Surgical Implications of Human Immunodeficiency Virus Infection in Children

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Abstract

According to the joint United Nations Program on HIV/AIDS (UNAIDS), 34 million people worldwide were estimated to be living with HIV or acquired immune deficiency syndrome (AIDS) at the end of 2011 (UNAIDS_Global_Report_2012_en.pdf. Accessed 19 Feb 2013). Most reside in the developing world, with approximately two-thirds in sub-Saharan Africa. The annual rate of incident (new) HIV infections is believed to have peaked at >3 million in the late 1990s and was 2.5 million in 2011 (UNAIDS_Global_Report_2012_en.pdf. Accessed 19 Feb 2013; Karpelowsky J, Millar AJ Semin Pediatr

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Surg 21(2):125–135, 2012). Approximately 12 percent of these infections (330,000 cases) occurred in children younger than 15 years of age (UNAIDS_Global_Report_2012_en.pdf. Accessed 19 Feb 2013). Thus pediatric HIV infection is a pandemic affecting children predominantly in sub-Saharan Africa but is also seen in Asia and sporadically elsewhere (UNAIDS_Global_Report_2012_en.pdf. Accessed 19 Feb 2013). The number of children newly infected with HIV has decreased dramatically. This decrease is a consequence of the success of interventions to prevent mother-to-child transmission (PMTCT) of HIV. These interventions include early identification of HIV infection in pregnant women through routine antenatal testing, provision of antiretroviral medications to the pregnant woman and her infant, delivery by elective Caesarean section when indicated and the complete avoidance of breastfeeding. In addition the widespread availability of educational programs addressing HIV infection, prevention of HIV perinatal transmission and HIV counselling and testing services have further reduced the incidence. HIV infected children may require surgery either as an emergency to deal with a life threatening condition or a complication of the disease, non-emergency procedures where surgery is required to assist is the diagnosis of an HIV related condition or for elective surgery for routine childhood procedures. Surgical problems associated with HIV infection are described under categories of soft tissue or organ specific infections requiring drainage or debridement, gastrointestinal tract disease and complications, infections in the perineal area, and malignancies. Although surgical outcomes are compromised in children with AIDS, current HAART (Highly Active Anti-retroviral Therapy) prognosis is, in the short term, excellent.

Keywords
Children · HIV · Surgery · Complications

Introduction

Pediatric HIV (Human immune deficiency virus) infection is a pandemic predominantly in sub-Saharan Africa. Approximately 2.2 million children under 15 years are infected with HIV, representing almost 95% of the total number of children globally infected with HIV (Karpelowsky and Millar 2012). Pediatric HIV is largely transmitted from an HIV infected mother to her infant either at the time of delivery or through breast feeding. The risk of transmission can be substantially reduced by mother to child transmission prevention (MTCT) programs that include use of antiretroviral therapy and formula feeding (Roider et al. 2016; Cotton and Rabie 2015). However in many areas of Sub Saharan Africa access to these interventions is unavailable or unaffordable and may be accompanied by unacceptable morbidity and mortality from enteric infection. Hence mother to child prevention programs have changed to emphasize that exclusive breast feeding is best provided the mother has been identified and treated antenatally with anti-retroviral therapy and does not have a low CD4 count. With the introduction of a breastfeeding-only policy late in 2011 in South Africa, staff working in prevention of mother to child transmission [PMTCT] programs now face the challenge of educating HIV-positive mothers on the correct care and dosing throughout the period of breastfeeding.

Whilst mothers previously had the option of formula feeding to minimize their babies' exposure to HIV, they are now encouraged to breastfeed exclusively as a means to reducing overall infant mortality from gastroenteritis (Johnson et al. 2016). However, this necessitates daily dosing with nevirapine syrup, and continued antiretrovirals for the mother, and requires that breastfeeding is exclusive i.e. no formula feeding at all. Where these PMTCT programs have been introduced transmission of HIV from infected mother to infant has been drastically reduced. Although the numbers have been considerably reduced, HIV infected or exposed but uninfected

children still present and can be expected to require a surgical procedure for the following reasons:

1. Emergency procedures to deal with a life threatening condition or a complication of the disease
2. Non-emergency procedures where surgery is required to assist is the diagnosis of an HIV related condition
3. Elective surgery for routine childhood procedures (UNAIDS 2012)

Most studies on the outcome of HIV infected patients undergoing surgery have been in adults (Yii et al. 1995; Shelburne et al. 2005; Horberg et al. 2006; Madiba et al. 2009). These have reported conflicting results but several suggest an increased morbidity associated with HIV infection with little or no impact on mortality. In contrast there is limited information on surgical presentations and outcomes in HIV infected children.

For children presenting with a life threatening complication of HIV/AIDS the same indications for surgery in HIV unexposed children exist. The emergent nature of these cases does not allow pre-operative correction of co-morbidities such as nutritional deficits or management of the immune-suppression with highly active antiretroviral therapy (HAART). Surgical procedures are frequently undertaken to assist in the diagnosis of an HIV/AIDS related pathology or complication. Most of these allow time for pre-operative correction of pre-morbid conditions (Stefanaki 2002; Shelburne et al. 2005; Madiba et al. 2009). Lastly there are an increasing number of HIV infected children who require routine pediatric surgical procedures. In children who are considered for elective surgery the health status and life expectancy should be taken into account when considering the timing and need for surgery. If surgery can be delayed then treatment with HAART should commence immediately and surgery should only be performed after a period of 8–12 weeks at which time viral levels should be low and the child's immune system should have reconstituted. If the child in question is infected with an opportunistic organism e.g. mycobacterium tuberculosis one must be aware of the added potential complication of the immune reconstitution inflammatory syndrome (IRIS) where in the first instance the infection should be treated and controlled before starting HAART. The term IRIS describes a collection of inflammatory disorders associated with paradoxical worsening of pre-existing infectious processes following the initiation of highly active antiretroviral therapy (HAART) in HIV-infected individuals especially if the CD4 count is <200 cells/μL. Pre-existing infections in individuals with IRIS may have been previously diagnosed and treated or they may be subclinical and later unmasked by the host's regained capacity to mount an inflammatory response. Pathogens particularly associated with IRIS are Mycobacterium tuberculosis, Mycobacterium avium complex, Cytomegalovirus, Cryptococcus, Pneumocystis, Herpes simplex, Hepatitis B and Human herpes virus 8 (associated with Kaposi sarcoma).

Surgical problems associated with HIV infection may be described under four major categories (Table 1)

1. Soft tissue or organ specific infections requiring drainage or debridement
2. Gastrointestinal tract disease and complications
3. Infections in the perineal area
4. Malignancies

Infections

Approximately 90% of HIV infected children will develop mucocutaneous disease, which may be infectious or non-infectious (Stefanaki et al. 2002). Children with symptomatic HIV infection have an increased incidence of soft tissue infections. The cutaneous manifestations of HIV are an

Table 1 Presentation, differential diagnosis and indications for surgery in HIV-infected children

	Clinical presentation	Differential diagnosis	Surgical Indications
Surgical infection	Abscess Necrotizing fasciitis Septicemia	Staphylococcus, Streptococcus Candida Herpes, CMV Tuberculosis Molluscum Gram negative e.g. Pseudomonas	Drain pus Debride necrotic tissue Obtain culture to direct antibiotic therapy
Esophageal diseases	Esophagitis Esophageal stricture	Candida CMV, Herpes Idiopathic ulcers (HIV) Malignancy e.g. Kaposi Non-HIV related pathogens GOR	Contrast swallow to identify strictures Endoscopy with biopsy for histology and culture
Intra-abdominal problems	Gastrointestinal bleeding Gastrointestinal perforation Gastrointestinal obstruction	CMV Mycobacterium *tuberculosis* and *avium-intracelularae* Candida Malignancy e.g. lymphoma	Endoscopy to diagnose GI bleeding Surgery for perforation and obstruction
Perineal disease	Ano-cutaneous fistula Condyloma Rectovaginal fistula Rectourethral fistula	CMV Papilloma virus	Colostomy for sepsis with rectovaginal, rectourethral fistulae Cryotherapy or laser for Condylomata
Malignancy	Depend on site and extent of disease	Non-Hodgkins lymphoma Karposisarcoma Leiomyosarcoma B-cell lymphoma	Biopsy of mass Surgical excision

indicator of underlying immune status. Bacterial skin infections are often recurrent, in atypical sites or due to atypical organisms (Prose 1991).

The most common organisms causing skin infections are Staphylococcal and Streptococcus species. These usually present as cellulitis, ecthyma, erysipelas, furunculosis (occasionally of disseminated nature), persistent and recurrent folliculitis and impetigo. Pyomyositis is also increasingly reported possibly associated with an increased rate of *Staphylococcus aureus* colonization. Gram negative organisms may also cause severe skin infection in HIV infected children. Pseudomonas organisms may produce cutaneous manifestations, including ecthyma gangrenosum and a papular rash, often in the perineal area (Flores et al. 1993) (Fig. 1).

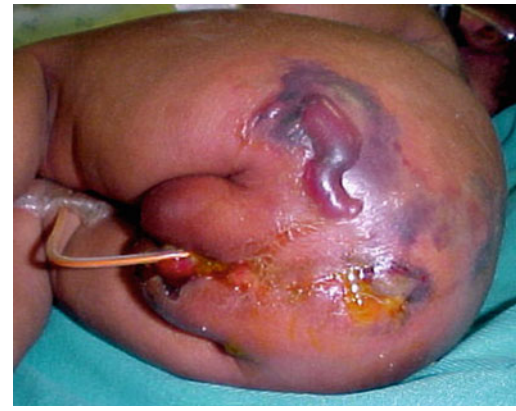

Fig. 1 Necrotizing fasciitis in a newborn infant with an ano-rectal malformation

The principles of management of bacterial skin infection are as for HIV unexposed children including the use of appropriate antibiotics and surgical drainage or debridement when needed. A high index of suspicion for rapidly spreading infection or necrotizing fasciitis must be maintained (Pijnenburg and Cotton 2001) specifically as the immune compromised patient may not mount a clinically evident initial systemic response.

Infection with Molluscum contagiosum, a common viral infection due the DNA poxvirus is frequent and is identical in appearance to HIV unexposed patients but tends to be more extensive

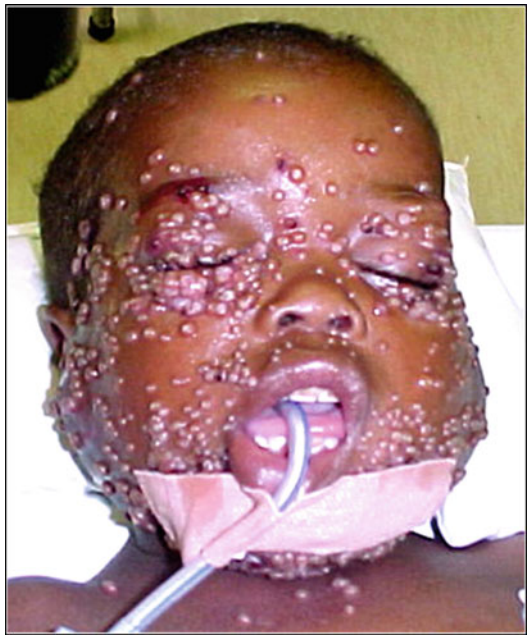

Fig. 2 An HIV infected child with florid facial Molluscum Contagiosum

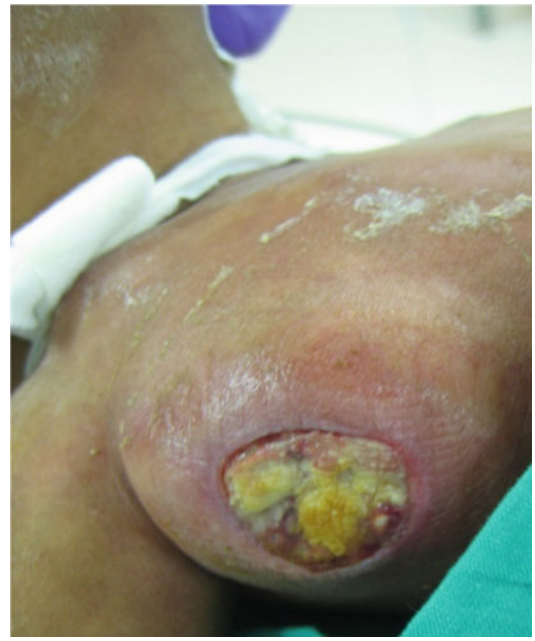

Fig. 3 BCG-associated ulcerating caseous axillary lymphadenopathy

and recurrent, usually occurring on the face and neck (Prose 1992) (Fig. 2).

Complications after BCG (Bacillus Calmette Guerin) vaccination are also commonly seen (Alexander and Rode 2007). Following vaccination with BCG (routinely given in developing countries at birth) children may present with a local reaction and localized non progressive axillary lymphadenopathy. HIV infected children however may develop complications of ulcerating lymphadenopathy especially when starting HAART due to the immune reconstitution inflammatory syndrome (Puthanakit et al. 2006) (Fig. 3).

A conservative approach to treatment is recommended (Zar 2004) but large ulcerating caseating lymph nodes are best treated by excision or curettage. Disseminated BCG disease may occur in HIV infected children and may be indistinguishable from miliary tuberculosis.

Gastrointestinal Tract Disease

Esophagitis is a common problem in HIV infected children that can cause prolonged discomfort and malnutrition, compromise adherence to HAART and lead to increased morbidity and mortality (Fantry 2003). Esophageal symptoms rank second only to diarrhea in frequency of gastrointestinal complaints in children with acquired immune deficiency syndrome (AIDS) (Fantry 2003). Esophageal disease may be a predictor of poor long-term prognosis, as it reflects severe underlying HIV immunodeficiency. Opportunistic infections are the leading cause of esophageal complaints. Treatment for most etiologies of esophagitis generally has a high degree of success, with a resultant improvement in quality of life especially with HAART (Cooke et al. 2009).

The differential diagnosis for esophageal disease includes:

(a) Esophagitis or ulceration. The causes are usually infective in origin, Candida species being the most frequent infection, followed by cytomegalovirus (CMV), herpes simplex virus and idiopathic infective ulceration. Due to overlap of symptoms, endoscopy and biopsy are essential in identifying the pathology (Cooke et al. 2009). The growing number of effective antiviral and antifungal agents has mandated a more goal directed approach to therapy. As

with all severe esophageal infections the motility of the esophagus is adversely affected and this may lead to acid gastro-esophageal reflux which compounds the inflammatory process.

(b) Esophageal strictures. The end result of untreated or extensive ulceration is likely to be stricture formation, occurring in approximately 10% of patients (Cooke et al. 2009). Strictures can be difficult to treat as they respond poorly to dilation and may require esophageal replacement surgery (Issa et al. 2004).

Intra-abdominal Pathology

The diagnosis and management of children with intra-abdominal surgical pathology can be challenging. Localizing signs and symptoms are frequently misleading due to underlying immune-suppression, debilitation, and antibiotic use. Gastrointestinal (GI) bleeding, distension, obstruction, perforation with abdominal pain and tenderness are the most common clinical presentations associated with intra-abdominal diseases in HIV infected children (Bowley et al. 2007).

Gastrointestinal bleeding represents an important source of morbidity and can result from opportunistic infections (CMV or Candida infection), HIV associated malignancies, (Kaposi's sarcoma, leiomyosarcoma or lymphoma) or may be unrelated to HIV infection (Balderas and Spechler 2006). Lower GI bleeding may be caused by CMV colitis, Mycobacterium tuberculosis (TB), malignancy or idiopathic colonic ulceration. Aggressive investigation with endoscopy to find the source of bleeding is required due to the wide differential diagnosis (Zanolla et al. 2001).

Abdominal distension may develop secondary to chronic diarrhea, ileus or obstruction. There are many causes for obstruction including inflammatory and infective causes with TB predominating. Less commonly neoplastic obstruction develops secondary to lymphoma or Kaposi's sarcoma. The obstruction may present due to invasive bowel infiltration by the tumor or from more localized disease and intussusception (Cairncross et al. 2009). In neonates, the use of HAART may mimic functional bowel obstruction.

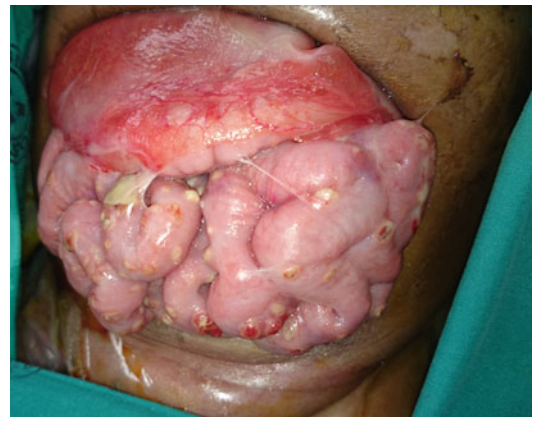

Fig. 4 Multiple perforations of both small and large bowel in an HIV infected infant presenting with peritonitis. CMV as the cause was identified on biopsy

Gastrointestinal perforations may be secondary to CMV, TB, or lymphoma. CMV infections frequently lead to multiple areas of ulceration and perforation with peritonitis (Fig. 4).

Infants with chronic diarrhea may also develop peritonitis due to intestinal perforation (Kahn 1997). HIV infected and HIV exposed uninfected neonates with necrotizing enterocolitis may have a higher mortality and develop more extensive disease than unexposed infants (Karpelowsky et al. 2010). Likewise, infants outside the neonatal period may develop necrotizing enterocolitis type pathology after acute gastroenteritis with shock, which can result in extensive small and large bowel necrosis.

Abdominal pain as a presenting symptom may be due to medical or surgical causes. Both infective and neoplastic conditions may present with abdominal pain. Several unique problems arise however. The taking of HAART may lead to abdominal pain due to pancreatitis or lactic acidosis. Pain in the HIV infected child must be fully investigated for medical, drug induced or surgical causes.

Perineal Disease

HIV infected children have an increased rate of peri-rectal abscess and ano-cutaneous fistula. There are several reports of recto vaginal fistula

and recto urethral fistulae or multiple fistulae with an increased rate of sepsis (Wiersma 2003; Banieghbal and Fonseca 1997). Management includes debridement and antibiotics and on occasion stool diversion with a proximal divided colostomy. Definitive repair without previous anti-retroviral therapy has been reported to have poor results but after several weeks of HAART may be successful.

Anal condylomata are rare in children but an increased incidence has been noted in HIV infected children presenting with extensive and recurrent lesions. Most cases of anal condylomata can be managed with cryotherapy, electrocoagulation or ideally CO2 laser ablation under general anesthesia, taking care not to include the whole anal circumference to avoid anal stricture. A staged approach may be indicated if the lesions are very extensive and may require prior stool diversion with colostomy (Johnson et al. 1997).

Malignancy

Children with HIV infection are at higher risk than HIV unexposed children for malignancy, with tumors representing 2% of AIDS defining events (Hadley and Naude 2009). It is important to exclude with tissue biopsy mycobacterium-avium-intracellulare infection associated pseudotumor or other viral induced lymphadenopathy in any child presenting with a mass. Therefore, for any spindle cell lesion in the setting of HIV infection, it is important to order an acid fast stain to see if these S100- and CD68-positive spindle cells contain mycobacterial organisms. A high incidence of EBV-related smooth muscle neoplasms including leiomyomas and leiomyosarcomas has also been reported in various anatomic sites (mainly central nervous system, but also the gastrointestinal tract, liver, spleen, lung, adrenal, and skin) in HIV-infected adults and children. Detection of EBV (e.g., EBER in situ hybridization) along with smooth muscle markers (e.g., smooth muscle actin) may be of diagnostic aid. HIV-associated malignancies include B-cell lymphoma, mixed-cellularity Hodgkin's disease, leiomyosarcoma and Kaposi sarcoma (Stefan 2014; Stefan et al. 2011).

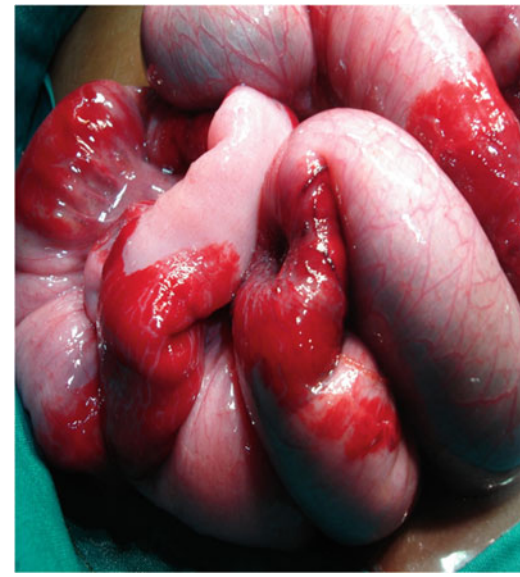

Fig. 5 Small bowel Kaposi sarcoma presenting as intussusception in an HIV infected child

In developed countries 2–3% of HIV infected children will develop an HIV-associated malignancy of which B-cell lymphomas constitute about 80% and Kaposi sarcoma 20% of cases. In contrast Kaposi sarcoma, followed by Burkitt's lymphoma, represent the most significant HIV-associated malignancies in African children due to the epidemiology of herpes virus-8 and Epstein-Barr Virus. Surgery is usually limited to tissue biopsy or to the treatment of complications (Fig. 5).

Incidental solid tumors must be treated as for HIV unexposed children, although coexisting disease, specifically TB, should be considered during the investigation of solid tumors for metastatic spread (Hadley and Naude 2009). This group of co-infected patients has been reported to have a high mortality independent of the primary tumor type. An HIV infected child with a malignancy should be started on HAART as soon as possible. The widespread introduction of HAART has greatly lengthened life expectancy, which may result in an increased lifetime incidence of solid organ malignancy in HIV infected children (Biggar et al. 2000; Caselli et al. 2000).

Medical Aspects of Pediatric HIV Infection and Their Effects on Surgery

HIV infected children have a greater risk of community and nosocomial acquired bacterial infections which are more severe, and have a worse outcome than their HIV unexposed counterparts. Bacterial infection can involve any organ system, and concomitant bacteremia is common. Infections may be polymicrobial and drug resistant, which has implications for use of prophylactic antibiotics given at surgery (Zar 2004; George et al. 2009).

Reduced pulmonary reserve and an increase in pulmonary complications are of concern after major surgery (Zar 2004). HIV infected children have a high incidence of pulmonary complications which may be infective or non-infective. Respiratory involvement in HIV infected children can involve either the upper or lower airway with implications for airway management during anesthesia (Bosenberg 2007). Adeno-tonsillar enlargement can cause upper airway obstruction and difficult endotracheal intubation. There is an increased incidence of chronic lung disease in HIV infected children; this may impact on the anesthetic and peri-operative management (Leelanukrom 2007). Lastly the increased risk of infection may lead to nosocomial pneumonia complicating the post-operative course.

Hematological manifestations of HIV include anemia, neutropenia, lymphopenia and thrombocytopenia (Calis et al. 2008; Eley et al. 2002). Anemia has been repeatedly identified as a strong, independent risk factor for HIV disease progression and death. Severe thrombocytopenia and anemia correlate with advanced disease and poor prognosis. Thrombocytopenia can complicate surgical procedures by increasing bleeding and the need for blood products, leading to increased complications in the peri-operative period.

Gastro-intestinal dysfunction including diarrhea, nausea and vomiting, dysphagia or odynophagia causes significant morbidity among HIV infected children. Abdominal surgery may result in a post-operative ileus. This together with pre-existing intestinal dysfunction can make post-operative fluid management and feeding challenging. Furthermore odynophagia and dysphagia may be secondary to lesions which are friable and thus easily traumatized during airway instrumentation or insertion of a naso-enteric tube causing bleeding or perforation.

Children experience mouth pain from oral lesions and aphthous ulcers associated with candidiasis. Abdominal pain is very common, caused by pancreatitis or colitis. Acute pancreatitis causes severe and diffuse abdominal pain with distention and vomiting. Chronic diarrhea is common in HIV disease and is associated with abdominal cramping. Pain in the mouth and gut may lead to reduced food intake, malnutrition and failure to thrive. Even in the early stages of HIV disease, difficulties with oral intake can have a significant impact on a child's quality of life.

Malnutrition is one of the most frequent and severe complications of pediatric HIV infection, increasing morbidity and mortality. Malnutrition has been reported to be an independent risk factor for an adverse surgical outcome.

HIV infected children are at risk for the development of metabolic complications, which may be secondary to HIV or to HAART. The surgical and anesthetic implications of such complications must be considered (Bosenberg 2007; Leelanukrom and Pancharoen 2007).

Post-operative pain control in HIV infected children can also be challenging. For adequate pain control a combination of medications may be needed, increasing the potential for drug interactions in children who are often taking HAART or other drugs (Abuzaitoun and Hanson 2000).

Outcomes of HIV Infected Children Undergoing Surgery

Few prospective data exist on the outcomes on HIV infected children undergoing surgery (Nelson et al. 2009; Mattioli et al. 2009). The first reports of surgical outcomes in children with HIV infection were brief, focusing on the procedures performed and risk of transmission of HIV to health care workers. Subsequently a few case series reported HIV specific surgical conditions in

children without describing the outcome or complications of surgical intervention, although a neonatal subgroup were reported to have a high post-operative mortality of 30%. Most of these children reported on did not receive HAART.

Several case reports or case series of procedures have been published, raising concerns of poor wound healing, breakdown of anastomoses and surgical site infections (Kleinhaus et al. 1985; Beaver et al. 1990). A recent series of 48 HIV infected children undergoing minimally invasive surgery (MIS) for diagnostic and therapeutic procedures (Banieghbal 2009) concluded that MIS could be safely performed on HIV infected children but that certain routine procedures such as fundoplication were more difficult and prone to complication. The largest series of HIV infected and HIV exposed children undergoing surgical admission was published in 2009 but the report focused on the disease presentations and only alluded to a higher morbidity, furthermore no control group existed in that study (Karpelowsky et al. 2009). There is only one prospective cohort study undertaken comparing the outcomes of HIV infected and HIV unexposed children which noted that HIV infection was the most important risk factor for development of a complication post-surgery, associated with an almost 12-fold higher risk. There was also a significantly higher mortality and longer length of stay (Karpelowsky et al. 2012).

Factors Influencing Post-surgical Complications in HIV Infected Children

Several factors may impact on the incidence of post-operative complications in HIV infected children (Desfrere et al. 2005; Karpelowsky et al. 2012). Highly active antiretroviral therapy (HAART) has reduced mortality and morbidity and improved the quality of life of HIV infected children (Violari et al. 2008). Use of HAART increases the CD4 cell count and reduces the plasma HIV viral load, thus restoring immune function, reducing the direct cytotoxic effect of the virus on some tissues and slowing the progression of HIV disease. Two adult studies have investigated the use of HAART as an independent predictor of surgical complications. Both defined the use of HAART as three drugs for at least 2–3 months prior to surgery. Neither found that the use of HAART reduced post-operative complications. In pediatric studies HAART was not found to be associated with a statistically significant decreased rate of post-operative complications, thus delaying elective surgery for the institution of HAART, which is currently a standard of care may not be warranted although intuitively restoring a compromised immune system prior to surgery and reducing viral load would seem sensible (Karpelowsky et al. 2011a).

Few studies have addressed the clinical stage of HIV as a predictor of surgical complications. Earlier studies, in the absence of CD4 counts or HIV viral load, used CDC clinical definitions to stratify patients (Tran et al. 2000).

Indicators of the stage of HIV infection include an absolute CD4 T-lymphocyte count, percentage of CD4 lymphocytes, and plasma HIV viral load. Most work on the prognosis in HIV infected adults has been based on absolute CD4 counts. Studies assessing the role of CD4 counts in predicting wound healing have drawn conflicting results. A postoperative CD4 count of <18 cells/mm^3 and a pre to postoperative CD4 percentage change of 3% were shown to be independent risk factors for postoperative morbidity (Lord 1997). CD4 counts of <50 cells/mm^3 or an absolute CD4 count of <200 cells/mm^3 i.e. in severe immune-suppression are predictive of an increased incidence of complications. Apart from AIDS other conditions such as severe intra-abdominal infections or trauma can lead to low CD4 counts. There is thus little agreement as to the level of CD4 count that might be predictive of complications in adults.

Viral load indicates the intensity of HIV infection. A postoperative viral load greater than 10,000 copies/ml have been found to be independent risk factors for complications. However, acute medical conditions may transiently increase viral load. No published study to date focuses on the combination of low CD4 counts and a viral load to predict the risk of complications.

Poor nutrition has long been associated with a poor surgical outcome. Increased complications may manifest as higher rates of infection, poor wound healing and an increased postoperative mortality rate. No study on the outcomes of HIV infected patients undergoing surgery has investigated nutrition as a co-morbid factor for adverse outcome. Albumin as a surrogate marker has been used and was found to be a predictor of poor outcome in several studies, but was refuted in another as an independent risk factor. Albumin levels, however may be affected by acute stress and hepatic or adrenal disease thus making them an inaccurate surrogate of nutrition.

Only one pediatric study has assessed predictors of post-operative complications in HIV-infected children undergoing surgery. Although this study was limited by sample size and a high proportion of children with advanced HIV disease it found only age less than 1 year and major surgery to predict post-operative complications. There was no association between poor nutrition, clinical or immunological stage of disease or the use of HAART with post-operative complications (Karpelowsky et al. 2011b).

HIV Exposed Uninfected (HIVe) Children

Children who are HIVe have a higher risk of morbidity and mortality compared to HIV unexposed children (Slogrove et al. 2010; Karpelowsky et al. 2011a). HIVe children have a greater susceptibility to infections including opportunistic infections that tend to be more severe than in HIV unexposed children (Karpelowsky et al. 2011a). Susceptibility to infections may increase the risk for developing complications in the post-operative period.

Poorer growth and nutrition in HIVe compared to HIV unexposed children have been reported. Thus, HIVe children are more likely to be at risk for malnutrition which may impact on outcomes post-surgery.

HIVe children have an increased mortality compared with HIV unexposed children but lower than that of HIV infected children (Karpelowsky et al. 2011a). The risk of death amongst HIVe children was highest in cases of maternal death, low maternal CD4 count or low birth weight.

The increased morbidity and mortality in HIVe children is multi-factorial relating to maternal, environmental and immunological factors all playing significant roles in the morbidity and mortality of HIVe children. These include impaired passive immunity from an HIV infected mother, exposure to a higher disease burden innate immune abnormalities and concomitant impact of maternal HIV illness on child health (Slogrove et al. 2010). T-Cell immunity cytokine abnormalities and antibody function in the HIVe child have also been implicated in the pathogenesis. Currently maternal CD4 count seems to be the strongest variable correlated to the outcomes of HIVe children.

In a prospective study it was noted that HIVe children had a risk of postoperative complications and mortality higher than that of HIV unexposed children but less than HIV infected children (Karpelowsky et al. 2011b).

Conclusion and Future Directions

HIV infected children may present with both conditions unique to HIV infection and surgical conditions routine in pediatric surgical practice. HIV exposure confers an increased risk of complications and mortality for all children following surgery, whether they are HIV infected or not. This risk of complications is higher in the HIV infected group of patients. These findings seem to be independent of whether patients undergo an elective or emergency procedure, but the risk of an adverse outcome is higher for a major procedure. Early treatment with HAART is associated with reduced mortality in HIV infected infants and children. The incidence of infected children presenting for surgery should be significantly reduced by the effective implementation of PMTCT programs. The danger is one of complacency as although once infected by HIV there is yet to be a cure but HAART therapy can virtually clear virus and enable children to live near normal lives. Great emphasis should be placed on PMTCT. The hope for the future is the development of an effective vaccine.

Cross-References

▶ Immunology and Immunodeficiencies in Children

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