Presentation and outcome of varicella pneumonia in adults

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Chickenpox (varicella), caused by the DNA virus varicella zoster virus, is a highly infectious and common disease in childhood. The disease has a high attack rate of approximately 90% within 2 weeks among household contacts. Consequently most adults in developed countries have experienced infection during childhood and retain life-long immunity. Although a trivial illness in childhood it carries a 25-fold greater risk of complications in adults compared to children.[1] These include respiratory, neurologic, renal and hematologic complications. Varicella pneumonia (VP), first described in 1942[2] is the most common complication and the leading cause of death in adults with chickenpox. Mortality is reported to range from 10-30%[1] and can be as high as 50% in patients admitted to intensive care units.[3]

Records of 12 adults admitted to Riyadh Medical Complex, Riyadh, Kingdom of Saudi Arabia with a diagnosis of VP were studied. Demographic data, clinical features, contact history, risk factors for VP, laboratory investigations, radiologic changes, treatment and outcome were documented. The mean age was 35.6 years (range 22-45). There were 10 males (83.3%) and 7 Saudis (58.3%). Seven patients were smokers and one was on immunosuppressants after a kidney transplant. The mean duration between the onset of rash and respiratory symptoms was 3 days (range 0-7). Three patients had no respiratory symptoms on presentation while 2 had symptoms at the onset of rash. In 5 patients (41.67%) there was no clear contact history. None of the patients had prior vaccination against varicella. All patients were febrile on presentation. Cough (91.7%), sputum production (58.3%), and dyspnea (50%) were the most common symptoms. Three patients (25%) had no detectable signs on examination of the chest. None of the patients had neurological or renal complications. Thrombocytopenia was noted in 11 patients (91.7%) but none had bleeding events. Leucocytosis was present in 2 cases, both of whom had an evidence of super-added bacterial infection. Although transaminases were elevated in all there were no clinical hepatitis in any of them except for one patient. Bilateral nodular or interstitial infiltrates were noted in 10 patients (83.3%) on chest radiography with the lower zones being involved in all patients. The right lung was involved in all cases. Eight patients (66.67%) had hypoxia on presentation. **Table 1** gives the details of the clinical features and investigations of cases and **Figure 1** shows the chest radiograph of patient 9. All patients received oxygen supplementation in addition to intravenous acyclovir at a dose of 10mg/kg body-weight. Two patients received corticosteroids and, in spite of poor clinical state and the presence of super-added bacterial infection, made unremarkable recovery. The mean duration of stay was 8.67 days (range 1-28). Two patients (16.67%) died on days 1 and 2 of admission.

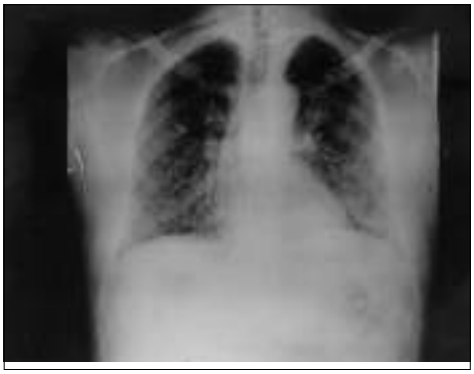

Figure 1 - Chest radiograph showing the characteristic diffuse nodular infiltrates of varicella pneumonia.

There is an evidence that the incidence of varicella zoster infection in adults is increasing over the last 2 decades with proportionately more deaths occurring in adults.[4] Several risk factors for the development of VP have been identified. These include male gender, smoking, chronic lung disease, pre-existing neoplasm, immunosuppression and pregnancy. The findings in our study are in consonance with earlier studies. Males are more at risk from VP probably due to the higher prevalence of smokers among this group. All patients in this study were smokers. Smoking is an important risk factor due to its effect on the nasal mucosa leading to enhanced primary viremia and a higher possibility of pneumonia. It has also been shown that smoking renders alveolar macrophages more susceptible to infection by herpes viruses. Thus, in 2 studies, 23 of 53 patients who smoked developed pneumonia compared to one of 43 patients who did not.[5,6] Household contacts, usually children, were responsible for the infection in 58.3% of our cases. Close contact with a patient's child has recently been identified as an independent risk factor for VP in adults. This is believed to be due to the larger infecting dose due to the closer contact and therefore an enhanced primary viremia. Children who contract chickenpox from their siblings also tend to have more severe disease, as do patients who contract the disease from index cases. Respiratory

Table 1 - Clinical presentation, treatment and outcome in 12 patients with *Varicella pneumonia.*

Nationality and patients number	Gender/ Age	Risk factors	Duration of rash before respiratory symptomes (days)	Contact history	WCC/ PLC	LFTS	ABG's	CXR	Sputum cultures	Treatment	Duration of stay days
1) Indian	42/M	Smoker	3	Unknown	6.4/76	AST 226 ALT 149	pH 7.41 PO_2 241.3 PCO_2 31.7 SAT 77.4%	Bilateral lower and mid zone infiltrates	Negative	Acyclovir Antibiotics	11
2) Nigerian	34/M	Smoker	0	Household contact	7.5/132	AST 66 ALT 119	pH 7.41 PO_2 67.4 PCO_2 30.8 SAT 93%	Bilateral lower zone infiltrates	Negative	Acyclovir Antibiotics	5
3) Saudi	22/M	Smoker	7	Unknown	8.4/130	AST 68 ALT 83	pH 7.4 PO_2 97 PCO_2 31.4 SAT 93.8%	® lower zone infiltrates	*Staphylococcus aereus*	Acyclovir Antibiotics	10
4) Saudi	30/F	Post-renal transplant	2	Household contacts	5.7/130	AST 41 ALT 47	pH 7.27 PO_2 98.2 PCO_2 41.1 HCO_3 18.6 SAT 97%	® lower zone infiltrates	Negative	Acyclovir Antibiotics	6
5) Saudi	30/M	Smoker	1	Household contact	4.5/137	AST 62 ALT 54	pH 7.37 PO_2 83 PCO_2 33 SAT 95%	Bilateral lower zone infiltrates	Negative	Acyclovir Antibiotics	6
6) Indian	28/F	Nil	0	Household contact	9/91	ASTu	pH 7.45 PCO_2 32.1 PO_2 45.2 SAT 71.4%	Bilateral infiltrates R>L	*Pseudomonas*	Acyclovir Antibiotics	7
7)Bangladeshi	45/M	Smoker	0	Casual contact	7.3/115	AST 63 ALT 113	pH 7.46 PO_2 73.9 PCO_2 25.5 SAT 95.2%	Bilateral infiltrates LZ+MZ	Negative	Acyclovir Antibiotics	28
8) Saudi	31/M	- -	3	Unknown	4.4/134	AST 71 ALT 50	pH 7.42 PO_2 61.7 PCO_2 32.8 SAT 91.8%	Bilateral modula infiltrates lower zones R>L	*Haemophilus influenzae*	Acyclovir Antibiotics	7
9) Saudi	38/M	Smoker	4	Casual contact	11.4/211	AST 149 ALT 182	pH 7.43 PO_2 46.0 PCO_2 28.3 SAT7 5.4%	Bilateral diffuse infiltrates	*Pseudomonas*	Acyclovir Antibiotics	1*
10) Saudi	35/M	Smoker	0	Unknown	4.6/106	AST 81 ALT 172	pH 7.42 PCO_2 26.6 PO_2 58 SAT 90.3%	Bilateral modular infiltrates LZ+MZ	*Klebsiella*	Acyclovir Antibiotics	2*
11) Saudi	44/M	- -	6	Unknown	5/98		pH 7.37 PO_2 41.3 PCO_2 27.2 SAT 75%	Bilateral LZ infiltrates	*Staph aureus*	Acyclovir Methyl prednisolone Antibiotics	9
12) Yemeni	44/M	--	0	Household contact	13.5/119		pH 7.50 PO_2 47.16 PCO_2 37.5 SAT 87%	Bilateral MZ+L Z infiltrates	*Staphylococcus aereus*	Acyclovir Antibiotics methylpredni solone.	12

*died, M - Male, F- Female, LFTs - liver function tests, ALT - alanine transaminase, AST - aspartate transaminase, R - right, L- left, LZ - lower zone, MZ - middle zone,, CxR - chest radiograph ABG - arterial blood gases, WCC - whitecell count, PLC - platelet count,

symptoms may precede, coincide with or present after the rash. The mean period between the onset of rash and respiratory symptoms is 0-4 days. The cardinal symptoms of pneumonia in this study were fever, cough and dyspnea. The persistence of fever and the development of new onset cough when new lesions are still erupting are considered to be the best indicators of VP. Three patients (25%) in this study presented with hemoptysis. Although this symptom seems to be common, there is a need to ensure that certain sinister causes of hemoptysis are considered and if necessary, excluded. These include pulmonary embolism (a consequence of immobility) and bronchogenic carcinoma (in smokers) among others. The radiological sign of VP is diffuse nodular infiltrates that tend to be discrete at the periphery and to coalesce towards the hila and bases of the lungs as seen in **Figure 1**. Hilar lymph node enlargement may be seen although this may be masked by the coalescence of infiltrates in that region. Pleural effusion is uncommon and never large. Clearing of radiologic shadows usually takes from 9 days to several months. Widespread miliary foci of calcification may follow VP and, although a common examination question, occurs in only 1.7% of patients with presumed VP and approximately one in every 2000 chest radiographs in the general population. In general, radiologic changes are far more common than symptoms.

Approximately 91.7% of our patients had thrombocytopenia (platelet count of <150,000/mm^3) on admission, which subsequently normalized and was not associated with bleeding. Thrombocytopenia is believed to be due to the direct effect of the virus on platelets leading to shortening of the platelet survival rather than to immunologic mechanisms, which manifest at a later stage. Biochemical hepatitis is a common phenomenon but clinical hepatitis with liver failure is rare in immunocompetent patients. In adults, alanine transaminase was found to be higher in patients with VP and the only factor strongly associated with severe disease. It is therefore prudent to evaluate the liver functions in patients at risk of severe disease and VP in particular. All our patients received acyclovir (ACV) intravenously within 24 hours of admission. It has been recommended for use in immunocompetent adults with varicella. In a multicenter retrospective controlled study, Haake et al[7] demonstrated that early administration of ACV (namely within 36 hours of admission) is associated with a reduction of fever and tachypnea and improvement in oxygenation in healthy adults with VP. The early oral administration of ACV has also been shown to reduce the time of cutaneous healing, fever and severity of symptoms. Recent studies in other centers in which intravenous ACV was used early in the course of management have demonstrated substantial reduction in mortality ranging from 3.3-6.7%. Even in patients requiring intensive care, the mortality has substantially decreased from 13.6-25%.

The use of adjuvant steroids is controversial as there is, to date, no controlled study evaluating this aspect of therapy. A recent uncontrolled study has however demonstrated that patients who received steroids had shorter hospitalization, shorter ICU stay and lower mortality compared to those who did not.[5] Controlled studies are obviously needed before categorical recommendations can be made regarding the routine use of steroids. Four of our patients underwent mechanical ventilation. Continuous positive airway pressure (CPAP) ventilation has been proven to be an effective modality and should be considered before resorting to mechanical ventilation in patients with progressive respiratory fatigue. Where conventional ventilation proves refractory, extracorporeal membrane oxygenation (ECMO) may be used.

Emphasis should be placed on prevention of varicella especially in patients at increased risk of VP. Varicella vaccine has been shown to prevent or modify varicella infection if used less than 3 days after exposure. Similarly acyclovir and varicella zoster immunoglobulins (VZIG) are also increasingly being used as prophylaxis/treatment during the incubation period in order to prevent or modify the disease in patients at high risk of complications. Varicella zoster immunoglobulins is particularly useful as postexposure prophylaxis in pregnant patients in whom varicella vaccine is contraindicated.

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References

1. Centers for Disease Control. Varicella-zoster immune globulin for the prevention of chickenpox. ***MMWR Morb Mortal Wkly Rep*** 1984; 33: 84-90, 95-100.
2. Waring JJ, Neuberger K, Geever EF. Severe forms of chickenpox in adults. ***Arch Intern Med*** 1942; 69: 384-408.
3. Mer M, Richards GA. Corticosteroids in life threatening varicella pneumonia. ***Chest*** 1998; 114: 426-431.
4. Gray GC, Palinkas LA, Kelley PW. Increasing incidence of varicella hospitalizations in United States Army and Navy personnel: are today's teenagers more susceptible? Should recruits be vaccinated? ***Paediatrics*** 1990; 86: 867-873.
5. Grayson ML, Newton-John H. Smoking and varicella pneumonia. ***J Infect*** 1988; 16: 312.
6. Ellis ME, Neal KR, Webb AK. Is smoking a risk factor for pneumonia in adults with chickenpox? ***Br Med J (Clin Res Ed)*** 1987; 294: 1002.
7. Haake DA, Zakowski PC, Haake DL, Bryson YJ. Early treatment with acyclovir for varicella pneumonia in otherwise healthy adults: Retrospective controlled study and review. ***Review of Infectious Diseases*** 1990 12: 788-798.