ORIGINAL ARTICLES

Assesment of Paediatric Varicella Pneumonia

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ABSTRACT

Background: *The objective of the study was to determine the clinical presentation, diagnosis, treatment, and respiratory complications of varicella zoster pneumonia (VZP) in children.*

Material and methods: *Relevant data, age, gender, month of admission, demographic data, past medical and family histories, physical findings during admission, laboratory findings, treatments given, and outcome of these treatments with diagnosis of varicella pneumonia were collected retrospectively.*

Results: *In a two-year period, 15 cases were identified and their data were analysed. Eight patients were male (53%) and seven were female (43%). The mean age was 4.7 ± 3.7 months. Twelve cases (80%) were under six months of age and nine patients (60%) had household contact with persons with chicken pox infection. After onset of the chicken pox rash, the mean time for development of respiratory symptoms was 3.5 ± 1.0 days. The mean hospital stay was 13 ± 1.8 days and ranged from 9−17 days. The persisting fever, fatigue, and cough episodes were major presenting symptoms upon admission in almost all the patients. All patients received acyclovir and non-specific pneumonia treatment and all recovered. None of the children were previously immunized against varicella.*

Conclusions: *Varicella zoster pneumonia should be considered in patients with prolonged fever and accompanying cough in patients with chicken pox. Probably the best approach would be a trial of high dose acyclovir treatment in children who develop VZP.*

Keywords: Acyclovir, child, pneumonia, varicella zoster

Evaluación de la Neumonía por Varicela en los Niños

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RESUMEN

Antecedentes: *El objetivo del estudio fue determinar la presentación clínica, el diagnóstico, el tratamiento, y las complicaciones respiratorias de la neumonía causada por el virus varicela-zóster (VVZ) en niños.*

Materiales y métodos: *Datos relevantes, edad, sexo, mes de ingreso, datos demográficos, historia médica y familiar, hallazgos físicos durante la hospitalización, resultados de laboratorio, tratamientos dados, y resultados de estos tratamientos con diagnóstico de neumonía por varicela, fueron recopilados retrospectivamente.*

Resultados: *En un período de dos años, se identificaron 15 casos y se analizaron sus datos. Ocho pacientes eran varones (53%) y siete eran mujeres (43%). La edad promedio a fue de 4.7 ± 3.7 meses. Doce casos (80%) tenían menos de seis meses y nueve pacientes (60%) tuvieron contacto doméstico con personas con infección por varicela. Después del comienzo de la erupción de la varicela, el tiempo promedio para el desarrollo de los síntomas respiratorios fue 3.5 ± 1.0 días. La estancia hospitalaria promedio fue de 13 ± 1.8 días y varió de 9−17 días. La persistencia de la fiebre, la fatiga, y los episodios de tos fueron los principales síntomas observados a la hora del ingreso en casi todos los pacientes. Todos*

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los pacientes recibieron Aciclovir y tratamiento no específico para la neumonía, y todos se recuperaron. Ninguno de los niños fue previamente vacunado contra la varicela.
Conclusiones: *La neumonía por varicela-zóster debe ser parte de las consideraciones en torno a los pacientes con varicela que presentan fiebre prolongada y acompañamiento de tos. Probablemente el mejor enfoque con los niños que desarrollan neumonía por VVZ sería un tratamiento con una alta dosificación de Aciclovir.*

Palabras claves: Aciclovir, neumonía, niño, varicela-zóster

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INTRODUCTION

Chickenpox is a very contagious disease caused by the varicella-zoster virus, which mostly affects children in the course of epidemics (1, 2). Morbidity and mortality from chickenpox can now be regarded as preventable by vaccine (3). Varicella is usually a benign disease in children, but the rate of complications increase in adulthood. In spite of the high morbidity of varicella zoster related pneumonia (VZP) in adults, cases in children are very rare in the literature (4−6). There is a paucity of data on the incidence of severe complications and death in children. In this study, we aimed to evaluate the clinical presentation, diagnosis, and treatment of rare cases of varicella pneumonia in children, a serious health problem in developing countries.

SUBJECTS AND METHODS

We studied characteristics of pneumonia associated with varicella infection in the South of Anatolia in Turkey, between March 2011 and March 2013. Clinical records of the children hospitalized for varicella and pneumonia were reviewed. Rashes were evaluated by a paediatrician and dermatologist. Chest X-rays were evaluated by a paediatrician and radiologist. Relevant data; age, gender, month of admission, demographic data, family histories, physical findings during admission, laboratory findings, treatments given, and outcome of these treatments of paediatric patients admitted to Van Research Hospital with a diagnosis of varicella pneumonia were collected.

Chicken pox was diagnosed using the clinical findings of fever and a typical polymorphic vesicular skin rash. Varicella pneumonia was diagnosed based on the development of respiratory symptoms and fever within seven days following the onset of the chicken pox rash in the paediatric age group (0−16 years). Pneumonia was diagnosed when cough, tachypnoea or reduced oxygen saturation, and fever higher than 38.5 ˚C occurred. Finally, based on blood gases, chest X-rays, and clinical symptoms, pneumonia was diagnosed in children with complicated varicella. Blood and sputum cultures were taken from all these patients. Patients with bacterial infection, aspiration and secondary causes of pneumonia (cystic fibrosis, malignancy, tuberculosis, *etc*) were excluded from the study.

Data collected were analysed by SPSS v16.0 statistical software. Descriptive statistics were provided for all the study and outcome variables. The categorical variables were expressed as percentages and continuous variables were expressed as mean ± standard deviation.

RESULTS

A total of 139 children were admitted to the university hospital with a diagnosis of VZV infection in a study period. Fifteen cases (10.7%) were diagnosed with varicella pneumonia. All patients had a recent history (within the last 21 days prior to admission) of exposure to VZV infection from their family or neighbours. In a two-year period, 15 cases were identified and their data analysed. Eight patients were male (53%) and seven were female (47%). The mean age was 4.7 ± 3.7 months. Twelve cases (80%) were under six months of age, and nine cases (60%) were between two and six years of age. Nine patients (60%) had household contacts with persons with chicken pox infection. After onset of the chicken pox rash, the mean time for development of respiratory symptoms was 3.5 ± 1.0 days, and the mean hospital stay was 13.0 ± 1.8 days and ranged from 9−17 days. The clinical characteristics of the 15 varicella pneumonia cases are summarized (Table).

Table: Demographic features, clinical features on admission, treatment and outcomes in patients with varicella zoster releated pneumonia

Clinical features of VZP	Mean ± SD or number (%) (n:15)
Age (month)	4.7 ± 3.7
0−6	3 (20%)
6–24	1 (6.6%)
24−72	9 (60%)
72−144	2 (13.3%)
Gender	
Male	8 (53.3%)
Female	7 (46.6%)

Table (Cont'd): Demographic features, clinical features on admission, treatment and outcomes in patients with varicella zoster releated pneumonia

Interval from varicella onset to hospital admission (days)	3.5 ± 1
Duration of hospitalization	13 ± 1.8
Treatment	
Acyclovir	15 (100%)
Antibiotic	9 (60%)
Dijitalizasyon	5 (33.3%)
Seasonal case number	
Spring (March to May)	7 (46.6%)
Summer (June to August)	2 (13.3%)
Autumn (September to November)	–
Winter (December to February)	6 (40%)
Symptoms and clinical findings (%)	
Fatigue	15 (100%)
Cough	15 (100%)
Persisting fever	15 (100%)
Tachycardia	15 (100%)
Tachypnea	8 (53.3%)
Abnormal breathing sounds	8 (38.1%)
Cardiac insufficiency signs	5 (33.3%)
Retractions	4 (26.6%)
Hepatomegaly	4 (26.6%)
Laboratory results	
Anaemia	3 (20%)
Leucocytosis (> 10 000/mm^3)	9 (60%)
Neutropenia-trombocytopenia	1 (6.6%)
Elevated ESR (> 20 mm/hr)	15 (100%)
CRP (> 5 mg/L)	6 (40%)
Roentgenographic findings	
Reticular densities	8 (53.3%)
Reticulonodular densities	5 (33.3%)
Patchy airspace consolidation	4 (19%)
Diffuse alveolar infiltrates	4 (19%)
Risk factors	
Exposure to VZV infection from their family	5 (33.3%)
Exposure to VZV infection from their neighbors	4 (26.6%)
Undetermined	6 (40%)
Clinical outcomes	
Non-complication recovery	14 (93.3%)
ARDS	1 (6.6%)
Mortality	–

VZP: varicella zoster releated pneumonia; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ARDS: acute respiratory distress syndrome

Persisting fever, fatigue, and cough episodes were major presenting symptoms at the time of admission in almost all patients. All patients were treated immediately after the diagnosis of VZP with intravenous acyclovir in a dose of 10 mg/kg every eight hours (600–900 mg intravenously, three times a day). Five of 15 patients (33%) presented with signs of respiratory distress and cardiac insufficiency (retractions, hepatomegaly and tachycardia), requiring digoxin therapy. In three patients, moderate anaemia was observed; one of them had neutropenia-thrombocytopenia at admission and developed cardiac and respiratory insufficiency requiring mechanical ventilation support and intensive care during follow-up. One patient needed intensive care admission (Figure). The same organism was cultured in both skin and blood culture of six patients. Nine (60%) patients developed secondary bacterial infection; all recovered with appropriate antibiotic treatment.

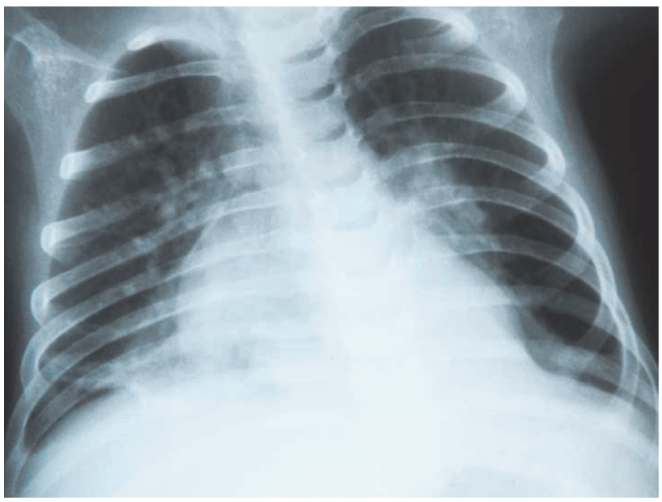

Figure: Chest radiography of the patient with severe disease. Note the perihilar patchy infiltrates and cardiomegaly superimposed on reticulogranular pattern.

DISCUSSION

Varicella pneumonia is 10 times more prevalent in the adult population than in the paediatric population after chicken pox infection. Previous studies have reported rates of pneumonia ranging from 7−25% in children hospitalized for varicella complications (1). Despite its role as an important cause of complications in the course of varicella infection, few studies deal with varicella associated pneumonia in children. However, it seems to be infrequent in children as suggested by the few reports on this topic. To date, most cases of varicella associated pneumonia have been reported in adult patients. In our study, the number of varicella associated pneumonia cases was 10.7%, which is similar to that in the previous study outlined above.

The epidemiology of the varicella differs in temperate and tropical climates. In most temperate climates, more than 90% of people are infected before adolescence, whereas in tropical climates the disease is acquired later in life and adults are more susceptible than children. Epidemiological variation might relate to the differences in population, density and risk of exposure, differences in transmissibility of the heat-labile varicella-zoster virus in hot, humid conditions, environmental and social factors, or a combination of all these factors. Varicella shows pronounced seasonality in temperate climates and most tropical climates, with peak incidence in the cooler, drier months during winter or spring. In temperate climates, studies have shown that disease incidence in the total population is in the range of 13–16 cases per 1000 people per year, with substantial year-to-year variation (2, 6). In the present study, children 2–6 years were more affected and in the winter and spring months; household contact with chicken pox should be accepted as risk factors for varicella pneumonia. The epidemiology of varicella pneumonia is observed to follow the epidemiology of primary chicken pox infection with respect to similar age and seasonal characteristics.

The clinical manifestations of VZP cover a wide spectrum, from asymptomatic to mild illness to death**.** The symptoms and the observations of chicken pox pneumonia start 1–6 days after the development of skin lesions. Cough, haemoptysis, chest-pain, difficulty in breathing and in severe cases, respiratory insufficiency and cyanosis may be observed in these patients. Prolonged fever and cough are considered to be indicators of pneumonia (6–8). In our study, all patients admitted with the complaints of persistent fever, fatigue and cough episodes during chicken pox infection were considered as VZP pneumonia.

The characteristic radiological aspect is reticular or nodular opacities with clear limits of 5–10 mm diameter and the consolidations formed by the aggregation of these masses. These are more frequent near the hilus and basal regions. However, the growth in the hilar lymph tissues and occurrence of pleural effusions is not frequent. Usually, these lesions start to disappear one week after the recovery of skin rashes. Sometimes, radiological observations may last for months. In some patients, calcifications of 2–3 mm diameter in both lungs may remain as sequelae (9). These radiological observations when observed together with skin lesions are used for diagnosis. Two-thirds of patients diagnosed with chicken pox pneumonia have normal lung radiograph, therefore, chickenpox pneumonia should be considered in all patients with respiratory complaints.

In these patients, high resolution computed tomography (HRCT) is an alternative for diagnosis. The HRCT findings of varicella pneumonia have been previously reported, including small, well-defined and ill-defined nodules, centrilobular nodules, nodules with surrounding ground-glass attenuation, patchy ground-glass attenuation and coalescence of nodules (10, 11). In our study, eight patients had reticular and five patients had reticulonodular densities in chest radiography which are characteristic in varicella pneumonia. Unfortunately, none of our patients had an HRCT.

The reported death rate for VZP without acyclovir treatment varies between 7.0 and 11.0%. Should pneumonia be suspected, chest roentgenogram and blood gas analysis should be requested, especially in immunocompromised patients. Intravenous acyclovir in a dosage of 10 mg/kg three times a day for 5–10 days is effective for VZP or other complications in children if started early. Although no controlled trials have been performed, acyclovir seems to prevent the development of severe acute respiratory failure and generally decreases the morbidity and mortality in severe cases of varicella. Intravenous acyclovir was well tolerated, and no drug related complications were observed in our study as well as others (2, 8, 12). Early antiviral treatment reduces developing complications, duration of hospitalization and mortality in patients with VZP.

The utilization of corticosteroids in chicken pox pneumonia should also be discussed (8, 12). Steroids were administered to six of the 15 patients with chicken pox pneumonia in the intensive care. The duration of hospitalization and inten-

sive care stay of patients treated with steroids were statistically significantly shorter. No mortality was observed in that group (13). Moreover, further controlled random studies on larger patient populations are required.

In patients with VZP, late diagnosis and delayed treatment, various complications and respiratory insufficiency may develop.

The patients with respiratory insufficiency should be monitored in an intensive care unit, and followed-up closely for potential complications such as acute respiratory distress syndrome (ARDS). Treatment for acute respiratory failure due to VZVP depends upon the severity of the hypoxaemia. In mild or moderate hypoxaemia, the administration of oxygen *via* a simple face or Venturi-type mask will usually correct the hypoxaemia. Severe hypoxaemia may respond better to continuous positive airway pressure (CPAP) or noninvasive positive pressure ventilation *via* a special facemask. Continuous positive airway pressure has been tried successfully in patients with VZP. Although early cardiac support was given in a third of the patients due to signs of cardiac insufficiency at admission, only one patient developed cardiopulmonary insufficiency requiring mechanical ventilation (8, 12). In our study, ARDS developed in one case. In particular, when respiratory distress develops in patients with varicella zoster, they should be monitored in an intensive care unit and early intubation and close monitoring can prevent mortality and complications.

The recommendation of chicken pox vaccination in routine vaccination programmes has led to a dramatic decrease in the incidence of the disease and in the rate of hospitalization and death in relation to chicken pox. Effective vaccination programmes in some countries have been reported to successfully eradicate severe complications of chicken pox in the paediatric population. However, the major concern about this vaccination intervention is that the increasing percentage of chronic diseases in the adult population, and signs of decreasing antibody titers formed after varicella vaccination with advancing age may increase the risk of serious varicella zoster virus associated infections in later decades (3, 14).

Our study has some limitations. First, it is a retrospective study with its drawbacks and biases. Secondly, the number of the sample size was small. Lastly VZV has not been verified by the polymerase chain reaction and none of patients had HRCT findings for VZP.

CONCLUSION

In conclusion, VZP should be considered in patients with prolonged fever and accompanying cough in patients having chicken pox. Children with severe VZP must be treated in the ICU. Early diagnosis and early treatment using acyclovir will reduce both mortality and potential complications. Besides all of these, long-term effects of mass vaccination programmes in populations should be evaluated carefully and continually.

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