SHORT REPORT

Transient lymphopenia in acutely unwell young infants

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The clinical outcome of 42 acutely unwell infants <3 months old with lymphopenia was retrospectively compared with that of 42 controls. Lymphopenic infants were significantly more likely to require active resuscitation and intensive care, independent of total leucocyte count, gender, degree of prematurity, and diagnosis.

As lymphocytes have a central role in orchestrating the immune response to environmental pathogens, lymphopenic infants might be expected to mount an inadequate protective immune response to common childhood illnesses and thus develop more severe disease.^{1–3} The degree of active medical intervention required by previously healthy infants or children who present with transient lymphopenia at the time of acute illnesses has, to our knowledge, not been previously studied. The perceived limited usefulness of the absolute lymphocyte counts compared with neutrophil counts among doctors means that physicians are likely to overlook this parameter when reviewing full blood counts on young children presenting with acute illnesses. In this study we examined whether active medical intervention of young infants who present with a significant lymphopenia is greater than that of infants with normal absolute lymphocyte numbers.

METHODS

A total of 229 infants <3 months old presenting acutely unwell to a regional children's hospital accident and emergency (A&E) department from May 1999 to April 2000, identified by reviewing haematology department full blood count records, were selected for this retrospective study. Children who were seen as planned admissions, or who had a known chronic illnesses, were excluded. Of the total cohort of 229 children, 42 (18%; 31 boys and 11 girls) had a lymphopenia, defined as a total lymphocyte count below the 3rd centile for children of this age group ($2.8 \times 10^9/l$) (lymphopenic group).³ A gender matched and randomly selected sample of the cohort who were not lymphopenic were studied as the control group. Clinical and laboratory data were obtained from the medical records. Leucocyte counts were determined using routine flow cytometry of peripheral venous blood samples.

RESULTS

Gender and gestational age at birth of the two groups were not different. None of the children had a past medical history of recurrent infections or immunodeficiency, nor were they being treated with glucocorticoids. All but two were admitted to hospital, with a median (interquartile range) length of stay in hospital of 5 (3–7) days. The median absolute lymphocyte count of the lymphopenic group was $1.8 \times 10^9/l$ (range 0.05 – $2.78 \times 10^9/l$); this was associated with a significantly lower total leucocyte count of $6.4 \times 10^9/l$ when compared with controls (lymphocyte count $6.3 \times 10^9/l$; total leucocyte count $11.5 \times 10^9/l$; $p = 0.0001$). The duration of lymphopenia was

Table 1 Treatment and outcome measures of study groups (univariate analysis)

	Lymphopenic group (n=42)	Control group (n=42)	p value*
Initial resuscitation	29 (69)	3 (7)	0.0001
Admission to PICU	26 (62)	1 (2)	0.0001
Mechanical ventilation	24 (57)	1 (2)	0.0001

Results expressed as number (percentage).
* χ^2 test.

studied in 26 infants and lymphocyte count returned to normal in all: within two days in 19 (73%) and within one week in all but one case (96%). The median neutrophil counts of the two groups did not differ significantly.

More infants in the lymphopenic group than in the control group had clinical features of an acute infection (88% v 52%; $p = 0.0001$). Significantly more lymphopenic infants than controls had respiratory syncytial virus bronchiolitis (33% v 5%; OR 10, 95% CI 2 to 47; $p = 0.004$). Blood cultures were positive in seven of the lymphopenic infants compared with none of the controls ($p = 0.006$). Of the 25 children with non-infective causes, 11 (44%) had pyloric stenosis; five (20%) had other gastrointestinal problems.

Acute resuscitation in the A&E department was required by 29 (69%) of the lymphopenic group (fluid boluses in eight, immediate intubation and fluid boluses in 19, cardiopulmonary resuscitation in two), compared with only three (7%) of the control group (fluid boluses in two, intubation and fluids in one; $p = 0.0001$). Twenty six (62%) of the lymphopenic group required admission to the paediatric intensive care unit (PICU) compared with only one (2%) of the control group ($p = 0.0001$; table 1). None of the children in the study died and no patients in either group were diagnosed as having severe combined immunodeficiency. The association between lymphopenia and need for resuscitative measures on presentation of infants to the A&E department remained significant (OR 29, 95% CI 5 to 175; $p = 0.0005$), even when absolute leucocyte count, gender, age, degree of prematurity, and whether the underlying diagnosis was infective or non-infective were taken into account. A lower total leucocyte count, male gender, and younger age were other independent factors associated with a significantly increased risk of infants requiring active resuscitation (table 2).

DISCUSSION

In this study we have shown for the first time, that previously well infants presenting to a paediatric A&E department with an acute illness are more likely to require any active resuscitation if they are lymphopenic. A significant proportion (90%) of these

Abbreviations: A&E, accident and emergency; CI, confidence interval; OR, odds ratio; PICU, paediatric intensive care unit

Table 2 Factors determining need for active resuscitation of infants presenting to an A&E department (multivariate analysis)

	Odds ratio	95% CI	p value
Lymphopenia/normopenia	27	5–175	0.0005
Absolute leucocyte count	0.81	0.66–0.99	0.03
Gender (male v female)	7	1–41	0.02
Age (wk)	0.74	0.57–0.97	0.03
Gestational age at birth	0.86	0.69–1.06	0.2
Infective v non-infective cause	0.86	0.10–3.44	0.6

Odds ratio (95% CI) using binary logistic regression of covariates.

lymphopenic patients required admission to a PICU. A number of confounding factors might be expected to influence the association between lymphopenia and the need for acute medical intervention. Males are thought to cope less well with illnesses than females, but the potential confounding effect of this factor was avoided by matching the study groups for gender. Possible confounding effects of age, gestational age at birth, and presenting diagnosis were excluded using multivariate analysis.⁴ Lymphopenia also appears to be associated with a poorer prognosis in non-infected as well as infected patients, in keeping with previous studies which have shown that up to 68% of adults in a surgical intensive care unit for management of acute trauma not associated with super added infection have significant lymphopenia.⁵ Further studies are required to determine whether lymphopenia in children requiring more active medical management is an epiphenomenon, or directly causes more severe disease.

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REFERENCES

- 1 **Lubin BH**. Reference values in infancy and childhood. In: Nathan DG, Oski FA, eds. *Hematology of infancy and childhood*. Philadelphia, PA: WB Saunders, 1987.
- 2 **Gossage DL**, Buckley RH. Prevalence of lymphocytopenia in severe combined immunodeficiency. *N Engl J Med* 1990;**323**:1422–3.
- 3 **Hague RA**, Rassam S, Morgan G, Cant AJ. Early diagnosis of severe combined immunodeficiency syndrome. *Arch Dis Child* 1994;**70**:260–3.
- 4 **Thomassen HV**, Boyko WJ, Montaner JS, et al. Absolute lymphocytosis associated with nonsurgical trauma. *Am J Clin Pathol* 1986;**86**:480–3.
- 5 **Grossbard LJ**, Desai MH, Lemeshow S, Teres D. Lymphocytopenia in the surgical intensive care unit patient. *Am Surg* 1984;**50**:209–12.

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