

A Caucasian male was delivered vaginally (gestational age: 26 weeks; weight 825 g) and showed signs of respiratory insufficiency, necessitating artificial ventilation for 39 days. On the 10th day after birth he developed a maculopapular rash which became scaly and later pustular. There were no signs of pulmonary infection or other organ involvement. After 1 week, cultures of the pustular cutaneous lesions yielded *A. fumigatus*. Histology with visualization of hyphae was not performed. Bacterial and viral cultures of blood, urine, skin, sputum and the conjunctival swab were sterile. Serologically, concomitant virus infections were not demonstrated. At that moment ophthalmological examination was not performed. The primary skin lesions were treated locally. Broad spectrum antibiotics (flucloxacillin and amoxicillin) were added when pustular lesions developed. After 3 days with broad spectrum antibiotics his clinical condition deteriorated and antifungal treatment (amphotericin B and flucytosine) were started. There was a gradual clinical improvement and the skin lesions healed, indirectly supporting the clinical diagnosis of *Aspergillus* disease. After 4 weeks, intravenous amphotericin B therapy was stopped, without signs of recurrence. Three weeks later during routine ophthalmological examination for retinopathy of prematurity, haziness of the media was seen. Ultrasonography of the eyes showed irregularities of the retina. Vitrectomy was performed and showed a distorted retina with microabscesses. The pus obtained from the vitreous cavity and retinal microabscesses showed no bacterial or fungal growth. Again histological sections were not performed. Thus possible fungal elements could not be looked for. Despite these negative findings a presumptive diagnosis of *Aspergillus* endophthalmitis was made based on the history of the skin lesions with positive cultures of *Aspergillus*, which healed with systemic antifungal treatment, and the known poor intraocular penetration of amphotericin B [3]. The subsequent clinical course was complicated by a patent ductus arteriosus, bronchopulmonary dysplasia and intracranial haemorrhage.

This case shows that in the preterm neonate with a severe or an expanding skin lesion the presence of *A. fumigatus* should be considered. To prove the diagnosis histology is obligatory. Ophthalmological examinations should be performed in preterm infants with suspected fungal infection in order to detect possible fungal endophthalmitis.

References

1. Granstein RD, First LR, Sober AJ (1980) Primary cutaneous aspergillosis in a premature neonate. *Br J Dermatol* 103: 681
2. Green WR, Bennet JE, Goos RD (1965) Ocular penetration of amphotericin B. *Arch Ophthalmol* 73: 769-775
3. Schwartz DA, Jacqueline M, Chawla HS (1988) Disseminated neonatal aspergillosis: report of a fatal case and analysis of risk factors. *Pediatr Infect Dis J* 7: 349-353

Vancomycin intoxication in a preterm neonate

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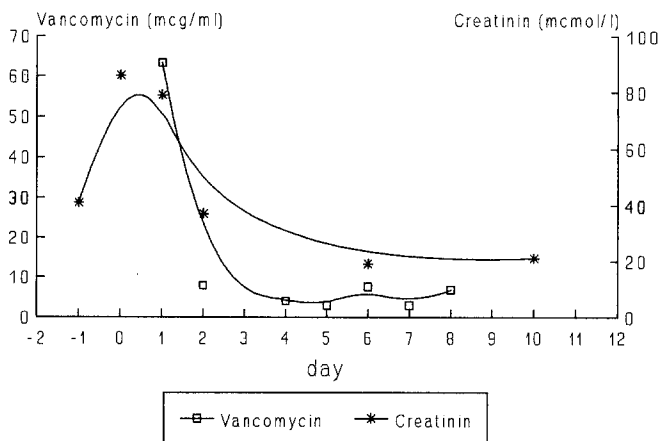
Sir: Neonatal bacterial sepsis is associated with a high risk of mortality and morbidity, especially in preterm infants.

Vancomycin therapy is usually started when septicaemia, presumed to be caused by multiple resistant *Staphylococcus epi-*

dermidis, is suspected. At present, there are no data available concerning possible side-effects of vancomycin in the premature neonate, related to serum concentrations. Nephrotoxic and ototoxic side-effects are reported in older children. Ototoxicity is reportedly caused by damage to the sensory cilia in the cochlea and is irreversible. It has been observed with serum concentrations of 80-100 mg/l [1, 2]. The nephrotoxic side-effects in older children are reported to be reversible and related to serum levels > 40 mg/l; the incidence is unknown [1, 3, 4]. We here describe acute vancomycin intoxication in a premature neonate.

A caucasian female was born at a gestational age of 29.3 weeks, weighing 1520 g. In the 4th week of life septicaemia was suspected. Tobramycin (2.5 mg/kg every 18 h) and vancomycin (15 mg/kg every 12 h according to the regimen suggested by Schaad et al.) were started [5]. Blood cultures grew *S. epidermidis*. Twenty-four hours after the start of therapy the child became oliguric and serum creatinine doubled from 41 to 86 µmol/l. Antibiotics were immediately discontinued. Serum vancomycin concentration was elevated (63.3 mg/l 12 h after becoming oliguric) while tobramycin concentration was normal (1.8 mg/l); so we concluded that the renal failure was secondary to vancomycin toxicity. The course of the serum concentrations of vancomycin and creatinine are shown in Fig. 1. During the episode of elevated serum vancomycin concentration no further clinical or biochemical abnormalities were noted. Repeated brainstem evoked auditory potentials showed no cochlear hearing impairment. Two months after the event, no nephrological abnormalities were demonstrated either biochemically or by ultrasonography.

This case suggests that vancomycin overdosage can produce reversible renal impairment in preterm neonates. Creatinine concentration and drug levels should be carefully monitored. If oliguria is observed vancomycin should be immediately withdrawn until serum creatinine and drug concentration are available.



day 0: start anuria, overdose
day 8: restart vancomycin therapy

Fig. 1. The course of vancomycin and creatinine serum concentrations in the days before and after vancomycin intoxication

References

1. Bailie GR, Neal D (1988) Vancomycin ototoxicity and nephrotoxicity - a review. *Med Toxicol* 3: 376-386
2. Brummett RE, Fox KE (1989) Vancomycin- and Erythromycin-induced hearing loss in humans. *Antimicrob Agents Chemother* 33: 791-796
3. Dean RP, Wagner DJ, Tolpin MD (1985) Vancomycin/aminoglycoside nephrotoxicity. *J Pediatr* 106: 861-862
4. Odio C, McCracken GH, Nelson JD (1984) Nephrotoxicity associated with Vancomycin-aminoglycoside therapy in four children. *J Pediatr* 105: 491-493
5. Schaad UB, McCracken GH, Nelson JD (1980) Clinical pharmacology and efficacy of Vancomycin in pediatric patients. *J Pediatr* 96: 119-126