Increased serum IgE concentrations during infection and graft versus host disease after bone marrow transplantation

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SUMMARY Serum IgE concentrations estimated in 25 bone marrow transplant recipients during episodes of infection or graft versus host disease, or both, were raised not only in some patients with acute graft versus host disease but also in many patients with infection. Raised values were not seen in chronic graft versus host disease. The routine estimation of serum IgE in bone marrow transplant recipients had minimal value because of the lack of specificity of the IgE response.

Two major causes of morbidity and mortality in bone marrow transplant recipients are infection and acute graft versus host disease, which may be difficult to distinguish clinically and may also occur simultaneously.¹ There would be obvious value for any laboratory investigation that could be used in the differential diagnosis and monitoring of these complications.

Increased concentrations of serum IgE have been reported after allogeneic bone marrow transplant,² and in some patients the rise accompanied clinical and biochemical evidence of acute graft versus host disease. Later studies³ suggested that monitoring serum IgE concentrations might be helpful in reaching an early diagnosis of acute graft versus host disease. The IgE response is T cell dependent, however, and it is possible that disturbed T cell regulation resulting from infection, particularly viral, might also be associated with raised serum IgE concentrations in the bone marrow transplant recipients. If this were so, a raised serum IgE would not be a specific and early indicator of acute graft versus host disease.

In the present study serum IgE concentrations were investigated in bone marrow transplant recipients in relation to graft versus host disease and infection.

Patients and methods

Forty episodes of infection, acute graft versus host

disease, or both, were clearly documented in 25 of 35 bone marrow transplant recipients studied. Patients had been transplanted for acute leukaemia (12), aplastic anaemia (4), or inborn errors of metabolism (9). There were 23 children (age range 11 months–15 years) and two adults (both with acute leukaemia). Serum IgE concentrations were also measured in 16 patients with chronic graft versus host disease, diagnosed clinically and histologically, who had no evidence of infection.

IgE was measured by the Phadebas IgE PRIST method (Pharmacia Diagnostics AB, Uppsala, Sweden).

Serum samples were taken before transplantation and weekly after transplantation until discharge unless infection or graft versus host disease developed, when samples were taken on alternate days. Serum samples were taken from patients with chronic graft versus host disease when they were reviewed as outpatients (range 3 months–4 years after transplantation).

Results

Serum IgE concentrations were determined during episodes of bacterial, viral, or mixed or other infections, including fungal; in acute graft versus host disease with and without intercurrent infection; and in chronic graft versus host disease. The sites and causative agents of infections occurring in the absence or presence of acute graft versus host disease are shown in Tables 1 and 2 respectively.

In all but three of the bacterial, fungal, and pro-

Table 1 Infections occurring in the absence of acute graft versus host disease in bone marrow transplant recipients

Infection	Causative agent
Bacterial	
*Pneumonia	<i>Streptococcus pneumoniae</i>
*Pneumonia	<i>Streptococcus pneumoniae</i>
Pneumonia	<i>Streptococcus pneumoniae</i>
Pneumonia and septicaemia	<i>Streptococcus pneumoniae</i>
*Septicaemia	<i>Streptococcus faecalis</i>
Pneumonia and septicaemia	<i>Streptococcus pneumoniae</i>
Pyogenic abscess at lumbar puncture site	Unknown—responded to laminectomy and drainage
Viral	
*Encephalitis	Varicella zoster
*Hepatitis	Hepatitis B
*Hepatitis	Non-A non-B hepatitis
*Rash on thigh	Varicella zoster
*Mucositis	Herpes simplex
Fungal/mixed	
*Mucositis	Herpes simplex <i>Candida albicans</i>
*Enteritis	<i>Giardia lamblia</i>
Mucositis	Herpes simplex <i>Cand albicans</i>
Vesicles on dorsal trunk	<i>Staphylococcus aureus</i> Herpes simplex
*Brain abscesses	<i>Cand albicans</i>
*Cystitis	<i>Escherichia coli</i>
Pneumonia	Unknown—responded to intravenous amphotericin
Pneumonia	Mixed coliforms
Mucositis	Herpes simplex <i>Cand albicans</i>

*Increased IgE concentration at the time of infection.

tozoal infections the diagnosis was confirmed by culture and the patients responded to appropriate treatment. Viral infection was diagnosed by electron microscopy, viral isolation, or rising viral antibody titres. In the few patients in whom a causative agent was not identified there was strong clinical indication of infection or response to treatment or both.

Serum IgE concentrations for all patient groups are shown in the Figure. The incremental rise in IgE was derived by subtracting the value before transplantation from the maximum value observed during an episode. Most of the patients were children with pretransplantation values below 5 IU/ml. In all episodes monitored the IgE concentrations returned

to baseline values at or soon after clinical improvement.

A rise of serum IgE concentration was associated with 3/7 bacterial infections, 5/5 viral infections, 4/6 mixed or other infections, 8/11 episodes of acute graft versus host disease with infection, and 6/11 episodes of acute graft versus host disease alone, but was invariably absent in chronic graft versus host disease.

Discussion

This study has confirmed previous reports of raised

Table 2 Infections occurring in the presence of acute graft versus host disease in bone marrow transplant recipients

Infection	Causative agent
*Septicaemia	<i>Streptococcus faecalis</i>
Septicaemia	<i>Streptococcus viridans</i>
Pneumonia and septicaemia	<i>Proteus mirabilis</i>
*Septicaemia	<i>Pseudomonas aeruginosa</i>
*Conjunctivitis	Adenovirus
Pneumonia	Parainfluenzavirus
*Mucositis	Herpes simplex
Intestinal candidiasis	<i>Cand albicans</i>
*Vesicles on dorsal trunk	<i>Staph aureus</i> Herpes simplex
*Hickman catheter infection	Unknown—improved when Hickman catheter was removed
Pharyngitis	Adenovirus
*Mucositis	Herpes simplex
Candidaemia	<i>Cand albicans</i>
Pharyngitis	<i>Cand albicans</i>
*Pharyngitis	Herpes simplex
Pneumonia	Cytomegalovirus
Enteritis	Adenovirus

*Increased IgE concentration at the time of infection.

Serum IgE increment in infection and in acute and chronic graft versus host disease (GVHD) in bone marrow transplant recipients.

serum IgE concentrations in acute graft versus host disease and unchanged values in chronic disease.¹ The maximum concentration seen in the present study was only 307 IU/ml, however, whereas Geha *et al*¹ reported values up to 9500 IU/ml. Differences in patient management and treatment as a factor in modifying the IgE response cannot be excluded.

In the present study raised serum IgE concentrations seen in many infections with or without graft versus host disease. A number of infections have been reported to be associated with raised serum IgE.⁴⁻⁶ In one study⁷ various respiratory viral infections were associated with higher IgE values in the acute compared with the convalescent phase of infection. This was interpreted as resulting from viral suppression of the IgE response. No preinfection values were quoted, however, and these results could equally well represent an acute IgE response to the viral infection, similar to the pattern seen in the figure. Other workers^{8,9} found an increase in IgE in the acute phase of cytomegalovirus and Epstein-Barr virus mononucleosis compared with preinfection values.

An interesting finding in our study was the invariant rise of serum IgE concentrations in patients with viral infections. T lymphopaenia or a disturbed T cell subset ratio has been reported in viral infections.¹⁰⁻¹² A similar pattern of raised serum IgE concentrations and T lymphopenia has been shown in children with asthma¹³ and atopic eczema.¹⁴ The raised IgE concentrations found in acute graft versus host disease might also be associated with T lymphocyte imbalance, but occult viral or other infections, exacerbating or initiating acute graft versus host disease, cannot be excluded.

In conclusion, the use of raised serum IgE concentration as an early indicator of acute graft versus host disease has been precluded by the finding of raised values in a large number of infective episodes.

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