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Can General Anesthesia Trigger The Activation of Latent Measles Infection?

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ÖZET

Genel anestezi latent kizamik enfeksiyonunu aktive edebilir mi?

Genel anestezi altında travmatik katarakt cerrahisi geçiren sonrasında subakut sklerozan panensefalit (SSPE) tanısı konan hastada olası fizyopatolojik mekanizmaları tartışmak. On bir yaşındaki erkek hastaya sağ travmatik katarakt nedeniyle genel anestezi altında komplikasyonsuz katarakt cerrahisi uygulandı. Cerrahiden 10 gün sonra hastada dizartri, serebellar disfonksiyon ve mental yavaşlama gelişti. Klinik ve laboratuvar bulguları ile hastaya SSPE tanısı kondu ve tedaviye başlandı. Genel anestezinin immün sistem üzerindeki muhtemel olumsuz etkileri ve SSPE'nin patofizyolojisi göz önüne alındığında, genel anestezi ile hastamızda önceden varolan subklinik enfeksiyonda hızlı bir ilerlemenin ya da latent SSPE'nin aktivasyonunun tetiklendiğini düşünmekteyiz. Özellikle aşılama durumunun veya kızamık öyküsünün şüpheli olduğu çocuk hastalarda patofizyolojinin tam olarak aydınlatılabilmesi mümkün olmayabilir.

Anahtar kelimeler: Genel anestezi, subakut sklerozan panensefalit, immun system

ABSTRACT

Can general anesthesia trigger the activation of latent measles infection?

We present a patient who was diagnosed as subacute sclerosing panencephalitis (SSPE) following a cataract surgery under general anesthesia and we discuss the possible physiopathological mechanisms in this disease.

An 11 years old boy presenting with right traumatic cataract and underwent an uncomplicated cataract surgery under general anesthesia. Ten days following the surgery, the patient developed dysartria, cerebellar dysfunction and mental deterioration. The patient was diagnosed as SSPE with the clinical and laboratory findings, and treatment was started.

Considering the pathophysiology of SSPE and effect of general anesthesia on the immune system, we think either a latent SSPE infection was activated or subclinically present infection started a rapid progression following an operation under general anesthesia. Nevertheless particularly in patients with suspicious vaccination and previous measles infection, it may not be possible to enlighten the actual pathophysiology.

Key words: General anesthesia, subacute sclerosing panencephalitis, immune system

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INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a progressive neurodegenerative disorder of central nervous system related to a persistent and aberrant measles virus infection. The disease can be endemic in regions of inadequate vaccination and the incidence is 1-10:100.000 following measles infection (1). The symptoms mostly appear by the end of the first decade or in early adolescence. Behavioral and mental changes, myoclonus, epileptic seizure, extrapyramidal dysfunction and visual disturbances are the main findings of the disease. The diagnosis is made due to Dyken criteria, which includes; (1) progressive deterioration of cognitive functions and myoclonus, (2) characteristic electroencephalography (EEG) findings, (3) increased globulin levels in cerebrospinal fluid (CSF) without

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pleocytosis, (4) increased measles antibody titers in CSF, and (5) classical histopathological findings in brain biopsy (2). Here we present a patient who was diagnosed with SSPE following a cataract surgery under general anesthesia and we discuss the possible physiopathological mechanisms in this disease.

CASE REPORT

An 11 years old boy presented with a decrease in vision in his right eye following a blunt ocular trauma. Best corrected visual acuity (BCVA) in the right eye was counting fingers from 1 meter, and 10/10 in the left eye. The patient was diagnosed with a right traumatic cataract. Other ocular examination findings (intraocular pressure, fundus examination) in both eyes and systemic examination were otherwise normal. He underwent an uncomplicated lensectomy and intraocular lens implantation surgery under sevoflorane, nitrous oxide and thiopenthal anesthesia. In the postoperative period, the patient was treated with topical prednisolone acetate (5x1/day), moxifloxacine (5x1/day) and cyclopentolate (1x1/day) drops for 3 weeks. The day after examination was without any problems and the patient was discharged. The patient presented to the clinic on 10th postoperative day with the complaints of difficulty in speaking and behavioral disturbances. The patient was consulted to pediatric neurology and the examination revealed psychomotor retardation and postural imbalance. EEG showed bilaterally synchronic sharp and wave complexes in both hemispheres and following diazepam infusion, bilateral synchronic asymmetric sharp and slow waves did not disappear. Considering the clinical and EEG findings, a diagnosis of SSPE was suspected and a lomber puncture was done. CSF culture, measles immunoglobulins in both serum and CSF, immunoglobulin indices, total immunoglobulin levels of blood and CSF was studied. No microorganisms were isolated in CSF cultures, but CSF measles IgG level was >100 IU/ML (<25 IU/ML), IgG index was 2.37 (0.20-0.60) and CSF total IgG level was 7.4 mg/dl (1.5-5.50 mg/dl). Total measles IgG level in serum was within normal limits (1340 mg/dl, N: 650-1600 mg/dl). Cranial magnetic resonance imaging came out as normal. The patient was diagnosed with SSPE with these clinical and laboratory findings. The vaccination and previous measles infection history in early childhood was not reliable as the patient came from a rural area. Treatment with carbamazepine (16 mg/kg/day) and isoprinosine (100 mg/kg/day) was started. Although the clinical findings started regression in the first days of the treatment, myoclonus and postural imbalance deteriorated significantly by time. The visual acuity could not be evaluated due to lack of cooperation in the following days, but the anterior segment was silent and posterior segment examination did not reveal any pathologic findings, as chorioretinitis, maculopathy or optic nerve edema.

DISCUSSION

Pathophysiology of SSPE is still full of unknowns. Brain autopsies and postmortem histopathological examinations demonstrated demyelinization, inflammatory cell infiltration, neuronal loss, degeneration in dendrites and neurofibrillary tangles (2). These findings point the possible effects of cellular immunity and inflammatory cytokins in development and progress of the disease. Tekgül et al. evaluated the relationship of lymphocyte subtypes and cytokine profiles before and after the treatment of 3 SSPE patients (3). They reported a high number of CD8+ cells (T suppressor cell) and CD56+ cells (natural killer cell) and low number of CD3+ cells (activated T cell) in serum before the treatment. In a study examining a larger group of SSPE patients, a positive correlation was found between the increase in CD4+ cell number and rapid progression of the disease

Table 1: Brief review of the literature about the analysis of serum and cerebrospinal fluid cytokine levels and cellular immunity in subacute sclerosing panencephalitis.

	IL2		IL4		IL6		IL10		IFN-γ		TNF-α		CD8+	CD3+
	S	CSF	S	CSF	S	CSF	S	CSF	S	CSF	S	CSF	S	S
Tekgül[3]	2P↓,1P↑	2P↓,1P↑	-	-	-	-	-	-	-	-	2P↓,1P↑	2P↓,1P↑	↑	↓
Anlar[4]	-	-	ND	-	-	-	-	-	-	-	ND	-	↑	↓
Aydın[5]	↑	ND	↓	↓	ND	↓	↓	ND	↑	ND	ND	ND	-	-
Ichiyama[6]	ND	ND	ND	ND	↑	↑	↑	ND	ND	ND	ND	ND	-	-

S: serum, CSF: cerebrospinal fluid, P: patient, ND: no difference from control group, -: not studied

(4). Aydın et al. reported a reduced concentration of serum IL4 and IL10, CSF IL4 and IL6 and a significant increase in serum IL2 and IFN γ concentration (5). Ichiyama et al. also demonstrated an increase in serum IL6 and IL10 levels (6). The controversy in the results of cytokine and cellular immune system studies presented in the literature is obvious (Table 1). But almost all of them point out the role of immune system in both appearance and progress of SSPE. Moreover preventing the progression of the disease with immunomodulator treatment is another point verifying the effect of immune system in the pathophysiology of SSPE.

The increased infection rates in postoperative periods and adverse effects of general anesthesia on immunocompromised and oncology patients reveals the possible effects of general anesthesia and surgery on the immune system. On the contrary, SSPE patients have been treated with intraventricular alpha interferon, administered under general anesthesia (7). The course after such operations have not been reported to be deterioration, as therapeutic agent is also administered at the same time with general anesthesic agents. Besides many studies were reported on inhalation and intravenous anesthetic agents' effects on the immune system. Sevoflorane and enflorane were shown to induce apoptosis in peripheral lymphocytes and cause diminished release of IL-1β and IFN γ from mononuclear cells (8). Similarly thiopenthal was reported to induce apoptosis in T lymphocytes (9). Schneemilch demonstrated the immunsupressive effect of thiopenthal andnitrous oxide on mononuclear cells (10). Moreover the unfavorable effects of surgical stress on the immune system is a well known truth and must be recognized. In conjunction with this stress, anesthetic agents may cause a more severe immunosuppression in some patients.

In our case, the symptoms and findings aroused following an uncomplicated cataract surgery under general anesthesia. It would be a pretentious idea to admit general anesthetics as the reason of SSPE in this patient, but considering the effect of general anesthesia on the immune system and the pathophysiology of SSPE, we think either a latent SSPE infection was activated or subclinically present infection started a rapid progression. Nevertheless the manifestation of the disease after general anesthesia may also be coincidental. We think it is not likely to make a distinct comment in the possible pathophysiology of this patient, as the age of the patient is eligible with the natural course of SSPE as well. Moreover, particularly in patients with suspicious vaccination and previous measles infection, it may not be always possible to enlighten the actual pathophysiology.

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