Early thrombocytopenia in HIV infection

R M Beattie, J Q Trounce, E G Hermione Lyall, D M Gibb

Abstract

Three children aged between 7 months and 2 years developed thrombocytopenia as an early feature of HIV infection. The prevalence of this condition, possible pathogenesis, and options for treatment are discussed. HIV testing should be considered in the investigation of a child with thrombocytopenia.

(*Arch Dis Child* 1992;67:1093-4)

As the incidence of HIV infection in children increases¹ and the various manifestations of the disease become apparent through studies of its natural history² it is clear that it needs to be considered in the differential diagnosis of many childhood diseases. We report here a series of children with HIV infection who presented with thrombocytopenia.

Case reports

CASE 1

A healthy 12 month old boy was referred to hospital with a five month history of bruising in areas of accidental trauma. He had no other abnormalities on clinical examination, was thriving, and was developmentally normal.

Laboratory investigation showed a platelet count of $8 \times 10^9/l$. The blood film was normal and his bone marrow showed an increase in megakaryocyte numbers consistent with peripheral platelet destruction. An initial diagnosis of idiopathic thrombocytopenic purpura was made. Only later was HIV considered in the differential diagnosis and after counselling the parents the child was tested. Tests for antibodies to HIV and the p24 antigen were positive. The CD4 count was low for his age with a reversal of the CD4:CD8 ratio, and hyperglobulinaemia was present. On the basis of these results a diagnosis of HIV infection with thrombocytopenia was made. His platelet count showed a good but temporary increase after treatment with intravenous immunoglobulin at a dose of 1 g/kg for two days. He has continued to receive this four times a week for six months.

Treatment with zidovudine (3'-azido-3'-deoxythymidine) for six months has not resulted in any permanent increase in platelet count and a trial of steroids by mouth was given. He became hyperactive and as there was no improvement in his platelet count they were stopped after three weeks. He has continued to have regular intravenous immunoglobulin treatment. He has no other manifestations of HIV infection.

The parents had no history of high risk behaviour for HIV infection but were subsequently shown to be positive for antibodies to HIV. The father's platelet count was $22 \times 10^9/l$ at presentation.

CASE 2

A 21 month old boy who had had a heart operation at the age of 4 months presented with a short history of bruising and had a platelet count of less than $10 \times 10^9/l$.

The bone marrow examination showed an increase in megakaryocyte numbers and a presumptive diagnosis of idiopathic thrombocytopenic purpura was made. There was no response to three courses of intravenous immunoglobulin and treatment with steroids was begun. Prednisolone was given at an initially high dose (2 mg/kg), decreasing slowly after two weeks to 5 mg on alternate days to keep the platelet count between 50 and $100 \times 10^9/l$.

At the age of 4 years (more than three years later) the child was found by donor tracing to have received a blood transfusion from donor positive for antibodies to HIV and subsequent testing showed the child to be infected with HIV. In addition to the thrombocytopenia he has since developed lymphocytic interstitial pneumonitis, encephalopathy, and is unwell. He currently receives regular intravenous immunoglobulin and prednisolone and zidovudine on alternate days. His platelet count has remained greater than $90 \times 10^9/l$.

CASE 3

A boy aged 7 months presented with petechiae and a platelet count of $6 \times 10^9/l$. His mother was known to be infected with HIV following a blood transfusion.

The T lymphocyte subsets were abnormal with reversal of the CD4:CD8 ratio and the p24 antigen was positive, indicating HIV infection. He received a short course of steroids which had no effect on the platelet count. A temporary increase in the platelet count occurred after intravenous immunoglobulin at a dose of 2 g/kg. The family then moved overseas. Regular treatment with intravenous immunoglobulin was recommended but not given. One year later, however, on returning to the United Kingdom his platelet count had recovered spontaneously without treatment.

He is currently well but remains positive for the p24 antigen and the CD4 count is slowly decreasing.

Department of
Paediatrics,
Royal Alexandra
Hospital for
Sick Children,
Brighton
R M Beattie
J Q Trounce

Royal Hospital for
Sick Children,
Edinburgh
E G Hermione Lyall
Institute of Child Health,
London
D M Gibb

Correspondence to:
Dr R M Beattie,
Division of Paediatrics,
Guy's Hospital,
St Thomas's Street,
London SE1 9RT.

Accepted 6 May 1992

Discussion

Chronic thrombocytopenia in childhood and an approach to its management has been reviewed by Chessells.³ Isolated thrombocytopenia can be the presenting feature of HIV infection in childhood as shown by the cases reported here and elsewhere.⁴⁻⁵ It should be included in the differential diagnosis of thrombocytopenia in an otherwise well child.

Thrombocytopenia is well recognised as a manifestation of HIV infection in adults and children. In adults with asymptomatic HIV infection the prevalence of thrombocytopenia (defined as a platelet count of less than $100 \times 10^9/l$) has been reported to be 3–12%; higher prevalences of up to 30% have been found in adults with AIDS.⁶ Of the children known to have HIV infection or AIDS in the United Kingdom about 10% are thrombocytopenic (C Davison, personal communication, British Paediatric Surveillance Unit). Higher prevalences have been reported in more selected groups of children with symptomatic HIV infection.⁷

Thrombocytopenia in HIV infection and AIDS is multifactorial and its aetiology and pathogenesis in adults has been described elsewhere.⁸ In the children described here (cases 1 and 2) the presence of bone marrow hyperplasia suggests peripheral platelet destruction. The likely mechanism is the deposition of immune complexes on the platelet Fc receptor with its subsequent uptake by phagocytes and destruction as in adult idiopathic thrombocytopenic purpura. Platelet antibodies have been reported in adults with HIV infection and thrombocytopenia.⁹

The major danger of HIV associated thrombocytopenia is cerebral haemorrhage and this has been reported.^{5, 10} Spontaneous remission may occur (as in case three) and has been described in adults and children.^{5, 11} If the platelet count is less than $20 \times 10^9/l$ there is a risk of bleeding and treatment is indicated. The treatment options include zidovudine, intravenous immunoglobulin, steroids, and splenectomy.

Zidovudine is known to increase the platelet count in HIV infected adults¹² and has been used effectively in the treatment of HIV associated thrombocytopenia. A response in 68% of adults has been reported, though treatment for over three months was required in some before an increase in the number of platelets was seen.¹³

Intravenous immunoglobulin has been found to be of value in HIV associated thrombocytopenia⁴ and it resulted in an improvement in the platelet count in two of the three children reported here. As a regular treatment (case 1), however, it does require regular cannula insertion and is expensive.

Prednisolone was effective in one of the two children in whom it was used. In the second its use was curtailed because of hyperactivity. The treatment of HIV associated thrombocytopenia in children with prednisolone has been reported

by Ellaure *et al* with success in five of seven cases.⁵ An appropriate regimen would be 2 mg/kg/day initially decreasing after a response has been seen to the lowest possible alternate day maintenance dose.¹⁴ There are concerns about using steroids in a disease where immunity is already suppressed and the incidence of infections is increased. Adverse effects have not been reported with the use of steroids in other diseases such as *Pneumocystis carinii* pneumonia associated with HIV infection in adults, however.¹⁵

Splenectomy has been reported to increase the platelet count in some adults with HIV associated thrombocytopenia.¹⁶ Its use in infants, however, would not be justified except as a last resort because of the subsequent adverse effects on immunity and the associated risk of sepsis particularly with *Streptococcus pneumoniae*.

In conclusion we stress the importance of considering HIV in the differential diagnosis of thrombocytopenia in children. The absence of symptoms or risk factors should not preclude suspicion of HIV infection.

In children with HIV associated thrombocytopenia treatment is indicated if the platelet count is low. Further investigation into the pathogenesis of the condition and the most appropriate forms of treatment for children is required.

We thank Dr J Y Q Mok for allowing us to report case 2.

- Chin J, Sankaran G, Mann JM. Mother to infant transmission of HIV: an increasing global problem. In: Kessel E, Awan AK, eds. *Maternal and child care in developing countries*. Thun: Ott, 1989.
- European collaborative study. Children born to women with HIV 1 infection: natural history and risk of transmission. *Lancet* 1991;337:253–60.
- Chessells J. Chronic idiopathic thrombocytopenic purpura; primum non nocere. *Arch Dis Child* 1989;64:1326–8.
- Salisbury FT, Boyle RJ, Wykoff RF, Howard TH. Thrombocytopenia as the presenting manifestation of human T-lymphotropic virus type III infection in infants. *J Pediatr* 1986;109:30–4.
- Ellaure M, Burns ER, Bernstein LJ, Shah K, Rubinstein A. Thrombocytopenia and the human immunodeficiency virus in children. *Pediatrics* 1988;82:905–8.
- Rossi G, Stellini R, Franceschini F. Prevalence and clinical features of thrombocytopenia in the HIV positive population. Biberfeld P, Gluckman JC, eds. *Proceedings of the 4th International Conference on AIDS*: Stockholm. Vol 1. 1988:2125.
- Ellaure M, Burns ER, Rubinstein A. Haematological manifestations of pediatric HIV infection: severe anemia as a prognostic factor. *Am J Pediatr Hematol Oncol* 1990;12:449–53.
- Karpatkin S. HIV 1 related thrombocytopenia. *Baillieres Clin Haematol* 1990;3:115–38.
- Magnac C, de Saint Martin J, Pidard D, Legrand C, Dighiero G. Platelet antibodies in the serum of patients with HIV infection. *AIDS Res Hum Retroviruses* 1990;6:1443–9.
- Park YD, Belman AL, Kim TS, *et al*. Stroke in paediatric immunodeficiency syndrome. *Ann Neurol* 1990;28:303–11.
- Goldswieg AHG, Grossman R, William D. Thrombocytopenia in homosexual men. *Am J Hematol* 1986;21:243–7.
- Flegg PJ, Jones ME, MacCallum LR, Williams KG, Cook MK, Brett RP. Effect of zidovudine on platelet count. *BMJ* 1989;298:1074–5.
- Rarick M, Espina B, Montgomery T, Easley A, Allen J, Levine AM. The long term use of zidovudine in patients with severe immune mediated thrombocytopenia secondary to infection with HIV. *AIDS* 1991;5:1357–61.
- Hilgartner M. Hematological manifestations in HIV infected children. *J Pediatr* 1991;119 suppl:S47–9.
- Consensus statement on the use of corticosteroids as adjunctive therapy for HIV-associated thrombocytopenia. *N Engl J Med* 1990;323:1501–4.
- Tyler DS, Shaunak S, Bartlett JA, Iglehart JD. HIV 1 associated thrombocytopenia: the role of splenectomy. *Ann Surg* 1990;211:211–5.

to primary. For example, I could find no mention in the relevant chapters of developmental delay associated with iron deficiency; no mention of district handicap teams; no mention of common sleep disorders; little discussion on asthma management at school, and also inappropriate advice such as 'stool examinations should include culture' in the home management of diarrhoea.

There are also deficiencies in the 'preventive' chapters. There is scanty discussion on the format, content, and evaluation of a surveillance programme that now forms a central part of child health in general practice (though the hard to credit statement is made on p 56 that 'for most children, pre-school surveillance is undertaken in child health clinics organised by the child health services'). The increasingly recognised public health aspects of child health in relation, for example, to accident prevention receive no mention. The contraindications to pertussis given on p 38 are incorrect and do not detail the definition of a severe reaction (which is the only absolute contraindication). I have some carping comments about omissions, too—hyperactivity, the distraction hearing test, torticollis, and blocked tear ducts are not to be found in the book but all may crop up in the examination, and are important problems in clinical practice.

There is much to learn in the chapters on epidemiology by Stuart Logan, on child abuse by Jane Wynne with its clear illustrations, and on genetics by Sarah Bunday, which has valuable data on recurrence risks.

I very much hope that the editors will take a fresh look at the format of the book before the

next edition to ensure that it is fully compatible with the reformed DCH.

TONY WATERSTON
Consultant community paediatrician

Handbook of Pediatric Imaging. Edited by Lori L Barr. (Pp 224; £80 hardback.) Churchill Livingstone, 1991. ISBN 0-443-08697-4.

'The *Handbook of Pediatric Imaging* guides the general radiologist through a thought provoking review of pediatric radiology'. This quotation from the preface provides a standard with which to compare this text.

In general, there is an uneven allocation of space to topics. It is a necessary editorial duty to control the enthusiasm of contributors for their special interests and to balance the content of the book.

There is a long contribution on dental radiology, mainly accurate and interesting, but out of proportion to other sections of wider interest. The pulmonary problems of the preterm infant receive less space and, due to the method of grouping by findings such as 'hypoaeration' and 'multiple cysts', some disease processes are described in several sections. The best description of pulmonary interstitial emphysema does not relate to respiratory distress syndrome, but appears under a section headed 'Mediastinal air'.

This system is of value in preparing candidates for examination where clinical information may be lacking, but does not help with clinicoradiological correlation. In the bone section, Scheuermann's disease has three short

and partly repetitive mentions, inaccurately recorded in the index.

In conclusion, this book is best used as a 'spot' primer for examinations: it is too uneven in content and style to be a major addition to the texts on paediatric radiology already available.

RICHARD KEITH LEVICK
Consultant radiologist

Atlas of Rare Chest Diseases in Children. Edited by J Rudnik and R Kurzawa. (Pp 192; no price stated, hardback.) Rabka, Poland: National Institute of Mother and Child, 1990. ISBN 83-00-03293-2.

The National Research Institute of Mother and Child in Rabka, Poland have put together a collection of interesting rarities in this book. They have impressive facilities, but the atlas unfortunately reflects their lack of access to modern investigative resources such as computed tomography, magnetic resonance imaging, and fiberoptic bronchoscopy. Bronchograms are used in most of their cases, whereas we rarely perform one, and the contrast medium may soon be unavailable. The illustrations, although lavish, are often poorly reproduced, and the reference list has important gaps. In summary, an enviable collection of material, but it is difficult to know to whom to recommend this book for purchase.

ANDREW BUSH
*Senior lecturer and
honorary consultant
paediatric chest physician*

Correction

Early thrombocytopenia in HIV infection

We wish to clarify any ambiguity in this paper by R M Beattie *et al* published in September (pp 1093-4). In case 1, the last sentence of the second paragraph should read: 'He continued to receive this [intravenous immunoglobulin] every four weeks for six months'. In case 2, the third sentence of the third paragraph should read: 'He is currently on intravenous immunoglobulin every four weeks, daily zidovudine, and alternate day prednisolone'.