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ORIGINAL ARTICLE

Subacute sclerosing panencephalitis – changes in phenotype during the last decade

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Summary

Introduction: Subacute sclerosing panencephalitis (SSPE) is a rare, progressive, neurodegenerative disease with poor outcome. Anti-measles vaccination contributed to a decreasing number of SSPE patients, but not to its eradication. The aim of our study is to evaluate the course of the disease in our SSPE patients with a focus on vaccinated children. The main goal is considering possibilities for improving prevention of the disease.

Methods: A retrospective study included the patients with SSPE treated in the period from December 2010 to December 2020 at the Pediatric Clinic of the Institute. The inclusion criteria were the patients with the diagnosis of SSPE based on clinical presentation, neuroimaging, electroencephalography and positive IgG anti-measles antibodies, both in serum and CSF.

Results: Five children with fulminant course of SSPE were included. All these patients were suffering from measles at an early age. Three of them had been vaccinated against measles and two had not. All of them had previously been healthy, immune-competent children, with normal general development. The course was extremely fulminant with lethal outcome within three months since the initial symptoms in four cases. Progressive motor and cognitive decline, behavior changes, movement disorders, myoclonic jerks and seizures were dominant in clinical presentation.

Conclusion: Despite vaccination, SSPE has not been eradicated. An increasing number of vaccinated immune-competent children with fulminant form of SSPE and history of measles infection at an early age were treated at our Clinic. As a measure for improving prevention, we suggest considering weaning of vaccine-derived immunity, and re-vaccination of girls at reproductive period.

Keywords: fulminant SSPE, vaccination, measles, children

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INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a rare, progressive, neurodegenerative disease caused by a persistent defective measles viral infection. The incidence of SSPE is inversely related to Measles-Mumps-Rubella (MMR) vaccination coverage. It is endemic throughout the world, mainly in the countries where effective vaccination programs have not been completely realized (1,2). Pathogenesis of the disease is very complex. Numerous mutations in the M gene have been noted in the brain tissues of SSPE patients. Defects in the M protein result in the failure to form the virus particle facilitating the persistence of measles virus in neuronal cells and initiate inflammatory response that leads to extensive tissue damage. SSPE usually occurs 5-10 years after the measles virus infection, in otherwise healthy immune-competent children. The disease usually develops within 1-2 years, while about 10% of cases have fulminant form of SSPE with developing symptoms and signs within 3 months (3-5). Typical clinical presentation includes progressive motor and cognitive decline, behavior changes, myoclonic jerks and seizures. With disease progression, myoclonic jerks increase in frequency, followed by motor and cognitive deterioration. Brain magnetic resonance (MR) shows nonspecific periventricular white matter signal abnormalities, but at early stages of the disease there are no abnormalities in neuroimaging. Definitive diagnosis is based on the Dyken's criteria, which include two major and four minor criteria. Major criteria are as follows: 1) increased anti-measles antibody titers in cerebrospinal fluid (CSF) greater than or equal to 1:4 or ratio greater than or equal to 1:256 in serum, and 2) typical or atypical clinical presentation. Minor criteria include: 1) characteristic electroencepahlograhic (EEG) findings that include periodic, generalized, bilaterally synchronous and symmetrical high-amplitude slow waves that recur at regular intervals of 5–15 seconds called periodic slow-wave complexes also known as "Radermecker" complexes, 2) CSF globulin levels greater than 20% of the total CSF protein, 3) characteristic histopathological findings on brain biopsy and 4) specialized molecular diagnostic test to identify wild-type measles virus mutated genome. There is no specific treatment for SSPE, although oral Isoprinosine combined with intravenous infusion of Ribavirin and Intrathecal /intraventricular interferon-alpha has been recommended. Prognosis is poor with lethal outcome in 95% of the patients (2).

It was believed that prevention of SSPE by measles vaccination was crucial for eradicating this devastating disease (5-7). The annual incidence of SSPE in both adults and children after measles infection declined from 1 per 100,000 in the pre-immunization era to 0.06 per 100,000, after the introduction of immunization against measles (8). The aim of our study is to evaluate the course of disease in SSPE patients treated at our clinic during the past ten years with a focus on regularly vaccinated children against measles infection who were suffering from SSPE. The main goal is to consider possibilities for improving the prevention of the disease.

MATERIAL AND METHODS

A retrospective study included the patients with SSPE treated in the period from December 2010 to December 2020 at the Pediatric Clinic of the Institute for Mother and Child Healthcare of Serbia „Dr Vukan ČupiĆ", Belgrade. The inclusion criteria were patients with the diagnosis of SSPE based on clinical presentation, neuroimaging, EEG and positive IgG anti-measles antibodies, both in serum and CSF. All cases had clinical, neurological, neuroradiologic, EEG, microbiological and serological evaluation. In all the cases, serum and CSF were analyzed by Polymerase Chain Reaction (PCR) for Herpes simplex virus (HSV), Varicella zoster virus (VZV), Epstein Barr virus (EBV), Human Immunodeficiency virus (HIV), West Nile virus (WNV) and Mycoplasma pneumoniae. Enzyme-linked immunosorbent assay (ELISA) test was used for anti-measles antibodies in serum and CSF. Concentration of immunoglobulin in serum and oligoclonal bands in CSF were evaluated. Medical charts were used for measles infection and vaccination status evaluation. The treatment included antiepileptic drugs, oral/parenteral corticosteroids, intravenous immunoglobulin, Isoprinosine, Ribavirin and interferon-alpha.

RESULTS

Five children with SSPE were treated at our Clinic during the past ten years, and all of them had a fulminant course of the disease. Four patients had measles during their childhood, and in one case (patient number 4) it is not clear whether the patient had measles infection or not, but since anti-measles IgG antibodies have been detected, it is supposed that the patient has had a subclinical form of measles. Two patients were not vaccinated, while three were vaccinated according to the regular schedule. The onset of SSPE varied and in two cases it was before the age of three. All the patients were previously healthy, immune-competent children, with normal general development. Progressive motor and cognitive decline, behavior changes, movement disorders, myoclonic jerks and different types of seizures were observed in clinical presentation of all patients. Two patients experienced *epilepsia partialis continua*, and one child had opsoclonus. In all patients, routine hematological, biochemical and acid-base profile, including renal function tests, liver enzymes, lactic acid, ammonia and creatine-kinase, and the concentration of immunoglobulin in blood were normal, so neurometabolic encephalopathy was excluded. Serological analyzes for HIV were negative. Interictal EEG showed slow background activity in all the cases, with epileptic discharges,

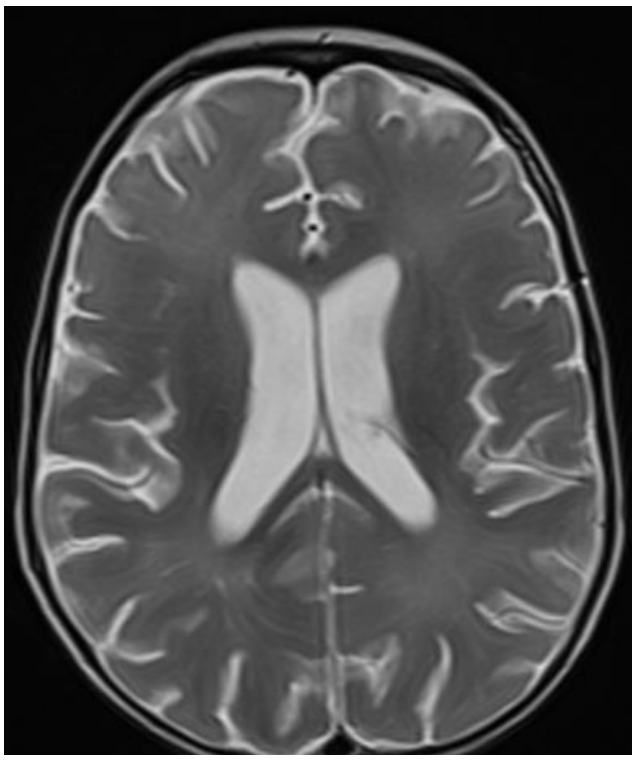

Figure 1. Brain MR in fulminant SSPE patient showed diffuse white matter T2W/FLAIR hypersignal abnormalites with supratentorial atrophy and ex vacuo ventriculomegaly

and periodic pattern in three patients. Brain MR revealed no abnormalities in two cases, diffuse white meter hypersignal in two cases, and brain MR was not available in one case. The clinical presentation and MR findings **(Figure 1)** were not consistent with the existence of leukodystrophy. In all the patients, IgG anti-measles antibodies in serum and CSF were detected by ELISA test, the index titer of IgG anti-measles antibodies in the serum vs. CSF is reduced, and oligoclonal bands were positive in CSF. IgM anti-measles antibodies were not detected in serum and CSF, and PCR test for measles was negative in serum and CSF. In all the patients, microbiological results were negative for bacterial agencies including tuberculosis, and PCR tests were negative for viruses (HSV, VZV, EBV, HIV) and Mycoplasma pneumoniae in both blood and CSF. Anti – NMDAR antibodies were negative in serum in two tested patients. The treatment of SSPE included:Isoprinosine 100mg/kg/day per os in all cases; Ribavirin at the dose of 10 mg/kg of body weight administered intravenously as a 30-min infusion three times a day for 7 days in three cases (patients 1, 2 and 3); intraventricular interferon IFN-α therapy (1 million IU three times a week (patients 4 and 5) and IFN-2α subcutaneous (70mcg/week) in patient 3. Despite the treatment, the course was extremely fulminant with lethal outcome within three months from the initial symptoms in four cases. Summarized results of all patients are presented in three tables. **Table 1** presents demographic and pre-morbidity features: sex (4 males, one female), perinatal history, and psychomotor development before SSPE onset, age and the course of measles infection, period from measles infection to SSPE onset, vaccination status, and immune-competence. The date from the table suggested that all the patients had normal perinatal history and early psychomotor development, with uncomplicated course of measles infection, and all of them were immune-competent. The age of measles infection was in range from 6 months to two years (mean age 12.5 months), while the onset of SSPE was in range from 2.5 to 16 years (mean age 8.1 years). Latency period from measles infection to SSPE onset was in range from 1.8 to 7 years (mean 4.32 years). **Table 2** shows that behavior changes, cognitive decline, dysarthria, ataxia, involuntary movements and seizures were the most common initial manifestations of the disease. The period from initial to full clinical presentation was very short, commonly about two months.

Table1. Demographic and pre-morbidity characteristics

Characteristics	Patient 1	Patient 2	Patient 3	Patient4	Patient 5
sex	male	female	male	male	male
age at admission (years)	2.6	8	3.2	16	7
calendar year at admission	2020.	2019.	2020.	2010.	2010.
perinatal history	normal	normal	normal	normal	normal
early psychomotor development	normal	normal	normal	normal	normal
age at measles infection (months)	8	12	6	no clear data	24
complicated course of measles infection	no	no	no	probably subclinical	no
age at SSPE onset (years)	2.5	8	3	16	7
latency period from measles infection to SSPE onset (years)	1.8	7	2.5	no clear data	6
age of MMR vaccination (months)	15	16	15	not vaccinated	not vaccinated
immune-competent	yes	yes	yes	yes	yes

Table 2. Clinical characteristics

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Initial manifestations	gait instability, speech difficulties, confusion, myoclonic jerks, seizures	behavior abnormalities, insomnia, ataxia, dysarthria	seizures, ataxia, weakness, lack of sphincters control, sleepiness, anxious when awake	ocular pain, cognitive dysfunctions, depression, behavioral problems	anxious, fears, language and behavior problems, drop attacks
Period from initial to full clinical presentation	2 months	3 months	2 months	2 months	2 months
Movement disorders	myoclonus, dystonia	myoclonus	myoclonus, dystonia, eyes deviation, opsoclonus	dystonia, decerebration, eyes deviation	tremor, myoclonus
Bulbar palsy development	within 3 months	within 2 months	within 1.5 months	within 2 months	within 6 weeks
Clinical finding on admission in our clinic	GCS 15, dysarthria, understanding the tasks, spastic hemiparesis, dystonia, tremor, Babinski's sign and clonus bilaterally, myoclonus, drop attacks, unable to walk	GCS 15, not following the gaze, horizontal nystagmus, mute, spastic quadriparesis, dystonic posture, unable to walk	GCS 15, not following the gaze, unable to sit and stand without support, dysarthria, spasticity, dystonia, flexion plantar response	GCS 8, no grimaces, spastic quadriparesis, decerebration position, no sitting and walking	bradykinesia, ataxia, tremor and myoclonic jerks
Types of seizures	myoclonus, atonic, atypical absence, GTC	myoclonic, atonic, GTC	myoclonic, atonic	episodes of focal onset clonic	atonic, focal onset nonmotor
Frequency of seizures	daily	daily	no seizure after admission	stopped by midazolam	stopped by midazolam
Continuous AED	valproate, levetiracetam, clonazepam	valproate, clobasm, clonazepam, topiramate	no	no	no

GTC – generalized tonic-clonic; AED – antiepileptic drugs

The table shows the type of movement disorders, the period within which bulbar palsy was developed, clinical findings at the admission to our clinic, the types and frequency of seizures and used antiepileptic drugs. **Table 3** presents brain MR finding, and the period from disease onset to brain MR, EEG features (background activity, epileptic discharges and periodical patterns), anti-measles antibodies in serum and CSF. All patients had positive oligoclonal bands and anti-measles IgG antibodies in serum and CSF, while both, IgM antibodies and PCR tests for measles were negative. There is no data about maternal vaccination status except for the mother of patient number three who had been vaccinated as a child, while none of the mothers had been revaccinated.

DISCUSSION

SSPE is a devastating disease and has been a big medical challenge since the disease has very poor prognosis and the treatment is of limited efficacy. The clinical course of typical SSPE is subdivided into four stages, unrecognized in fulminant forms (4). In fulminant SSPE cases, the course of disease is rapid with lethal outcome within a few months, even faster (8), as we showed in our group of patients. There is no data which prove that the children whose mothers have been vaccinated have more severe clinical presentation and earlier onset of disease, as we showed in our cases. Measles vaccination is supposed to be the best way of prevention and eradication of SSPE, and it is very important to increase awareness in population. In the post-vaccination era, measles virus infection in developed countries has drastically decreased, but anti-vaccination activity has led to measles epidemic, such as the one we experienced three years ago. The risk of SSPE is higher among persons infected with measles at an early age, especially in babyhood (9,10). According to the literature data, SSPE usually occurs 7–10 years after measles infection, but the latency varies from 1 month to 27 years, with shorter latency in children affected by measles at an earlier (<2 years) age (2). In our cases the range of latency was from 22 months to 7 years. All of our cases had a higher risk for SSPE since they suffered measles during babyhood, and in two of them, a fulminant SSPE started at a very early age, about three years of age.

Table 3. Brain magnetic resonance findings, laboratory results of blood and CSF analyzes

Analysis	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Brain MR	normal	normal	extensive white matter T2W/FLAIR hypersignal abnormalities with supratentorial atrophy and ex vacuo ventriculomegaly	diffuse white matter T2W/ FLAIR hypersignal abnormalities	not available
Period from initial symptoms to magnetic resonance	one month	two months	three months	one month	not available
EEG (from the onset to EEG)	one month	two months	one month	two months	one month
Background activity	slow	slow	slow	slow	slow
Epileptic discharges	generalized	generalized	no	no	yes
Periodic complexes	no	yes	yes	no	yes
Anti-measles antibodies					
Serum IgM	negative	negative	negative	negative	negative
CSF IgM	negative	negative	negative	negative	negative
Serum IgG	1:320	positive	1:320	1:320	1:640
CSF IgG	1:80	positive	1:5	1:40	1:32
PCR measles serum and CSF	negative	negative	negative	negative	negative
Oligoclonal bands	positive	positive	positive	positive	positive
Anti – NMDAR antibodies	negative	not done	negative	not done	not done

NMDAR - N-Methyl-D-Aspartate Receptor

Most infants are born immune to measles due to maternal antibodies transferred during pregnancy, regardless whether the mother had natural measles infection or was vaccinated. Measles antibody titers are lower in regularly vaccinated women than in those who had natural measles infection. So, the infants of vaccinated mothers have poorer protection, since they have lower titer and shorter duration of maternal anti-measles antibodies. In our last patient who got infected with measles at the age of six months, mother had the evidence that she had been regularly vaccinated. This contributes to the attitude that the infants of vaccinated mother are often left without transplacentally acquired measles antibodies before the age of one, even earlier, especially in preterm infants. Gestational age of the infant has an impact on the amount of transplacentally transferred antibodies, suggesting that premature infants receive lower titers of maternal antibodies (11,12). In none of our cases prematurity was a risk factor, and the mother of the last patient had data on regular anti-measles vaccination. A longitudinal prospective study reported progressive percentage decreasing of protected infants born to vaccinated mothers, from 69.6% at birth to 3.2% at six months and 0% at nine and twelve months (13). Low protection at the age of six months in our third case resulted by measles infection during measles epidemic in our country. According to these data, it is supposed that infants are vulnerable to measles infection in the period before regular vaccination schedule which included MMR vaccination between the age of 12 and 15 months. In addition to previous published SSPE cases, the data of our patients also support considering earlier measles vaccination compared to the current schedule, especially among premature infants and other infants of vaccinated mothers. There is a publication of SSPE in an HIV infected child, but none of our patients had inherited or acquired immunodeficiency (14).

The other observation from our practice and literature data is an increasing number of fulminant SSPE form in children. Retrospective evaluation of the total number of treated patients with SSPE at our Institute in the past ten years, suggested that all of them had fulminant course of the disease. Two of them, with *epilepsia partialis continua*, have already been published (4). Clinical presentation at the early stage of fulminant SSPE might be similar to the one in children with immune mediated encephalitis. Although immune mediated encephalitis is more frequent, SSPE has to be considered if the course is progressively deteriorating, in addition to the absence of certain antibodies and unresponsiveness to immune suppressive and immunomodulatory treatment. We suggest considering SSPE in all children with progressive neurological and cognitive deterioration, associated with movement disorders such as dystonia, insomnia, behavior problems and *de novo* epileptic events, even if the progression of deterioration is very fast. SSPE has to be evaluated in differential diagnosis of progressive deterioration in children, especially because valuable diagnostic procedures, such as serological CSF analyses, brain MR and EEG are non-invasive and available in most of the children hospitals. The observation in our cases is that brain MR in fulminant SSPE might be normal even in the stage when the patients are severely neurologically deteriorated. The other observation in our patients is that the stage with myoclonic jerks and atonic events associated with "Ra-

demecker's complexes", pathognomonic for SSPE, lasted only for a few weeks, and might be absent in some cases. We found pathognomonic EEG finding in three cases, in one short period of time. In all cases, EEG background activity was slow, even at the early stage of disease within the first month of the clinical onset. The treatment of epileptic seizures was challengeable in two of our patients and different antiepileptic drugs were given, especially at the onset of the disease.

CONCLUSION

In conclusion, five patients were reported, including three vaccinated children with fulminant SSPE associated with measles infection during babyhood. We pointed that scheduled measles vaccination of children contributed to a decrease in frequency but not to a complete eradication of SSPE. The explanation for this in our patients is that the children had measles before the scheduled vaccination.

The authors of this manuscript suggest two major issues. One is that in aiming to eradicate SSPE, we suggest considering weaning of vaccine-derived immunity, and re-vaccination of girls at reproductive period. The other issue is an increasing number of fulminant cases related to typical SSPE presentations and it might suggest upcoming changes in disease phenotype.

References

1. Mekki M, Eley B, Hardie D, et al. Subacute sclerosing panencephalitis: clinical phenotype, epidemiology, and preventive interventions. *Dev Med Child Neurol*. 2019;61(10):1139-1144.
2. Jafri SK, Kumar R, Ibrahim SH. Subacute sclerosing panencephalitis - current perspectives. *Pediatric Health Med Ther*. 2018;9:67-71.
3. Rota PA, Rota JS, Goodson JL. Subacute Sclerosing Panencephalitis. *Clin Infect Dis*. 2017;65(2):233-234.
4. Kravljanac R, Jovic N, Djuric M, et al. Epilepsia partialis continua in children with fulminant subacute sclerosing panencephalitis. *Neurol Sci*. 2011;32(6):1007-12.
5. Garg RK, Mahadevan A, Malhotra HS, et al. Subacute sclerosing panencephalitis. *Rev Med Virol*. 2019;29(5):e2058.
6. Masnada S, Zuccotti GV, Bova SM, et al. Re-emergence of SSPE: Consequence of the decline of adherence to vaccination programmes? *Eur J Paediatr Neurol*. 2019;23(2):338-340.
7. Pallivathucal LB, Noymer A. Subacute sclerosing panencephalitis mortality, United States, 1979-2016: Vaccine-induced declines in SSPE deaths. *Vaccine*. 2018;36(35):5222-5225.
8. Marjanović BD, Stojanov LM, Zamurović DR, et al. Fulminant subacute sclerosing panencephalitis:two cases with atypical presentation. *Pediatr Neurol*. 2003;29(1):63-5.
9. Wendorf KA, Winter K, Zipprich J, et al. Subacute Sclerosing Panencephalitis: The Devastating Measles Complication That Might Be More Common Than Previously Estimated. *Clin Infect Dis*. 2017;65(2):226-232.
10. Waaijenborg S, Hahné SJ, Mollema L, et al. Waning of maternal antibodies against measles, mumps, rubella, and varicella in communities with contrasting vaccination coverage. *J Infect Dis*. 2013;208(1):10-6.
11. Guerra FM, Crowcroft NS, Friedman L, et al. Immunity of Canadians and Risk of Epidemics (iCARE) Network. Waning of measles maternal antibody in infants in measles elimination settings - A systematic literature review. *Vaccine*. 2018;36(10):1248-1255.
12. Gershon AA. Measles virus (Rubeola). In: Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious disease. 8thed. Philadelphia: Elsevier Saunders; 2015:1967–1973.
13. Leuridan E, Hens N, Hutse V, et al. Early waning of maternal measles antibodies in era of measles elimination: longitudinal study. *BMJ*. 2010;340:c1626.
14. Kumari M, Shah I, Shetty NS, et al. Subacute Sclerosing Panencephalitis (SSPE) in HIV Infected Child. *Indian J Pediatr*. 2020;87(3):241.

SUBAKUTNI SKLEROZIRAJUĆI PANENCEFALITIS - PROMENE FENOTIPA TOKOM POSLEDNJE DECENIJE

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Sažetak

Uvod: Subakutni sklerozirajući panencefalitis (SSPE) je retka, progresivna, neurodegenerativna bolest sa lošim ishodom. Vakcinacija protiv malih boginja doprinela je smanjenju broja pacijenata sa SSPE, ali ne i eradikaciji. Cilj naše studije je da procenimo tok bolesti kod naših pacijenata sa SSPE sa fokusom na vakcinisanu decu. Osnovni cilj je sagledavanje mogućnosti za unapređenje prevencije bolesti.

Metod: Retrospektivnom studijom obuhvaćeni su pacijenti sa SSPE lečeni u periodu od decembra 2010. do decembra 2020. godine na Pedijatrijskoj klinici u Institutu. Kriterijumi za uključivanje su pacijenti sa dijagnozom SSPE na osnovu kliničke slike, neuromidžinga, elektroencefalografije i pozitivnih IgG antitela protiv morbila, kako u serumu, tako i u likvoru.

Rezultati: Uključeno je petoro dece sa fulminantnim tokom SSPE. Svi pacijenti su u detinjstvu bolovali od morbila. Troje ih je vakcinisano protiv morbila, dok dvoje nije vakcinisano. Radi se o zdravoj deci, bez poremećaja imuniteta i normalnog globalnog razvoja. Tok je bio izuzetno fulminantan, sa smrtnim ishodom u roku od tri meseca od početnih simptoma u četiri slučaja. U kliničkoj prezentaciji su dominirali progresivna regresija u motoričkom i kognitivnom razvoju, promene ponašanja, poremećaji pokreta, miokloničnі trzaji i napadi.

Zaključak: Uprkos sprovođenju vakcinacije, SSPE nije nestao. Sve veći broj vakcinisane imunokompetentne dece sa fulminantnim oblikom SSPE i anamnezom infekcije morbila u detinjstvu lečen je u našoj Klinici. Kao meru za poboljšanje prevencije, predlažemo da se razmotri mogućnost smanjenja imunskog odgovora nastalog vakcinom i revakcinacija devojčica u fertilnom periodu.

Ključne reči: fulminantni SSPE, vakcinacija, morbili, deca

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