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Chapter 7

A child with infant ALL and severe varicella-zoster pneumonia

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A little boy, presented at the age of 6 months with infant leukemia. He was started on the acute lymphoblastic leukemia protocol for children <1 year and had a good response. After the induction period he was in complete remission. After one year of intensive chemotherapy he started his maintenance therapy, consisting of dexamethasone 6mg/m²/day x 14 days with vincristine 1.5 mg/m² on day 1 and day 7 intravenously followed by 5 weeks oral 6-mercaptopurine 50 mg/m²/daily and methotrexate 20 mg/m² weekly, after this the cycle repeated.

He was on maintenance therapy for 3 months when he developed varicella zoster vesicles all over the body, but otherwise was not ill at that stage. It was known that this boy was IgG negative for varicella zoster. The contact of this varicella infection was not known, therefore he did not receive the passive immunization within 72 hours of zoster-immunoglobulin. On developing the vesicles he was started on high dose oral aciclovir and was admitted to hospital. Initially he was an otherwise well toddler except for the extensive vesicles. He did not improve and developed severe abdominal pain 10 days after the first vesicles had appeared. He was not vomiting, no diarrhea, and the pain did not seem related to the food intake. He was however not well at this stage, the vesicles were turning hemorrhagic (fig 1), and he was agitated, he did not want to walk anymore. He was started on i.v aciclovir and because of the possibility of secondary infection Augmentin® i.v. was started.

The following day this little boy deteriorated and was distressed. His respiration rate was 50/ min and on auscultation bilateral rhonchi were heard. His eyes were edematous and he was very irritated. He deteriorated rapidly that day and had to be transferred to the intensive care unit to be mechanically ventilated. At this stage he had an extreme high temperature and was neutropenic, therefore he was started on a cephalosporin and gentamycine. His chest X-ray showed bilateral infiltrative changes which progressed from fairly visible changes to a total white out (fig 2). The viral load of varicella measured with a PCR in blood was extremely high 1600.000c/ ml, also the PCR from the broncho-alveolar lavage was positive for VZV, therefore it was clear that the complication this boy had was a varicella-pneumonia.

Figure 1: skin lesions of the varicella zoster primary infection. Some lesions show a hemorrhagic aspect.
While on conventional ventilation he deteriorated despite pressures of 32/20 mm Hg, and FiO2 of 100%. Therefore he was started on high frequency oscillation ventilation. He reacted well to this form of ventilation, and could be extubated after 8 days. The viral load very slowly decreased. Slowly he improved and i.v. therapy was continued for 4 weeks, then his viral load showed 2500 c/ml and at this stage his therapy was switched from intravenous to oral therapy famciclovir.

**Figure 2:** Chest X ray presenting the varicella zoster pneumonia at time of HFO ventilation.

**Figure 3:** Viral load longitudinal data, showing that T cell response recovered after nearly one year and at that stage the viral load was 0.
which was continued another 9 months. Then he did show an adequate T-cell immune-response, and it was decided to stop the oral treatment (Fig 3).
He has done very well since. He finished his chemotherapy and has been in complete remission for over 2 years after stop of the chemotherapy.

Varicella pneumonia
This represents a severe complication of varicella, mostly seen in the immuno-compromised patients and in adults. This severe complication carries a mortality of 10-30% (1). However, when respiratory failure occurs and mechanical ventilation is necessary, mortality is as high as 50% (2,3). Although we know that aciclovir has limited efficacy it remains the first-line therapy (1). Varicella pneumonia causes an interstitial pneumonitis with impairment of pulmonary gas-exchange. The pneumonitis is probably due to host response rather than virally mediated tissue injury.
Corticosteroids may modify the inflammatory response. This results in a decrease in the release of macrophage-derived pro-inflammatory cytokines like interleukin-1 and Tumor necrosis factor-α (4, 5) and a decrease in production of membrane-derived products like leukotrienes and prostaglandins, leading to less edema and improved vascular permeability. Therefore it is recommended to start steroids in addition to anti-viral therapy and other supportive care measurements. This little boy did not cope on conventional chemotherapy, fortunately he responded to high frequency oscillation ventilation. Another form of ventilation these patients have been responding to fairly well is ECMO ventilation (extracorporeal membrane oxygenation). Early recognition of pulmonary failure and rapid institution of ECMO are critical in the successful management of this complication of varicella zoster infection. ECMO as such does little to reverse the course of the underlying disease. It’s role is one of support, during which time the lungs are rested and allowed to recover (6, 7).

References