

Blackwell Synergy

HomeBrowseSearchMy SynergyRegisterHelp

Username:

Password:

Athens Login

Login

Forgotten Password?Logout

You are at: [Home](#) > [List of Issues](#) > [Table of Contents](#) > Full Text



Univ di Roma Due Tor Vergata

Full Article

[Download](#) to reference manager

[Order Permissions](#)

[Alert me](#) when this article is cited | [Atom](#) | [RSS \(What is RSS?\)](#)

 [View/Print PDF article \(78K\)](#)

Journal of Paediatrics and Child Health

Volume 42 Page 319 - May 2006

doi:10.1111/j.1440-1754.2006.00863.x

Volume 42 Issue 5

CASE NOTE

Omenn syndrome: Therapeutic effects of cyclosporin

Sylvan Rego,¹ Andrew Kemp,¹ Melanie Wong¹ and Paul Knight²

Abstract: Omenn syndrome is a severe combined immunodeficiency with features of generalised erythroderma alopecia and evidence of Th2 inflammation (eosinophilia and raised IgE). We describe a differential effect of 2 calcineurin inhibitors, cyclosporine A (CsA) and tacrolimus, with CsA rapidly improving the erythroderma and lymphocytosis but tacrolimus having little effect.

List of Issues

Table of Contents

◀ Prev ArticleNext Article ▶

Add to Favorite Articles

E-mail this to a Friend



QuickSearch in:

- ☒ Synergy
☐ PubMed (MEDLINE)
☐ CrossRef
for

Authors:

- ☐ Sylvan Rego
☐ Andrew Kemp
☐ Melanie Wong
☐ Paul Knight
☐

Key words:

A female term infant (birth weight 2.965 kg), the second child of first cousin Egyptian parents, developed a generalised erythematous rash, poor feeding and perianal thrush at 3 weeks of age. At 4 weeks she developed a fever and skin desquamation. The fever subsided following intravenous antibiotics; however, the generalised erythroderma and desquamation persisted. Over the next 4 weeks she lost 0.5 kg and developed progressive hair loss from her scalp eyebrows and eyelashes, generalised lymphadenopathy and hepatomegaly. There was no family history of immunodeficiency.

Investigations at 10 weeks showed: Hb. 110 g/L, WCC $33.5 \times 10^9/L$ (normal 5–19) lymphocytes $12.4 \times 10^9/L$ (3.70–9.60), eosinophils $1.3 \times 10^9/L$ (0.1–1.1), normal liver function tests, serum cholesterol, triglycerides and hair microscopy. A urine metabolic screen was not consistent with biotinidase deficiency. There was generalised hypergammaglobulinemia with IgG 8.46 g/L (1.68–5.76), IgM 2.13 g/L (0.24–0.95), IgA 0.16 g/L (0.05–0.50) and IgE 24 993 kU/L (0–20); T cells CD3 $12.21 \times 10^9/L$ (normal 2.30–6.50), CD4 $5.96 \times 10^9/L$ (1.50–5), CD8 $6.82 \times 10^9/L$ (0.50–1.60), NK cells $2.13 \times 10^9/L$ (0.10–1.30), B cells $0 \times 10^9/L$ (0.6–3 $\times 10^9/L$). The mitogenic response to phytohemagglutinin was reduced. The absence of maternal DNA in peripheral blood excluded graft vs. host disease. The skin biopsy showed psoriatiform epidermal hyperplasia, basement membrane destruction and evidence of dermal inflammation consistent with Omenn Syndrome (OS).

The course was complicated by anaemia, hypoalbuminemia, hyponatremia and sepsis. Over 8 weeks *Klebsiella Oxytoca*, Beta haemolytic streptococci, *Acinetobacter* Methicillin Resistant *Staphylococcus Aureus* (MRSA) and *Candida* were isolated from blood cultures. Management included antibiotics, antifungals and intravenous immunoglobulin.

Oral cyclosporine (CsA) (5 mg/kg/day) was commenced at 11 weeks. Significant cutaneous improvement was noticed within 24 h. CsA was continued at 2–2.5 mg/kg/day for 2 weeks, resulting in blood levels between 50 and 100 ng/mL with complete resolution of erythroderma. The lymphocytosis resolved (Fig. 1). At 14 weeks, rifampicin was added because of ongoing sepsis and CsA was replaced by oral tacrolimus, as rifampicin inhibits CsA metabolism. Oral tacrolimus at doses between 0.025 and 0.12 mg/kg/day, resulted in blood levels between 1.8 and 4.4 ng/mL. On switching to tacrolimus, lymphocytosis rapidly recurred and erythroderma returned within 72 h. At 16 weeks tacrolimus was replaced by CsA 2 mg/kg/day. There was a dramatic improvement in the erythroderma and desquamation within 24 h.

The child underwent a bone marrow transplant from her mother at 4 months of age.

Key Points

- 1 Omenn syndrome is characterised by severe erythroderma in infancy.
- 2 Oral cyclosporine rapidly improved the erythroderma and lymphocytosis.
- 3 Another calcineurin inhibitor tacrolimus was not as effective as cyclosporine.

Discussion

Go to:

Choose

Go



Omenn Syndrome is an autosomal recessive immunodeficiency which usually leads to death owing to recurrent life threatening infections before 6 months of age, unless treated by bone marrow or cord blood stem cell transplantation.¹ Our patient manifested many of the key clinical features identified in a recent review of 68 cases of OS;¹ erythroderma (98%), alopecia (57%), lymphadenopathy (80%) recurrent infections (72%) and *Candida* (32%). Consistent laboratory features were eosinophilia (91%), lymphocytosis (19%) high serum IgE (91%) and absent or markedly decreased B Cells (81%). An unusual feature was hypergammaglobulinemia with raised levels of IgG and IgM, as hypogammaglobulinemia is usual (80%).

- ☐ cyclosporine
- ☐ erythroderma
- ☐ immunodeficiency
- ☐ reticuloendotheliosis
- ☐ tacrolimus.
- ☐

Search

Accepted for publication 12 January 2006.

Affiliations

¹Department of Immunology and Infectious Diseases and

²Department of General Paediatrics, The Children's Hospital at Westmead, Sydney, New South Wales, Australia

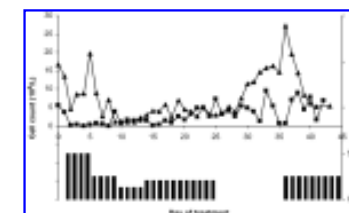
Correspondence

Professor Andrew Kemp, The Department of Allergy Immunology and Infectious Diseases, The Children's Hospital at Westmead, Locked Bag 4001, Westmead Sydney, NSW 2145, Australia. Fax: +61 298453421; email: andrewk5@chw.edu.au

We report the successful use of oral CsA at a dose between 2 and 2.5 mg/kg/day and the failure of tacrolimus to control the erythroderma in a child with OS. CsA blood levels ranged between 50 and 100 ng/mL and were below that usually recommended to maintain post transplant immunosuppression (range 100–300 ng/mL). A similar effect was recently reported in an infant with OS with a higher CsA doses (up to 9 mg/kg/day).²

The differences observed between CsA and tacrolimus do not appear to be due to a significant disparity in dosage. Tacrolimus has been estimated to be 25 fold more potent than CsA in lymphocyte blastogenesis inhibition³ A tacrolimus dose of 0.12 mg/kg is equivalent in potency to that of CSA 3 mg/kg. CsA and tacrolimus act through ligation of different intracellular binding protein targets (cyclophilin A for CsA, FK binding protein for tacrolimus). Both drugs inhibit the function of calcineurin, and reduce the activation of the transcription factor nuclear factor of activated T cells (NFAT), which regulates the expression of key cytokines and signalling proteins. Both promote down regulation of human Th1 and Th2 cytokines. The inhibition of cytokine IL 5, which is a principal driver of eosinophil production, appears to less than that of other cytokines and may explain our observation that the eosinophilia appeared more resistant to CsA than the cutaneous inflammation or the lymphocytosis. NFAT is also expressed in keratinocytes and reduction in keratinocyte differentiation may explain the dramatic effect of CsA on the desquamation.⁴ That these agents do have differing effects is demonstrated by the observation that CsA, but not tacrolimus, induces collagen production resulting in gingival overgrowth. OS has features of Th2 mediated inflammation. Tacrolimus but not CsA appears to promote Th2 type allergies in liver transplant recipients.⁵ This may be one reason why CsA was more effective than tacrolimus in the present case.

Image Previews



[Full Size]

Fig. 1 () Cyclosporin dose, (—▲—) lymphocyte and (—■—) eosinophil counts.

To cite this article

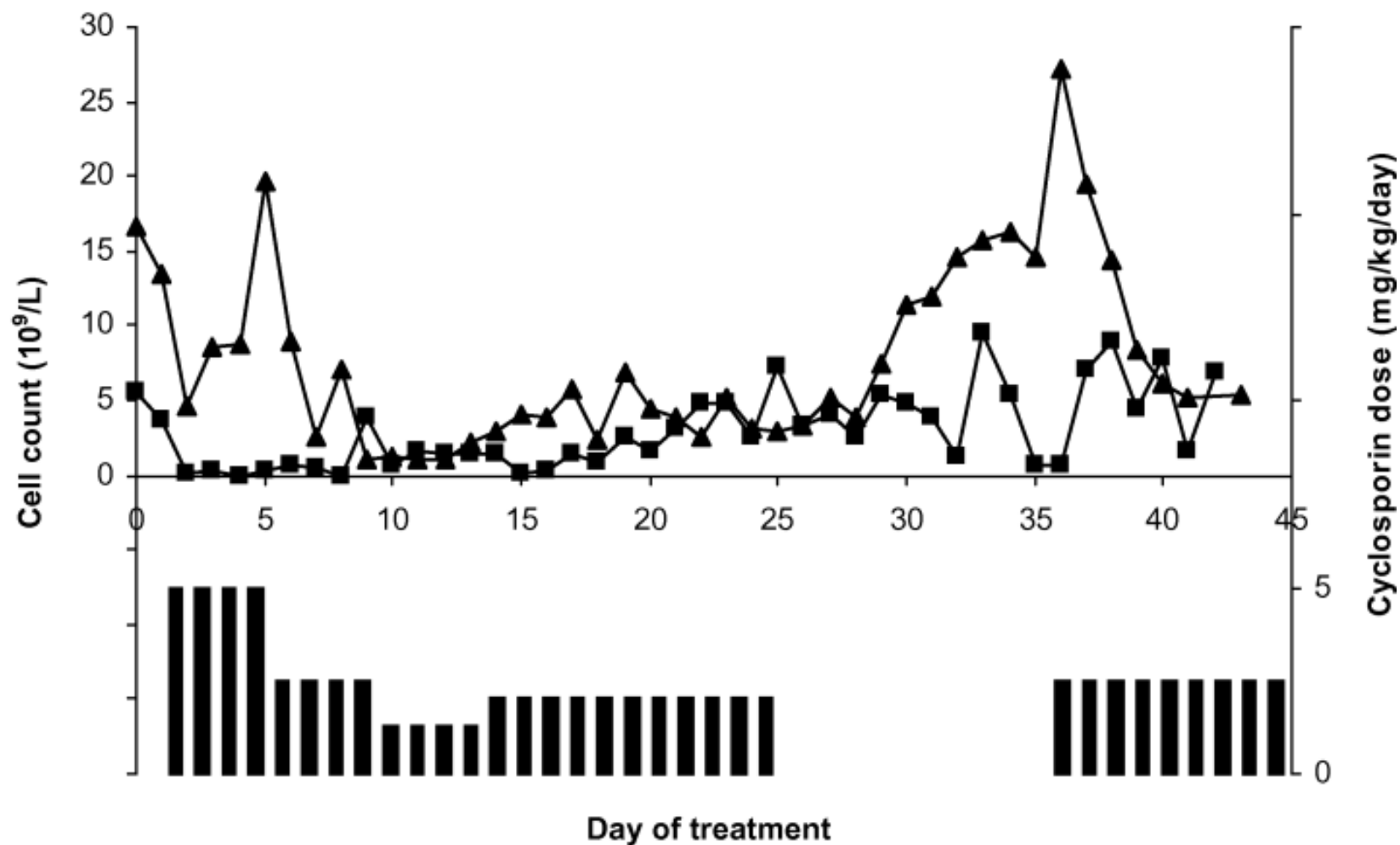
Rego, Sylvan, Kemp, Andrew, Wong, Melanie & Knight, Paul (2006)

Omenn syndrome: Therapeutic effects of cyclosporin.

Journal of Paediatrics and Child Health **42** (5), 319-320.

doi: 10.1111/

j.1440-1754.2006.00863.x



References

Go to:

Choose

Go

- Aleman K, Noordzij JG, De Groot R. Reviewing Omenn Syndrome. *Eur J. Pediatr* 2001; **160**: 718–25.
[MEDLINE](#) [MEDLINE](#) [ISI Abstract](#) [ISI Abstract](#) [CSA Abstract](#) [CSA](#)
- Meyer- Bahlburg A, Haas JP, Haase R *et al.* Treatment with cyclosporine A in a patient with Omenn's syndrome. *Arch. Dis. Child* 2002; **87**: 231–3.
[CrossRef](#) [crossref](#) [MEDLINE](#) [MEDLINE](#) [ISI Abstract](#) [ISI Abstract](#)
- Takeuchi H, Okuyama K, Konno O *et al.* Optimal dose and target trough level in cyclosporine and tacrolimus conversion in renal transplantation as evaluated by lymphocyte drug sensitivity and pharmacokinetic parameters. *Transplant. Proc.* 2005; **37**: 1745–7.
[CrossRef](#) [crossref](#) [MEDLINE](#) [MEDLINE](#) [ISI Abstract](#) [ISI Abstract](#)

- 4 Al Daraji WI, Grant KR, Ryan K, Saxton A, Reynolds NJ. Localization of calcineurin/NFAT in human skin and psoriasis and inhibition of calcineurin/NFAT activation in human keratinocytes by CsA. *J. Invest Dermatol.* 2002; **118**: 779–88.

[CrossRef](#)



[MEDLINE](#)

[MEDLINE](#)

[ISI Abstract](#)

[ISI Abstract](#)

- 5 Arikan C, Killie M, Tokat Y, Aydoglu S. Allergic disease after pediatric liver transplantation with systemic tacrolimus and cyclosporine therapy. *Transplant. Proc.* 2003; **35**: 3039–41.

[CrossRef](#)



[MEDLINE](#)

[MEDLINE](#)

[ISI Abstract](#)

[ISI Abstract](#)

Journal of Paediatrics and Child Health

Volume 42 Page 319 - May 2006

Blackwell Synergy® is a Blackwell Publishing, Inc. registered trademark

[More information](#) about Blackwell Synergy - online journals from www.blackwellpublishing.com.

We welcome your [Feedback](#). See our [Privacy Statement](#) and [Terms and Conditions](#).

Technology Partner - [Atypon Systems, Inc.](#)



Blackwell
Publishing