Case report
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Not All Hemiplegia is Stroke: a case report of a five-year-old girl with Familial Hemiplegic Migraine and an unusual clinical course

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Familial hemiplegic migraine (FHM) is a rare, inherited subtype of migraine with aura, classified among the “channelopathies” due to mutations affecting ion channels. Diagnosis typically combines clinical criteria with imaging studies, particularly MRI. We present a case of a 5-year-old girl who arrived at our clinic with sudden right-sided weakness and tingling, initially raising suspicion of a stroke. Laboratory tests, including lumbar puncture, were unremarkable, and empirical treatment with antibiotics and corticosteroids showed no effect. On the sixth day, her mother experienced similar symptoms and revealed a history of identical episodes in herself and milder ones in the patient’s younger sister. A joint evaluation by pediatric and adult neurologists raised suspicion of a familial disorder. Genetic testing confirmed a CACNA1A mutation in both mother and daughter, consistent with FHM. The

patient began treatment with acetazolamide and was followed by a neurologist and physiotherapist. She has remained symptom-free for several years.

Keywords: treatment, MRI, rare diseases, differential diagnosis, headache

Prikaz slučaja

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Nije svaka hemiplegija moždani udar: prikaz slučaja petogodišnje devojčice sa porodičnom hemiplegičnom migrenom i neobičnim kliničkim tokom

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Familijarna hemiplegična migrena (FHM) je retka, nasledna forma migrene sa aurom, koja spada u grupu „kanalopatija“, zbog mutacija koje utiču na jonske kanale. Dijagnoza se postavlja na osnovu kliničkih i radioloških kriterijuma , najčešće magnetna rezonanca (MRI). Prikazaćemo slučaj devojčice uzrasta 5 godina koja je primljena zbog iznenadne slabosti i trnjenja desne strane tela, što je inicijalno ukazivalo na moždani udar. Laboratorijske analize i lumbalna punkcija nisu pokazale abnormalnosti, a lečenje antibioticima i kortikosteroidima nije dalo efekta. Šestog dana hospitalizacije, majka deteta razvija slične simptome i prijavljuje da su slične epizode prisutne i kod nje, ali i kod pacijentkinjine mlađe sestre. Sagledavanjem od strane pedijatra, dečijeg neurologa i adultnog neurologa, shvaćeno je da se radi o verovatnom genetskom poremećaju. Testiranjem potvrđena je mutacija CACNA1A kod majke i ćerke, što

je potvrdilo dijagnozu FHM. Terapija je započeta acetazolamidom. Praćena je od strane neurologa i fizijatra i nije bilo ponavljanih epizoda hemiplegije.

Ključne reči: terapija, MRI, retke bolesti, diferencijalna dijagnoza, glavobolja

Introduction

Familial hemiplegic migraine (FHM) is a spectrum of a rare subtype of migraine with aura, that is inherited in an autosomal dominant fashion with variable penetrance and is closely related to the Proline-rich transmembrane protein 2 (PRRT2) gene. FHM is actually a migraine with a complex aura characterized by motor weakness and at least one symptom that may include speech disturbances, visual or sensory disturbances. These symptoms make it different from migraines with motor aura. This spectrum of disorders is called channelopathies (1, 2). In order to diagnose FHM, a clinician must be aware of and use clinical criteria complementary to imaging tools. MRI is the preferred imaging method, but it is not always readily available. Various treatments for hemiplegic migraine have been tried with variable success and include, but are not limited to verapamil, ketamine, naloxone, corticosteroids, and acetazolamide in case of familial form (2). Here we present a case of FHM in a female child that first presented at our clinic as a stroke-like illness. Most of the data for this case report was provided from the Medical Database System.

Case report

A 5-year-old female child, presented at our Clinic with sudden onset weakness of the right arm and leg. She also complained of feeling tingling in those extremities. The father first noticed the symptoms when the girl avoided using her right arm and had difficulty walking after she woke up. A week before admission the child had a mild respiratory infection with fever up to 38 °C. On examination vital signs were normal: HR 117/min, BP 90/55 mmHg, RR 24/min, SaO2 98%. On neurologic examination: facial asymmetry, left-sided flaccid hemiparesis with 1+ reflex on the left upper extremity, and positive Babinski on the left lower extremity were noted.

Height and weight were at the 40th percentile. She was born at term with no complications during delivery and has been vaccinated by the schedule. No other significant illness was noted, except the information given by the mother about previous hospitalization, 4 years before current admission at the age of 15 months, when the girl presented with sudden onset weakness in extremities. She was treated aggressively with intravenous corticosteroids and immunoglobulins due to suspicion of acute disseminated encephalomyelitis (ADEM) and symptoms resolved after two weeks of hospitalization. Mother had a history of migraines treated by a neurologist. The patient was admitted to the pediatric neurology department of the Pediatric clinic. Her condition soon worsened. She became soporose and developed a high fever, non-responsive to antipyretic treatment. Accordingly, a lumbar puncture was done, followed by broad treatment with empiric antibiotics, mannitol, corticosteroids, and IV rehydration, all of which didn't improve her condition. The cerebrospinal fluid (CSF) came back sterile. MRI was done, which showed T2 hyperintensities subcortically most prominent in the right occipital lobe described initially as ischemic (Figure 1). Symptoms persisted during hospitalization, and her overall condition was stable, followed by gradual spontaneous recovery, but on the 6th day of hospitalization, her mother complained of headache and soon developed right-sided hemiplegia after which she was urgently transferred to the adult neurology department. The mother then revealed that she has similar episodes as her daughter and that the younger child (the patient's sister), also has similar and repeating but milder symptoms, which resolve spontaneously. In the following days, due to suspicion of a genetic cause of the disease and after a consult was done between adult and pediatric neurologists, a presumptive diagnosis of familial hemiplegic migraine was made. Mother and daughter underwent genetic testing that revealed a CACNA1 mutation. The treatment was started with acetazolamide. She was followed by a neurologist and

physiotherapist for a few years with no recurring episodes since.

Discussion

This case report outlines the challenges in diagnosis and treatment of FHM in pediatric patients, where clinical features may often resemble different neurological disorders, such as stroke, transitory ischemic attack (TIA), acute disseminated encephalomyelitis (ADEM), and other rare conditions (CADASIL, HaNDL syndromes, etc.) (3, 4). Genetic background of FHM with repercussion to involved ion channels is shown in Table 1. Clinical features of the FHM spectrum are shown in Table 2. Although well-studied in adults, FHM in children is not well understood by clinicians and as such has many uncertainties regarding the preferred treatment (5). In our case, a sudden motor weakness at first resembled a stroke - a presentation not so common for FHM. Nevertheless, the emerging symptoms of fever and altered state of consciousness required an extensive diagnostic evaluation. The initial treatment plan consisted of corticosteroids and antibiotics and reflected our suspicions of an inflammatory disorder because the clinical course resembled an inflammatory disorder. The absence of inflammatory markers (cerebrospinal fluid analysis was negative for infection), along with lacking response to our treatment, evoke a need for more broad diagnostic evaluation. A positive genetic test result underscored the importance of considering the diagnosis of FHM in all pediatric patients with an initial presentation of neurological deficit. As we searched the literature, we found only a few case reports with abnormal imaging findings in patients with hemiplegic migraine, showing cortical thickening (6), and biphasic neurological changes with alteration of hypoperfusion and hyperperfusion (7). One report mentions regressive diffuse hemispheric cortical enhancement in sporadic hemiplegic migraine (8). Authors of this case report theorize

that cortical contrast enhancement on the T1 sequence can correlate with the severity of migraine attack, and such finding can be predictive of neuronal loss. The finding of hyperintense changes on MRI that our patient had is not a common finding in patients with FHM1. Therefore, we consider this a significant contribution to the literature regarding imaging characteristics of FHM. These T2 changes could result from alterations in cerebral perfusion and neuronal excitability during migraine attacks and may likely be directly related to the duration and severity of the attacks (9). There also remains the possibility that this is an incidental finding, unrelated to FHM. All in all, MRI findings can sometimes correlate with the genetics of FHM (10). Treatment with acetazolamide has proven positive in the control of headache in patients with FHM (5, 11). Our Previous experiences were also the reason why we chose this medication in treating our patient. Further follow-up can give us more information on the efficacy of the chosen therapeutic strategy. For severe cases, literature mentions intranasal Ketamine, which has shown clinical benefit in reducing the severity and duration of neurologic deficits in 5 of 11 patients included in one study. In acute management, methylprednisolone and dexamethasone were used and described in several case reports (12, 13).

Conclusion

This case report illustrates the diagnostic complexity of FHM in pediatric patients and emphasizes the need for increased vigilance and a tailored therapeutic approach when it comes to migraine syndromes in pediatric neurology. Several points were unique to our case presentation. The diagnosis was successfully made by the cooperation of the adult Neurology Clinic and Pediatric Clinic. It was noticeable that using clinical features or MRI alone can be

misleading. Physicians should be mindful of the rare causes of migraines in pediatric patients and include those in their differential when other more common diseases are excluded.

The case was managed and documented at the Pediatric Clinic of the University Clinical Center Niš.

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Migraine Subtype (FHM)	**Gene Name**	**Mutation Type**	**Functional Impact**	**Channel or Pump Affected**
FHM1	*CACNA1A*	GOF*	Increased calcium influx	Cav2.1 calcium channel, α1-subunit
FHM2	*ATP1A2*	LOF*	Reduced ion exchange	Na+/K+ ATPase pump, α2-subunit
FHM3	*SCN1A*	GOF*	Increased sodium influx	Nav1.1 sodium channel, α1-subunit

TABLE 1: Familial hemiplegic migraine common types.
*GOF – gain of function, LOF – loss of function (1, 2).

Criteria for FHM Diagnosis	Criteria for Migraine with Aura
At least two attacks fulfilling criteria for migraine with aura (see right column).	**A**. At least two attacks fulfilling criteria B and C.
Aura consisting of both of the following:	**B**. One or more of the following fully reversible aura symptoms: visual, sensory, speech and/or language, motor, brainstem, or retinal.
- Fully reversible motor weakness*.	**C**. At least three of the following six characteristics:
- Fully reversible visual, sensory, and/or speech or language symptoms*.	- At least one aura symptom spreads gradually over ≥5 minutes.
Not better accounted for by another ICHD-3 diagnosis	- Two or more symptoms occur in succession.
	- Each individual aura symptom lasts 5 to 60 minutes.
	- At least one aura symptom is unilateral.
	- At least one aura symptom is positive†.
	D. Not better accounted for by another ICHD-3 diagnosis.

TABLE 2: International Classification of Headache Disorders, 3rd Edition (ICHD-3).

*Sometimes motor symptoms may be prolonged up to 72 hours but they rarely lead to permanent neurologic deficits; +e.g. scintillations and pins and needles. According to (4).

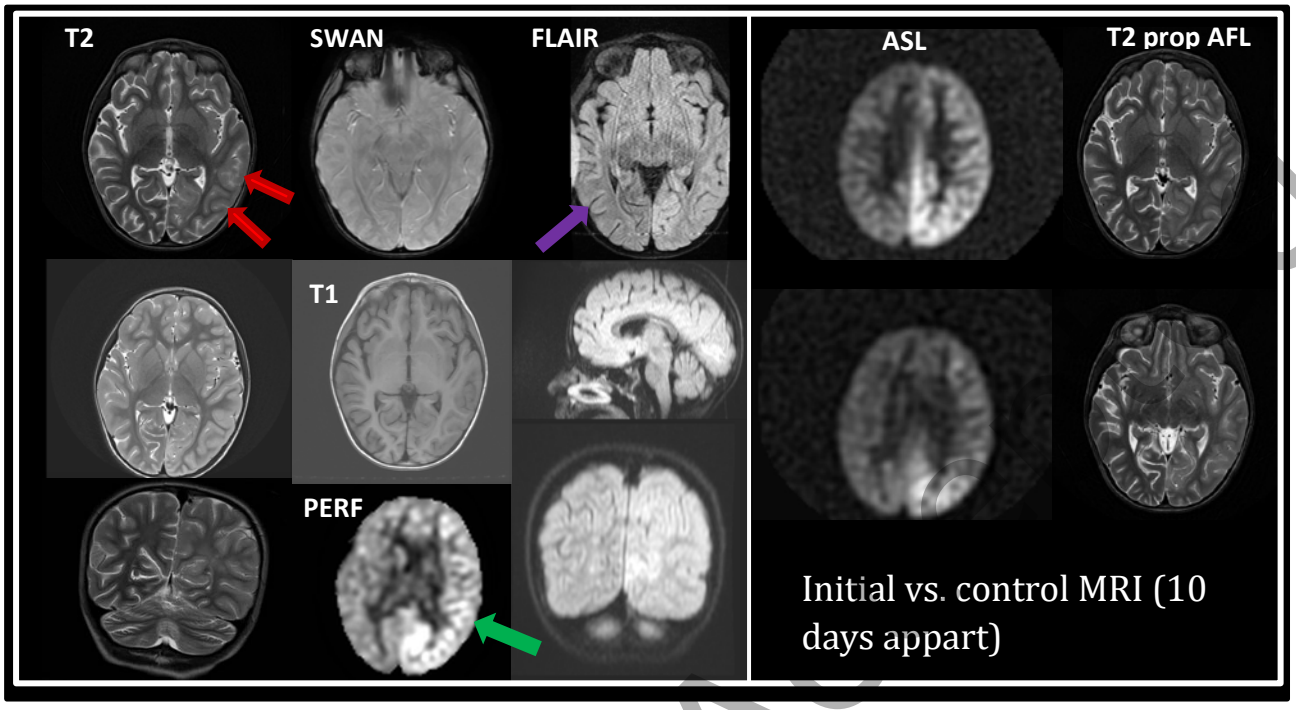

FIGURE 1: MRI of the patient.

Left panel: Initial MRI on admission (various sequences).

Red arrow – Discrete cortical thickening and increased T2 signal intensity in the right cerebral hemisphere.

Purple arrow – T2W/FLAIR hyperintensities in the occipital lobe with corresponding hyperperfusion on ASL (Arterial Spin Labeling) sequence.

Green arrow – T2W/FLAIR hyperintense changes without restricted diffusion (on perfusion sequence).

Right panel: Control MRI performed 10 days later, showing resolution or progression of findings across the same sequences (ASL/perfusion and T2 Prop AFL).