

SHORT REPORT

Chitotriosidase in neonates with fungal and bacterial infections

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Increased plasma and/or urine chitotriosidase activity was found in neonates with fungal infection changing in parallel with their clinical condition. Increased levels were also found in neonates with bacterial infection. Chitotriosidase activity increase is not a response specific to fungi, but serial assays could monitor the course of neonatal fungal infection.

Human chitotriosidase is a fully active chitinase, specifically expressed by activated phagocytes. Observations support its possible role in the defence against chitin containing pathogens, such as fungi. The human gene is homologous to other chitinase genes found in nature. Approximately 6% of the general population cannot synthesise an active enzyme.^{1–3}

Increased chitotriosidase activity was reported in a neonate with systemic *Candida albicans* infection.⁴ Here we report the levels of chitotriosidase in a number of neonates with fungal and bacterial infections.

METHODS

Eight neonates with fungal (group A) and 15 with bacterial infection (group B) were studied. Group A neonates I, II, and IV–VII had blood cultures positive for *C albicans*, also cultured post mortem from the peritoneal fluid, tracheal tube, and umbilical catheter of neonates II and IV. Neonate III gave a positive blood culture for fungus identified as *Aspergillus niger* through the detection of fungus DNA (PCR)⁵ and elevated antigen titre (Platelia Aspergillus, Sanofi Diagnostics Pasteur, Marnes La Coquette, France).

Antifungal treatment (amphotericin B liposome and flucytosine) was initiated following the diagnosis of fungal infection in all neonates except II, III, and IV who died around the time of diagnosis. Of the treated neonates, four (V–VIII) recovered and one (I) died in septic shock (table 1).

Group B comprised neonates with positive blood culture for *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Serratia marcescens*, or *Citrobacter* sp.

Chitotriosidase was assayed in plasma and urine samples from all neonates as follows: group A, at least four times, at weekly intervals; group B once only, on diagnosis.

This study was approved by the Ethical Committee of the Institute of Child Health.

RESULTS

Increased activity of chitotriosidase in plasma and/or urine was observed in 7/8 of group A neonates on diagnosis of the fungal infection.

Serial assays showed changes in chitotriosidase activity, more evident in urine, in parallel with the clinical condition (fig 1 and table 2). One neonate (VIII) had zero activity in both biological fluids at all time points studied (table 1).

Increased chitotriosidase activity was observed on diagnosis of bacterial infection in group B neonates. Three had increased activity in plasma and 12 in urine (1.9–12.5 and 1.5–40 times the upper normal values, respectively).

DISCUSSION

Chitinases are ubiquitous chitin fragmenting enzymes, identified in various organisms and involved in several biological processes including defence against chitin containing pathogens, such as fungi.⁶

Despite detailed characterisation of human chitotriosidase, its biological role is still unclear. Evidence suggests that it also plays a role in defence against fungi. Macrophages, one of the primary defences against fungal intruders, are the main source of chitotriosidase, which degrades both colloidal chitin and chitin in the cell wall of *C albicans*.¹ Increased activity has been reported in tissues and plasma of guinea

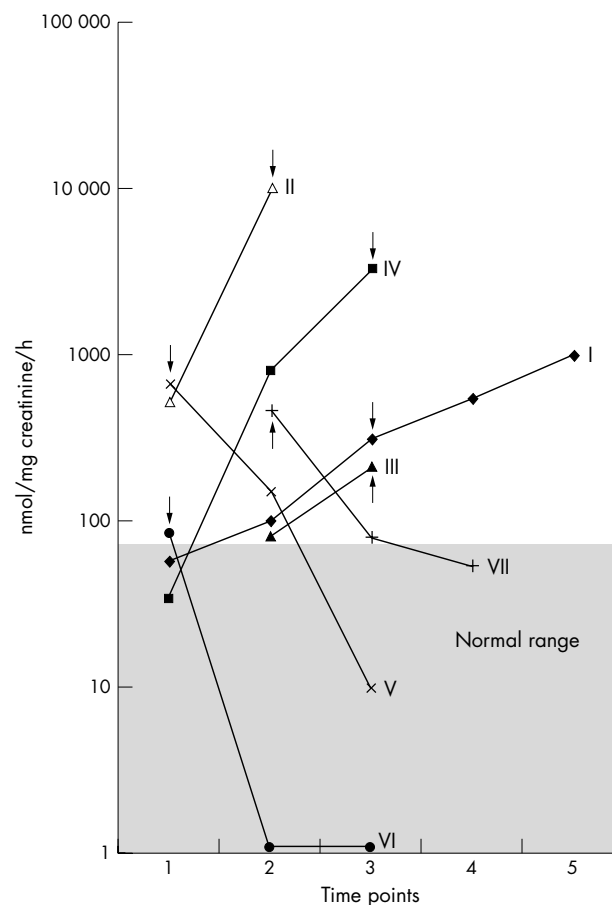


Figure 1 Chitotriosidase activity in urine of neonates with fungal infection (I–VII). Arrows indicate time of diagnosis of the infection.

Table 1 Case summaries of neonates and chitotriosidase activity on diagnosis of the fungal infection

Neonate	BW (g)	EGA (week)	Fungal species	Neonatal problems	Chitotriosidase	
					Plasma (nmol/ml/h)	Urine (nmol/mg creatine/h)
I	950	27	<i>C albicans</i>	RDS, apnea, IPPV, PDA, septic shock	59	312
II	720	25	<i>C albicans</i>	RDS, IPPV, IVH, PDA, BPD, NEC, DIC, ascites, septic shock	432	10 060
III	830	25	<i>A niger</i>	Asphyxia, RDS, IPPV, pneumonothorax, septic shock	32	210
IV	900	28	<i>C albicans</i>	RDS, IPPV, PDA, septic shock	123	3275
V	1000	29	<i>C albicans</i>	RDS, IPPV, PDA	46	661
VI	3620	Term	<i>C albicans</i>	Lethargy, seizures, meningitis, CT scan (+), EEG (-)	40	83
VII	3870	Term	<i>C albicans</i>	Renal failure, osteomyelitis	95	560
VIII	1750	Term	<i>C albicans</i>	Meconium staining, hypoglycaemia, abscess	0.0	0.0
Normal (n = 10)	-	-	-	-	0-48	0-70

BPD, bronchopulmonary dysplasia; BW, birth weight; DIC, disseminated intravascular coagulation; EGA, estimated gestational age; IPPV, intermediate positive pressure ventilation; IVH, intraventricular haemorrhage; NEC, necrotising enterocolitis; PDA, patent ductus arteriosus; RDS, respiratory distress syndrome.

Table 2 Chitotriosidase activity in urine (nmol/mg creatine/h) of neonates with fungal infection

Patient	Time point				
	1	2	3	4	5
I	56	100	312	550	1010
II	512	10 060			
III		80	210		
IV	34	808	3275		
V	661	150	10		
VI	83	2	2		
VII		560	80	54	

pigs infected by *Aspergillus fumigatus* and in plasma and urine of a neonate with *C albicans* infection.^{3,4} The present study, involving a larger number of neonates, also demonstrated increased activity, mainly in urine, in neonates with fungal infections. Improvement in their clinical condition was associated with a decline in chitotriosidase activity. Increased activity was also detected in neonates with Gram-negative and Gram-positive bacterial infections, indicating that increase in chitotriosidase activity is not a specific response to fungal infections but rather reflects phagocyte activation.

Fungal infections are an increasingly serious problem in neonatal intensive care units. Their diagnosis is often difficult, with a false negative culture rate of 20–50%. Early diagnosis is essential for survival, but often diagnosis is only established post mortem.⁷

Our results show that although increased chitotriosidase activity is not a response specific to fungal infection, it could, particularly in the absence of microbial infection, alert the physician to possible fungal infection. Furthermore, serial urine assays could be exploited for monitoring the response

of neonates to anti-fungal treatment. Studies of the behaviour of human chitotriosidase in relation to innate and acquired defence mechanisms are needed in order for its role to be elucidated.

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