



**Date:** October 12, 2024

**Re:** Seela Khalid Mohamed Attya

**DOB:** 14-10-2012

Seela Khalid is a 12-year-old girl, the second in birth order of first cousin marriage diagnosed as **biotinidase deficiency**. I had the pleasure to first meet her On April 11, 2023, after her discharge from the PICU. According to parents' reports, her condition started on August 2022 with abnormal gait that progressively worsened over time. She did MRI brain in October 2022 that showed patchy signal alteration (demyelination), cervical MRI showed diffuse signal alteration (demyelination) while lumbosacral MRI was normal. VEP showed neuromyelitis optica (please see the attached reports)

She was referred to the neurology department, Ain Shams University hospital where she received pulse steroids and IVIG followed by plasmapheresis with no response. In November 2022, the diagnosis of HLH was suggested and she received two doses of rituximab. She was discharged from PICU on December 14, 2022. A third dose of rituximab and IVIG was given on December 26, 2022.

Sample for WES was taken on December and result was received on January 2023 with no clinically relevant pathogenic variant and a potentially relevant finding of a homozygous missense VUS variant in *BTD* gene (c.520A>G, p. Asn174Asp). I was consulted about the WES result without seeing the patient and advised to do biotinidase enzyme assay which was significantly low (patient's level was 0.3 nmol/ml/min , reference range 5.3-12.2). Please see the attached reports.

She was prescribed biotin capsules that gradually increased from 20 mg/day to 100 mg/day.

I had the pleasure of seeing her after 3 months of diagnosis. She was cachectic, had rough scanty hair, very weak upper and lower limbs, hypotonia , increased deep reflexes and decreased sensation of lower limbs till the mid knee level. She was incontinent to urine and stools, but she regained her vision. She was advised to do physiotherapy and nutritional rehabilitation and to continue biotin.

In her second vision in June, 2023, she showed improvement regarding sensation, as she started to feel touch sensation of her arms and feet, feels urine when it touches her skin. Her sensation was lost only on the lower thirds of both feet but her tone started to increase as well as some limitation of movements of ankles and hips. She was able to sit with support for few minutes. A trial of intramuscular biotin started with no better response and therefore the same dose of 100 mg oral biotin was maintained with stress on the need of regular physiotherapy.

(DOB: Oct 14, 2012)



In October 2023, she showed improvement regarding sitting from supine position, feeling of pain in lower abdomen, and some control of urine excretion. But she was depressed with refusal to eat. Her lower limbs started to be spastic and started to have scoliosis. She developed also bed sores.

Baclofen was then started with small doses that increased gradually; Biotin was still on 100 mg/day. She was referred to back braces for scoliosis. Care of bed sores was advised in addition to nutritional therapy and increase time out of house.

MRI was repeated in January 2024 and it showed improvement regarding the brain stem, there was just barely faint signal alteration at periaqueductal region and just anterior to it. MRI spinal cord showed improvement of the cervical cord swelling and of the high signal alteration at the cervical cord with noted linear path along the lower aspect of the medulla and upper most cervical cord with normal other parts of the cord (please see attached report)

VEP was done that showed improvement as conduction showed moderate delay that was severe before. (please see attached reports)

On her visit in January 2024, she started to feel more deep touch and was able to control/maintain her leg position for 30 seconds. She regained strength of her upper limb and she was able to sit for long time but her lower limbs still showed spasticity in spite of continuous physiotherapy. Bed sores was more severe and so she was referred to pediatric surgery. Biotin dose was increased to 200 mg/day and then 300 mg/day. Baclofen dose was also increased and sirdaloud was added .

On May 2024, she started to better feel touch and pressure in her toes, soles , she was able to stand with maximum support with braces , her scoliosis improved .

On her recent visit, October 2024, she was able to sit for long time, maintain position of her lower limbs for longer periods, she was able to stand supported for long time, she was able to sit from supine position without help, she was able to raise her back in the supine position, she felt pain and touch in soles and toes. Her upper limbs showed no weakness and was able to support her trunk on extended arms. She still has spasticity of both lower limbs and her scoliosis significantly improved. Bed sores completely healed. DEXA scan was done and it showed osteoporosis and scheduled for bisphosphonate therapy next week.

Please feel free to contact me with any questions

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