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Neurological Complications of Chickenpox: Case Series Report and Literature Review

Neurološke komplikacije vodenih kozica: prikaz serije bolesnika i pregled literature

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Abstract

Chickenpox, as a self-limited disease, can result with a large spectrum of complications. Neurological complications are very rare, and among them acute cerebellar ataxia is the most frequent one. Also, varicella-zoster virus has been reported as the second infectious agent of acute encephalitis. We present neurological complications of chickenpox in a five year period of hospitalisation in the Infectious Diseases Clinic, Clinical Centre University of Sarajevo, Bosnia and Herzegovina. Among 181 hospitalised patients, nine of them had neurological complications. Acute cerebellitis was the most frequent diagnosis. All patients were treated with acyclovir, and the outcome was a major success.

Sažetak

Vodene kozice, kao samoograničavajuća bolest, može rezultirati velikim rasponom komplikacija. Neurološke komplikacije iznimno su rijetke, a među njima je akutna cerebelarna ataksija. Također, varicella-zoster virus naveden je kao drugi zarazni uzročnik akutnog encefalitisa. Predstavljamo neurološke komplikacije virusa u petogodišnjem razdoblju hospitalizacije u Klinici za zarazne bolesti Kliničkog centra Sveučilišta u Sarajevu, Bosna i Hercegovina. Među 181 hospitaliziranih pacijenata, njih devet imalo je neurološke komplikacije. Akutni cerebelitis bio je najčešća dijagnoza. Svi bolesnici su liječeni aciklovirom, što je rezultiralo ogromnim uspjehom.

Introduction

Varicella is a very contagious childhood disease with a worldwide distribution. It affects around 140 million new cases every year [1]. Even though it is often considered a self-limited disease, it may have a serious course with large spectrum of complications requiring hospitalization. Neurological complications during chickenpox are estimated to be very rare: 0.01-0.03% [2]. Among children, acute cerebellar ataxia is one of the most frequent complications, occurring in about 4-8% of those hospitalized for varicella. Rare varicella complications are meningitis, meningoencephalitis, rhombencephalitis, Guillain Barre etc. [3]. In recent years, varicella-zoster virus is the second most frequent virus causing encephalitis or meningitis, after herpes simplex virus [4].

The objective of this study is to determine the occurrence of neurological complications of chickenpox in our patients and present clinical symptoms, therapy and outcome of the disease.

Material and methods

We retrospectively analysed medical records of all the patients with chickenpox hospitalised in the period from

July 2013 to June 2018 in the Infectious Diseases Clinic, Sarajevo, Bosnia and Herzegovina. The diagnosis of varicella was based on clinical presentation of characteristic skin lesions in varying stages of development and resolution. Inclusion criteria were clinically confirmed diagnosis of chickenpox with any neurological complications. Exclusion criteria were neurological symptoms due to other possible cause. We used descriptive statistical methods, and presented specific data for each patient.

Results

181 patients with clinically confirmed diagnosis of chickenpox were hospitalised in the Infectious Diseases Clinic in the period from 01.07.2013 to 30.06.2018. Among them, nine patients (1.6%) had neurological complications. Six patients (66.6%) were male and three of them (33.3%) were female. The average age of the patients with neurological complications was 8.6 (range 3 – 29 years). Two of them (22%) had active skin lesions when admitted. The average time of onset for cerebellar symptoms was 7.48 days prior to hospitalization (range from 4 to 11 days). Typical clinical signs presented were ataxia (100%) and fever (56%), while individual patients had seizures, dysarthria or diplopia. Magnetic resonance imaging (MRI) was performed in seven patients and computed tomography (CT) in three, but all the findings were normal. In eight patients (89%) a lumbar puncture was performed, revealing clear cerebrospinal fluid (CSF) with presented cells in five patients (56%), range 32-180 cells/mm^3, and no microorganisms on gram stain. Clinical diagnosis for seven patients was acute cerebellitis, one patient had a meningitis with cerebellitis, and one patient was diagnosed with rhombencephalitis. They all received intravenous acyclovir (average 16 days, range from 7 to 32 days), and were discharged upon recovery.

Detailed data for all the patients with neurological complications of chickenpox are presented in **Table 1**.

Table 1. Detailed data for all patients with chickenpox neurological complications

No.	Age	Sex	Illness duration	Active skin lesion	Clinical presentation	Imaging	CSF	Diagnosis	Treatment	Hospital stay
1	6	M	8	No	Fever, headache, ataxia, vomiting	MRI, CT - referral	49 cells, increased proteins, glucose referral	Cerebellitis, Meningitis	Acy 14d	18
2	3	M	8	No	Ataxia	MRI- referral	Normal	Cerebellitis	Acy 10d	18
3	10	M	11	No	Ataxia, dysarthria	MRI-referral	Normal	Cerebellitis	Acy 7d	10
4	8	M	8	No	Ataxia	MRI-referral	32 cells, proteins and glucose referral	Cerebellitis	Acy 10d	14
5	29	F	4	Yes	Fever, vomiting, diplopia, ataxia	MRI, CT -referral	Normal	Rhombencephalitis	Acy 15d	32
6	7	M	6	Yes	Fever, seizures, ataxia	Not done	Not done	Cerebellitis	Acy 14d	14
7	3	F	7	No	Ataxia, fever	MRI- referral	170 cells, increased proteins, glucose referral	Cerebellitis	Acy 10d	22
8	8	M	10	No	Fever, ataxia, headache	MRI, CT - referral	78 cells, proteins and glucose referral	Cerebellitis	Acy 9d	11
9	4	F	9	No	Ataxia, vomiting	Not done	22 cells, proteins and glucose referral	Cerebellitis	Acy 7d	10

M – male, F – female, Acy – acyclovir

Discussion

Chickenpox most commonly occurs in childhood, and even normally benign, it can occasionally develop into a more serious illness with some serious complications. Usual findings are Staphylococcus aureus skin infections, otitis media, endocarditis, pneumonia, and rare central nervous system (CNS) conditions, like cerebellar ataxia and encephalitis [5]. Neurologic complications associated with varicella are estimated to be 1 to 3 per 10000 cases [6]. Cerebellar ataxia and encephalitis are usual findings, while other rare complications include transverse myelitis, aseptic meningitis, and Guillain-Barre´ syndrome [7-9]. Encephalitis, the most serious CNS complication of varicella, has an incidence of 1 to 2 episodes per 10000 varicella cases, with the highest incidence in adults and infants [10]. The mortality rate for varicella encephalitis is 5%–10%, but the majority of cases end with complete or nearly complete recovery [11]. Cerebellar ataxia is more frequent in younger children, and the prognosis of outcome is better if encephalitis is absent [12,13]. Ataxia may develop from several days before to 2 weeks after the onset of varicella, although the neurologic symptoms most often occur simultaneously with a rash [14]. It is still unknown whether it has a postinfectious, parainfectious, immunologic pathogenesis or a primarily infectious origin [3]. An extremely rare complication of chickenpox is rhombencephalitis, or meningo-rhomencephalitis that has, so far, been found in only few patients [15,16].

The prevalence of neurological complications in the paediatric age is between 13.9-20.4% [17]. Neurologic symptoms (headache, vomiting, and altered sensorium) most often occur about one week after the onset of the varicella rash. The onset of symptoms may be abrupt or gradual and is accompanied by seizures in 29–52% of cases [18,19]. CSF findings are usually normal, but a mild pleocytosis and increased proteins may accompany the condition [20,21]. We reported nine cases with different chickenpox neurological complications. Our patients presented dominantly with ataxia (100%), headache, vomiting, and few among them had ocular diplopia, dystartia and seizures. We did not have any cases with confirmed encephalitis among children. CSF findings in three patients were normal, and six had pleocytosis, range 32-180 cells/mm^3. Elevated proteins were presented in two patients. Radiological findings were normal in all patients. The median length of the hospital stay was 16.5 days (range from 10 to 32 days). All patients were treated with intravenous acyclovir (10mg/kg per dose). Average duration of antiviral therapy was 16 days (range from 7 to 32 days). According to previous studies, administration dose and route were equal, but duration of therapy was longer [22,23]. The vast majority of the patients recovered without apparent sequelae within 1 to 3 weeks. Although there is no substantial evidence that antiviral therapy alters the natural history of the cerebellar ataxia syndrome, it is probably appropriate [10]. The use of corticosteroids is still a dilemma. In a study performed by Bozzola et al., among 44 patients with cerebellar ataxia, 28 of them received corticosteroids (dexamethasone) due to clinical presentation and had a prolonged hospitalisation [3]. The outcome of the disease was favourable for all the patients. We had no long-term sequels, all patients had a complete recovery. Like all other countries in the region, Bosnia and Herzegovina does not carry out chickenpox vaccination. The reasons for it are mostly financial. Our authorities do not consider chickenpox as a big threat, even though we have had 6000-10.000 reported cases every year since 1995 [24]. On the other hand, all countries who introduced chickenpox vaccination reported significant decrease in new cases, from 55% in Germany up to 80% in USA [25,26,27]. Although there was a small number of patients included in the study, it can help us in further clinical approach and point out the importance of vaccination as the best prevention.

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