finding the disease specific antibodies anti AQP4. The antibodies are targeted against AQP 4 water channel proteins. Such protein is present in the astrocytic foot processes in the blood brain barrier, thus it is mainly found in the periaqueductal and periventricular regions. Some recent studies showed increased incidence of AQP 4 negative variants in pediatric cases and thus recommend testing for Anti MOG antibodies as a more sensitive alternative[2].

Abortive treatment of the relapses includes Intravenous immunoglobulin, pulse methylprednisolone and plasmapharesis. While long term maintenance management includes steroids, other steroid sparing immunosuppressive treatment including Azathioprine, Mycophenolate mofetil, Cyclophosphamide and rituximab. Rituximab was showing promising results but monitoring B-Cell count was essential in predictability of future relapse[3]. Our patient showed a significant response, but whether her being a pediatric has a role in the response is debatable. In adults the outcome depends on the aggressiveness of the relapse management as that disabilities arise from the acute attacks with estimated 50% ending up in paralysis or blindness within first five years of the onset of the disease. However, outcome in pediatric age of group was favorable compared to adults, but further follow up of such patients are needed[2].

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REFERENCES

1. Lechner C, Rostàsy K, Baumann M, et al. Neuromyelitis Optica Spectrum Disorders in Pediatric Patients. Neuropediatrics 2017;48(1):17.
2. Dahan A, Brilot F, Leventer R, et al. Neuromyelitis Optica Spectrum Disorder and Anti-Aquaporin 4 Channel Immunoglobulin in an Australian Pediatric Demyelination Cohort. J Child Neurol 2020; 35(4):291-6.
3. Nosadini M, Alper G, Riney CJ, et al. Rituximab monitoring and redosing in pediatric neuromyelitis optica spectrum disorder. Neurol Neuroimmunol Neuroinflamm 2016;3(1): e188.