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Otitis media in children with vertically-acquired HIV infection: the Great Ormond Street Hospital experience[1]

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Abstract

Human immunodeficiency virus (HIV) infection continues to be a vexing problem in the pediatric population. Otitis media, a common entity in immunocompetent as well as immunocompromised children, is prevalent in pediatric patients with HIV infection. Recurrent infections and complications secondary to otitis media are also common in this population. The purpose of this review was to evaluate the records of a large group of children with HIV infection undergoing treatment for otitis media at a tertiary care center. Incidence of infections, severity of infections, and pathogens responsible were the key points of data collection in relation to each patient's HIV clinical and immunologic classification. We reviewed 72 patients with vertically-acquired HIV infection undergoing treatment at the Hospital for Sick Children, Great Ormond Street, London. All patients were born to HIV infected mothers of sub-Saharan African origin. A total of 32 (44.4%) of these children presented to our institution with one or more episodes of otitis media, six of whom suffered systemic complications secondary to middle ear pathology. Middle ear culture data, when available from actively draining ears, was similar to those of immunocompetent children in the general population. The most common complications were systemic bacteremia and recalcitrant infections requiring intravenous antibiotic therapy. Severity of immunosuppression was associated with higher incidence and severity of otitis media. Otitis media in an HIV infected child must be treated aggressively at its outset in an attempt to minimize possible complications. Administration of prophylactic antibiotics to these children may reduce the frequency of acute and chronic infections. Improvement in immunologic status using antiretrovirals or protease inhibitors is a primary goal in diminishing the severity of otitis media as well as other infections in these children.

Keywords: Otitis media; Human immunodeficiency virus; Pediatric; Acquired immunodeficiency syndrome

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1. Introduction

The incidence of human immunodeficiency virus (HIV) infection in children is a worldwide problem of increasing concern. There are approximately 1 million children infected with HIV and it is estimated that approximately 4 million children will be infected by the year 2000 [11]. While horizontal transmission by sexual contact, intravenous drug use, and blood product transfusion are the most common modes of HIV transmission in adults, vertical transmission from mother to fetus is the primary mode of transmission in children [6,9]. With the advent of prenatal treatment of the HIV positive mother with antiretroviral agents, the infant seroreversion from carriage of maternal HIV IgG antibody to seronegative status has reached 90–97% in many cities in the United States. The spontaneous seroreversion rate after maternal exposure to HIV is closer to 70–85% [3].

Otitis media is a common illness of childhood, and is the most frequently seen acute illness by pediatricians [2,7]. In the immunocompromised child with HIV infection, the physician must consider potential complications secondary to middle ear disease [18]. Recurrent infections recalcitrant to oral antibiotic therapy, bacteremia, and meningitis are more frequently seen in the child with HIV infection [1,6]. Aggressive therapy, possibly with hospital admission for intravenous antibiotics, must be considered in treating this population.

2. Methods

We performed a retrospective review of all HIV infected children being treated at the Great Ormond Street Hospital for Sick Children, London, United Kingdom, from October 1988 through December 1996. We excluded patients who seroreverted to HIV seronegative status; once a child became a seroreverter, they were no longer followed at our institution. Polymerase chain reaction (PCR) for viral antibodies and more recently quantitative viral load are the most accurate means of assessing infection status in a given patient [3]. Several previous studies have compared seroreverted children with HIV infected mothers and seropositive children with respect to incidence of and complications secondary to otitis media. All noted a decline in episodes of otitis media in patients who seroreverted to HIV negative status [1,5] [12,15]. We did not have access to such a patient population in our review.

HIV classification in this study was based on the 1994 Centers for Disease Control 'Revised Classification System for Human Immunodeficiency Infection in Children Less than 13 Years of Age' (Table 1) [3]. In this system immunologic category is an age-adjusted level (Table 2) [3].

We reviewed the hospital records of all children with HIV infection at our center. In total, 72 patients were included. Variables included age, gender, CD_4 counts and percentage CD_4 counts over time. HIV classification and medication use were also included. Episodes of acute otitis media, recurrent otitis media, complications secondary to otitis media, and culture data when available were recorded. The control group in this study was the group of HIV infected children with no documented history of otitis media.

3. Results

A total of 72 patients with HIV infection were included in this review. Of these, 32 children (44.4%) presented with at least one episode of otitis media documented by either a pediatric infectious disease specialist or a pediatric otolaryngologist. Actual prevalence of episodes of acute otitis media may be higher in our population, as our data collection was based only on visits to a tertiary care center and did not include visits to primary care physicians. Diagnostic criteria for otitis media included evidence of purulent middle ear effusion with an intact tympanic membrane or purulent otorrhea in the presence of a normal external auditory canal.

Age distribution of children with and without history of otitis media was obtained based on age of the patient at the time of this study. The mean age of the patients with no history of otitis media was 64.4 months (median 52.5 months; range

7–172 months). The mean age of the patients with a history of otitis media was 80.4 months (median 79.0 months; range 22–156 months). The difference in the mean age in the two groups was statistically significant ($P = 0.04$, Mann Whitney U-test). Within the group of 32 patients with a history of otitis media, there were 69 episodes of documented infections. The mean age of patients during acute infections was 51.9 months (median 41.0 months; range 9–145 months).

There were 33 females and 39 males in this study. In the group of patients with no history of otitis media, there were 21 females and 19 males. In the group of patients with a history of otitis media, there were 12 females and 20 males. HIV classification in the group of patients with otitis media was similar to the HIV classification in patients with no episodes of otitis media (Table 3).

A total of six of the 32 patients with a history of otitis media developed systemic complications secondary to middle ear pathology despite treatment with oral antibiotic therapy. All of these patients were moderately to severely immunocompromised (Table 4). In the immunocompetent population, systemic complications secondary to otitis media, specifically bacteremia, are extremely rare [13,14]. In total, 14 of the 32 patients were noted to have otorrhea from either tympanic membrane perforation, presence of a tympanostomy tube, or middle ear granulation tissue. Culture data was available for six of these patients. Three of these cultures grew *Streptococcus pneumoniae*, which is similar to what is often seen in immunocompetent children. Three children with cultures of middle ear discharge demonstrated unusual middle ear pathogens without associated systemic sequelae: A 2 year old male with HIV classification B1 developed otorrhea which on culture demonstrated *Proteus sp*. A 6 year old male with HIV classification B3 grew Group A β-hemolytic *Streptococcus* on culture of middle ear drainage. A 7 year old male with HIV classification B3 developed otorrhea positive for *Staphylococcus aureus* on culture.

Table 1
Pediatric human immunodeficiency virus (HIV) classification

Immunologic categories	Clinical categories			
	N: No signs/symptoms	A: Mild signs/symptoms	B: Moderate signs/symptoms	C: Severe signs /symptoms
1. No Suppression	N1	A1	B1	C1
2. Moderate Suppression	N2	A2	B2	C2
3. Severe Suppression	N3	A3	B3	C3

Table 2
Immunologic categories based on age-specific CD4 T-lymphocyte counts and percent of total lymphocytes

Immunologic category	Age of child					
	<12 months		1–5 years		6–12 years	
	mml	(%)	mml	(%)	mml	(%)
1. No suppression	≥1500	(≥25)	≥1000	(≥25)	≥500	(≥25)
2. Moderate suppression	750–1499	(15–24)	500–999	(15–24)	200–499	(15–24)
3. Severe suppression	<750	(<15)	<500	(<15)	<200	(<15)

Table 3

Immunologic category	A. History of otitis media: HIV classification				
	Clinical category				
	N	A	B	C	Totals
1	0	4*	4	1	9
2	0	2	6	4	12
3	0	1	6	4	11
Totals	0	7	16	9	
	B. No history of otitis media: HIV classification				
1	1*	3	6	1	11
2	1	4	6	1	12
3	0	3	7	5	15
Totals	2	10	19	7	

* Denotes number of patients.

Table 4
Complications of otitis media

Age (years)	Gender	HIV classification	Complication/treatment
2	Male	B2	Bacteremia (*Str. viridans)*/intravenous antibiotics
3	Male	B3	Fever/acute otitis media/intravenous antibiotics
3	Male	B3	Fever/otorrhea/intravenous antibiotics
3	Female	A2	Bacteremia (*S. pneumoniae)*/intravenous antibiotics
2	Male	C1	Recalcitrant otorrhea (*P. aeruginosa; Enterobacter cloacae; Acinetobacter*)/intravenous antibiotics
11	Female	B3	Fever/acute otitis media/intravenous antibiotics

HIV immunologic classifications, based on both age adjusted CD_4 count and percentage CD_4 as well as AIDS associated illnesses [3] were similar in patients with episodes of otitis media and those with no history of otitis media. In the otitis media group, there were 20/32 with HIV classification B2-3 or C2-3. Similarly, in the non-otitis media group, there were 19/38 patients with B2-3 or C2-3 HIV classification. The HIV classification of the patients with systemic complications secondary to otitis media were A2, B2, B3 (three patients), and C1. All patients were either moderately to severely immunocompromised (A2, B2, B3) or had severe AIDS related illnesses (C1).

We noted a gradual decline in CD_4 count and percentage CD_4 over time. Utilization of antiretroviral therapy did not result in a long-term rise in CD_4 or percentage CD_4. The CD_4 and percentage CD_4 counts over time were plotted for the group of patients with otitis media. There was an overall decline in both CD_4 and percentage CD_4 over time. Episodes of otitis media did not show a particular trend based on age or CD_4 status (Fig. 1). Institution of antiretroviral therapy resulted in temporary, if any, rise in CD_4 count or percentage CD_4 levels (Fig. 2 and Fig. 3).

4. Discussion

This review evaluated the incidence and severity of otitis media in the HIV infected population at a tertiary care children's hospital in the United

Kingdom. All children had acquired HIV infection by maternal transmission, and were of sub-Saharan African descent.

Although the mean age of the study population with history of otitis media was older than the population with no history of otitis media, the patients were on average younger during acute episodes. There were more males in the group of patients with episodes of otitis media.

Current treatment goals of vertically-acquired HIV infection in the pediatric population focus on early detection of HIV in the gravid woman. Earlier identification of HIV seropositive women who are pregnant has allowed for drastic reduction in vertical transmission of the human immunodeficiency virus. Treatment options for the identified HIV seropositive pregnant patients include antiretroviral therapies with or without protease inhibitors. Antiretroviral therapy for the neonate born to an HIV seropositive mother in the first 6 weeks of life following maternal prenatal use of such therapy has reduced the vertical HIV transmission rates in many centers. Infants carry maternal HIV IgG antibody for the first 9–15 months of life, but with optimal perinatal therapies, they will have a greater than 90% chance of reverting to seronegative status by their 18th month of life [3].

Head and neck manifestations of HIV infection have been well documented in children [9,16,18]. Several otolaryngologic presentations are unique to pediatric patients with HIV infection or other immunosuppressed states. These include generalized cervical lymphadenopathy [9] [16], mucocutaneous candidiasis [18], parotid gland enlargement [4], and recurrent oro-esophageal herpes simplex viral eruptions [6]. Otitis media has been shown to be more prevalent and more severe in the immunosuppressed population [1,5] [12,15,17]. We noted a relatively high incidence of patients with systemic sequelae secondary to middle ear disease, which has been noted in previous studies [8]. All were treated with intravenous antibiotic therapy, and none succumbed to illness secondary to middle ear pathology.

Middle ear disease is prevalent in the general pediatric population. There were over 24 million visits to a physician's office for acute otitis media

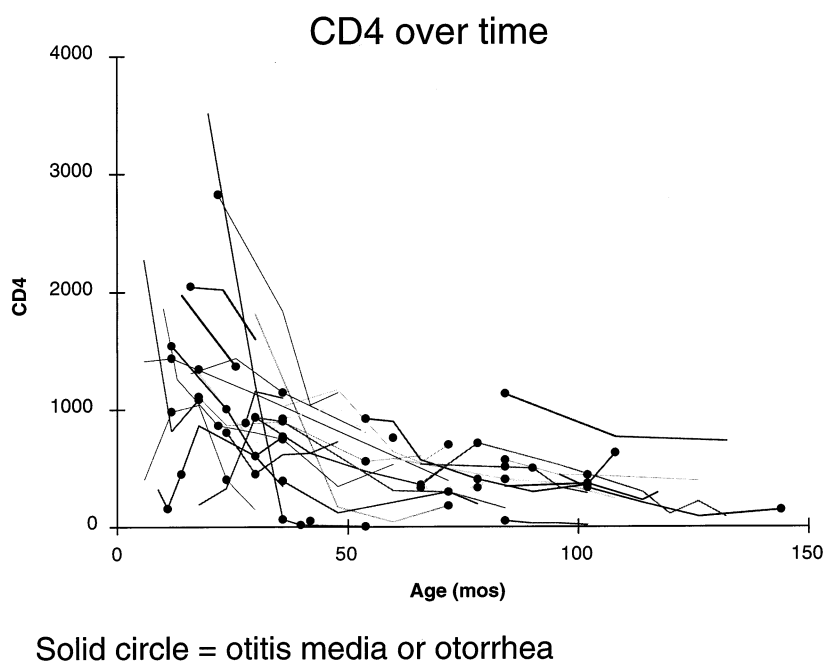

Fig. 1. Trend of CD_4 count over time. Each line represents individual patient. Solid circles indicate episodes of otitis media.

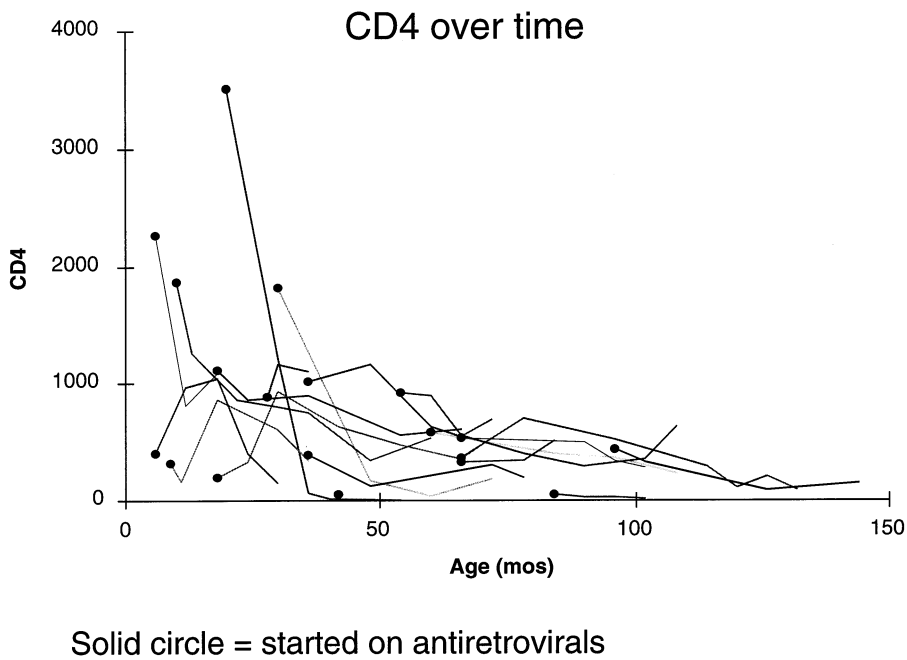

Fig. 2. CD_4 count over time in patients receiving antiretroviral therapy. Each line represents individual patient. Solid circles indicate initiation of antiretroviral therapy.

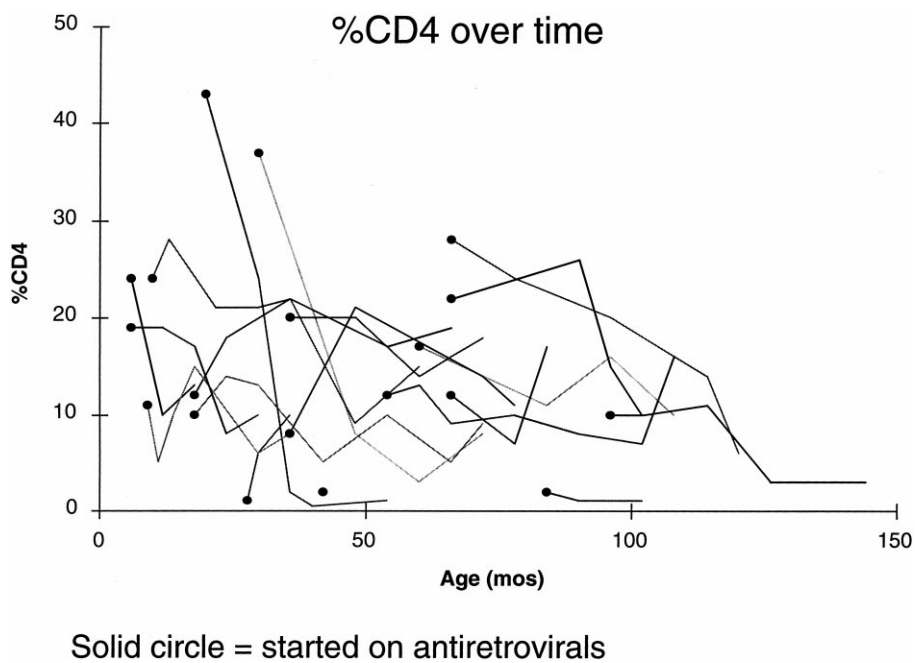

Fig. 3. Percent CD_4 over time in patients receiving antiretroviral therapy. Each line represents individual patient. Solid circles indicate initiation of antiretroviral therapy.

1990 in the United States [10]. Because of the frequent occurrence of otitis media in both immunocompetent and immunocompromised children, focus on systemic complications and unusual pathogens are of more import in the immunocompromised population [12]. Early perinatal identification, prevention, and/or treatment of HIV infection are clearly of primary interest in eradication of vertically transmitted HIV infection and its associated diseases.

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