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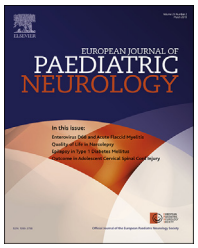

Letter to the Editor

Re-emergence of SSPE: Consequence of the decline of adherence to vaccination programmes?

Keywords:
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To the Editor,

Subacute Sclerosing Panecephalitis (SSPE) is a persistent and chronic encephalitis, which is well-known as an extremely severe complication of measles infection. Incidence of SSPE has dropped significantly since the introduction of mass campaigns for measles vaccination in most countries; in the United States of America, for instance, SSPE incidence decreased from 0.61 cases per million in 1963, when the measles vaccination program started, to 0.01 cases per million in 1997.[1] Despite in the last decades SSPE almost disappeared in Europe as well, in this letter we report two cases of early-onset SSPE recently observed in Italy, which can be both related to a fall in population immunity.

The first patient contracted congenital Cytomegalovirus infection and measles infection from the non-vaccinated mother at the age of 6 weeks (serum anti-measles IgM and IgG were 73 U/Ml/753 mU/mL, respectively). She was not administered antiviral therapy. At the age of 10 months she was hospitalized because of the onset of sudden head and upper limbs movements, associated with a progressive developmental regression. Neurological examination showed hypotonia, poor spontaneous movements, no head nor trunk control, no vocalization, irritability, absence of visual fixation, pyramidal signs. Electroencephalographic (EEG) registration revealed the periodic complexes typical of SSPE (Fig. 1) and epileptic and non epileptic myoclonic jerks. Brain MRI was unremarkable. Serological investigation documented high titers of anti-measles IgG (serum >300 UA/ml), anti-measles IgM were negative. The diagnosis was confirmed by high titers of anti-measles IgG in cerebrospinal fluid (CSF) (IgG 7,65 AI, v.n. 0,30-0,50) and absence of anti-measles IgM. Measles DNA was neither detected in blood, CSF, urine, nor in patient's throat swab specimen. Anti CMV IgG and IgM were negative both in serum and CSF. Oral antiviral therapy with inosine acedoben dimepranol and oral levetiracetam in order to control myoclonus were started. Interferon IFN-α was refused by parents. After four months, the patient showed progressive cognitive and motor deterioration, difficulty in swallowing, increase in number of periodic myoclonic jerks (>1/minute). At the age of 20 months, she is still alive; neurological examination shows severe hypotonia with dystonic movements, rare myoclonic jerks and absence of seizures; EEG periodic complexes disappeared, and delta slow wave activity is preminent.

The second patient contracted chickenpox at the age of 12 months and measles at the age of 26 months; both diagnoses were confirmed by serological investigations. He was not administered vaccinations by parents' decision. At the age of 5 years he presented a significant regression of language skills and after 11 months, he had a convulsive seizure and subsequently showed a rapid progressive motor and cognitive impairment. Neurological examination at the age of 6 years revealed severe ataxia, diffused tremors, periodic head and trunk falls, dysarthria. EEG revealed the typical periodic complexes. Brain MRI showed aspecific white matter alterations. High title of anti-measles IgG in CSF (IgG > 300 U/mL) confirmed the diagnosis of SSPE. Intratecal IFN-α-2b and oral methisoprinol were started with methisoprinol, carbamazepine, baclofen, trihexyphenidyl. Nowadays, at the age of 8 years, he shows a severe intellectual disability, spastic tetraparesis, tremors and dystonic-myoclonic movements.

In its typical form SSPE has a subtle onset characterized by behavioural changes (stage I), then patients deteriorate with the appearence of periodic myoclonic jerks (stage II), pyramidal and extrapyramidal disfunction (stage III), up to loss of cerebral cortex function and death (stage IV).[2] Our first patient, however, experienced a sudden clinical course, fairly different from the four-stage course. Indeed, a month after the first symptoms she exhibited simultaneously features typical of both stage II (repetitive myoclonic jerks, seizures) and stage III (poor spontaneous movements, lost of all acquisitions, absence of visual fixation, pyramidal signs). The second patient experienced a short latent period as well. The vertical

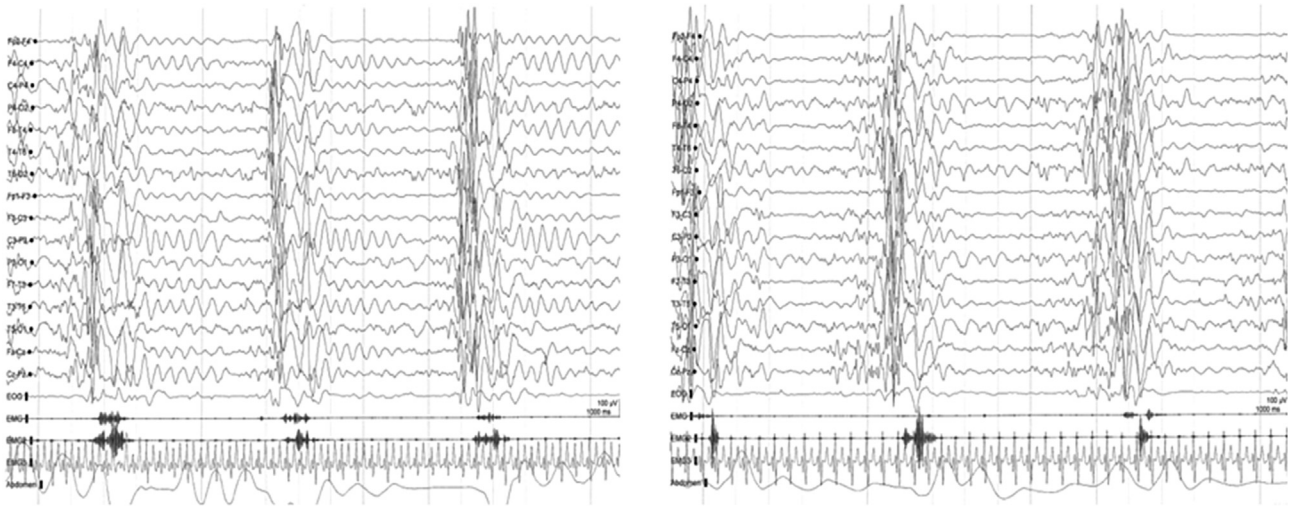

Fig. 1 – EEG-polygraphic registration (deltoids, electrocardiogram, breath), 15 mm/s, 150 μVcm. The EEG shows periodic complexes of bilateral and synchronous high voltage (300–500 μV) sharp waves, spikes and waves lasting 2–3 s and interbursts periods with diffuse hypovoltage EEG traces lasting 4–6 s; polygraphic traces showed upper limbs myoclonia concomitant with the burst.

transmission from a non-vaccinated mother to a very young baby with immature immune system, and a congenital infection (CMV), can explain the early onset and the rapid progression in the first patient; the second patient as well suffered a concomitant infection (chickenpox). However, the observed short latency and rapid/catastrophic disease progression might as well be age-dependent. In addition to our two early-onset SSPE cases, only a handful of SSPE cases were reported during the first two year of life, and in particular only two cases in the first year of life, namely at the ages of 4[3] and 11 months.[4] All these cases showed a course similar to the two patients described here, indicating that a fulminant course without well defined stages appears rather typical to SSPE triggered by very early measles infection, in contrast to the typical course of SSPE. Additional epidemiological and immunological studies may further clarify what underlies these different disease courses.

It should be emphasized that both of our cases can be directly related to a non-adherence to the vaccination campaign, a behaviour which is becoming increasingly common. Between August 2017 and July 2018, 28 EU/EEA countries reported 14,118 cases of measles.[5] The Italian Health Care System registered 256 new cases during 2015, increasing to 5.407 cases in 2017 and 2.368 during the first 10 months of year 2018; 91% of the patients diagnosed during 2018 were not vaccinated, 19,6% of them have less than 5 years of age and 153 have <1 year of age.[6] Currently, none of these reported measles infections, except for the case of our first patient, has developed SSPE. We nevertheless urge the community about the risks of life-threatening complications of measles infection, entirely avoidable by adhering the vaccination programs. Vaccination should be generally recommended to both adults and children in order to prevent the infection in children under two years of age, who are uncovered as measles vaccination is made mandatory only at the age of 2.

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Conflict of interest

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Consent

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