Acute arterial thrombotic purpura complicating varicella and the role of hyperbaric oxygen as an adjunctive therapy

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Chickenpox is a common infectious disease of the pediatric age group with rare complications such as hemorrhagic varicella and arterial thrombotic purpura. Medical support is the mainstay of treatment in such cases but for the rescue of necrotic tissues, hyperbaric oxygen (HBO) therapy should be applied in addition to anticoagulant intervention. We report an infant with acute arterial thrombotic purpura which developed after varicella eruption and who made full recovery with the help of HBO as an adjective treatment modality. Fresh frozen plasma and low molecular weight heparin were given for prolonged prothrombin time and thromboemboli on the 2nd-4th digits of his right foot. Protein C, protein S and factor V levels were found to be normal in our patient. Necrotic lesions on the toes regressed with repeated HBO treatment and amputation was not needed.

Key words: chickenpox, thrombotic purpura, hyperbaric oxygen therapy.

Chickenpox is a common contagious disease usually of childhood that can be seen at any age, and which is the result of primary infection with varicella-zoster virus (VZV). Although it usually has a good prognosis, hemorrhagic varicella and thrombotic purpura are well-defined serious but, fortunately, rarely seen forms of the disease. Besides medical treatment, hyperbaric oxygen therapy has increased options available to these patients, as the field for application of this method has apparently expanded with recent advances in technology. In this study, we present a case with acute thrombotic purpura during the course of chickenpox, which is reported very rarely, and discuss our modality of treatment.

Case Report

An eight-month-old infant was admitted to our clinic with the complaint of pruritic rash, beginning on his face and scalp one week previously and spreading throughout the whole body, eventually becoming crusty. This was followed by swelling of his right ankle for two days. Chickenpox was diagnosed with a typical rash and arthritis was considered secondary to infection. On the second day of admission swelling of the ankle regressed but pallor, hypothermia and then painful ecchymotic lesions developed on the second, third and fourth digits of the affected foot. Within less than 48 hours necrosis evolved on those digits and acute arterial thrombotic purpura was diagnosed as a complication of varicella. After presentation of thrombotic purpura, the patient’s general status rapidly worsened, with axillary (39.2°C) fever, respiratory distress, metabolic acidosis, heptomegaly and oliguria. Moderate anemia (Hb: 7.4 g/dl), leukocytosis (with neutrophil dominance), and severe thrombocytopenia (11,000/mm³) developed. C-reactive protein was found (++) qualitatively and erythrocyte sedimentation rate was 75 mm/hour. Prothrombin time prolonged to twice its normal value, whereas activated partial thromboplastin time was within normal range. The other biochemical analyses were insignificant.
After taking blood for hemoculture, cyclovir was prescribed for specific infection in addition to wide-spectrum antibacterials. Supportive therapy was given as appropriate fluid replacement for metabolic acidosis, vitamin K and fresh frozen plasma for abnormal prothrombin activity, and low molecular weight (LMW) heparin (nadroparin) for thromboemboli. Hyperbaric oxygen (HBO) therapy for necrotic digits was applied in a monoplace pressure room by oxygen cap under 2.5 atmosphere (ATA) pressure. During the first 10 days, therapy was given for two-hour periods with at least four-hour intervals. It was, continued for 60 minutes, six days a week. As protein C (Prot C) and protein S (Prot S) deficiencies and alteration of factor V (factor V Leiden mutation) can lead to a tendency to thrombosis, these parameters were analyzed in our patient. Prot C was measured as 0.42 u/ml and Prot S as 0.35 u/ml (normal ranges are 0.17-0.53 u/ml and 0.12-0.60 u/ml, respectively). The result of factor V Leiden mutation test was negative.

On the sixth day of admission, the platelet count increased to 100,000/mm³, and abnormal laboratory results normalized. No infectious agent could be isolated on cultures. The patient improved clinically and hematologically, and thrombopurpuric lesions showed no recurrence. The necrotic regions regressed to the pulpa of the affected digits at the end of the fourth week of HBO therapy. After 40 hours of HBO therapy overall, the whole necrotic region regenerated and amputation was not required.

Discussion

Chickenpox is seen during pediatric age in 90-95% of cases, and the systemic symptoms of the disease are generally mild in normal children; complications are observed infrequently. Purpura fulminans and necrosis localized to the extremities have been reported extremely rarely. Thrombotic purpura due to chickenpox can be seen at any age of childhood and no sex predilection is present. It has also been reported in adults. It appears suddenly and primarily on lower extremities approximately one week after the eruption of rash. There are thrombotic signs of affected capillaries and venules. In our case, the rapid development of necrosis preceded by pallor and hypothermia alerted us to the diagnosis of acute arterial insufficiency.

Fasciotomy and amputation may be implied for necrosis and tissue loss in cases with severe ischemia not treated properly. Disseminated intravascular coagulopathy (DIC) leads to thromboemboli in small vessels; intense capillary leakage and bleeding into tissues may occur as a result of endothelial damage. Therefore, early anticoagulation therapy is essential in purpura fulminans.

Protein S, Prot C and factor XII deficiency secondary to varicella infection have been implicated in pathogenesis. Acquired Prot S deficiency may be caused by a specific antibody against the protein or as a result of DIC. The transient character of deficiency has been shown with repeated enzyme studies. Factor Va in the coagulation cascade is inactivated by activated Prot C; the function of the latter is impaired in persons with the factor V Leiden mutation. This alteration confers increased risk of venous thrombosis. The natural anticoagulants, Prot C and Prot S, and genetic search for mutation of factor V were assessed normal in our case. Thus, we could not find any reason to explain the acute thrombosis other than the varicella infection itself.

Various treatment modalities have been discussed in the literature. Antithrombin III and Prot C concentrates may be effective if any of these factors are proven to be deficient. Intraarterial thrombotic treatment modalities with tissue plasminogen activator or urokinase have been applied successfully in patients with purpura fulminans. In our case, progression of ischemia was successfully impeded by early administration of LMW heparin treatment. There are several suggestions for the dosage of heparinization.

Hyperbaric oxygen therapy is a method of treatment applied in a closed pressure room under more than 1 atmosphere (1.0 ATA = 760 mmHg) pressure by giving 100% oxygen intermittently with a mask or hood. This mode of management has found many applications in medicine, such as for children with cerebral palsy, carbon monoxide poisoning or DIC. Using this method, sufficient oxygenation of the affected tissues will be assured without oxyhemoglobin being required. Dissolved oxygen in plasma can be utilized directly in cells. Using HBO therapy it is likely to sustain life without hemoglobin. On the other hand, angiogenesis is stimulated by hypoxia. Thus, application of hyperbaric oxygen for 2-4 hours
Hyperbaric oxygen therapy requires special equipment and trained personnel. The most satisfactory response will be achieved when this modality of treatment is applied together with the specific and supportive therapy. We found no report of use of HBO therapy in the literature for primary varicella other than a series of 12 pediatric patients with this infection complicated by group A Streptococcus necrotizing fasciitis. The use of HBO therapy in treatment of varicella infection with acute thrombocytopenia makes our case of interest. Report of this uncommon morbidity seen during the course of chickenpox will be of great assistance in deciding the best treatment.

REFERENCES


