Sexually transmitted diseases in children: herpes simplex virus infection, cytomegalovirus infection, hepatitis B virus infection and molluscum contagiosum

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Common sexually transmitted diseases (STD) in adults may occur in children as a result of vertical transmission, non-sexual child to child or adult to child contact, sexual abuse, or voluntary sexual activity. Viral STD are of particular concern as some viruses acquired through vertical transmission may result in fatal neonatal illness, permanent nervous system damage, recurrent disease in childhood and, as in the case of Hepatitis B infection, other long term complications. This review considers childhood illnesses caused by herpes simplex virus (HSV), cytomegalovirus (CMV), hepatitis B virus (HBV), and molluscum contagiosum.

Herpes simplex virus

An historical overview

Genital herpes infection was first clearly described by John Astruc, a French physician, in 1736.¹ By the end of the nineteenth century, the venereal transmission of genital herpes, the varying clinical presentations in both males and females, the recurrent nature of the condition and the histology of herpetic vesicle had all been described. Tissue culture of HSV in rabbit testicular fragments was first reported in 1925 and definitive diagnosis became possible from the late 1950s in conventional tissue culture systems.² Though a difference between herpes febrilis and venereal herpes was suggested by Lipshutz as early as 1921, it was only in the late 1960s that the existence of the two viral types, HSV1 and HSV2, was demonstrated. Thereafter, viral typing methods were developed which allowed the epidemiology of these infections to be clarified. The recognition of type-specific viral glycoproteins gG1 and gG2 in 1985, has now made serological differentiation possible and has facilitated new sero-epidemiological studies.³⁻⁵

In the neonatal period, HSV infections can cause high mortality and morbidity. The first written report of neonatal HSV infection appeared in 1935.⁶ After the neonatal period, genital HSV infection is rarely diagnosed in children. The first case of childhood genital herpes was described in 1853 in an abused 7 year old girl.⁷ Only relatively recently have further reports of transmission through sexual abuse appeared in the English literature.

Epidemiology

Intra-uterine infection is rare.⁸ It occurs as a consequence of transplacental or ascending infection. Although it is more likely to occur

with first episodes of maternal herpes, it has also been reported following recurrent infection and asymptomatic viral shedding. Risk factors associated with intra-uterine transmission require further clarification.

Neonatal HSV infections usually occur as a result of transmission during delivery. The incidence of neonatal HSV infection varies in different populations. In the UK, a rate of 2-3 per 100,000 births has been reported.⁹ In black populations in the USA the rate is about 13/100,000 births. In Africa, neonatal HSV is reportedly rare; the almost universal exposure to HSV2 prior to pregnancy has been postulated as an explanation for this observation.¹⁰

Although HSV1 infections are being more commonly diagnosed, around 80% of neonatal infections are caused by HSV2. The risk of acquiring neonatal infection from a recurrent maternal infection at term, is reported to be less than 8%. The risk is much higher with primary infection at term; as high as 50% was reported by Nahmias.¹¹ However, most infants with neonatal HSV are born to mothers with no history of symptomatic genital herpes at any time, who asymptotically shed HSV at delivery.^{12,13} This may occur in 10% or more of women who acquire primary herpes during pregnancy and in 1-2% of those who acquire the infection before pregnancy. Reports from the USA indicate a 10 fold increase in the incidence of neonatal HSV during the 1980s, following an increase in genital HSV in the general population.¹⁴ Although the incidence of adult genital herpes shows a similar rising trend in the UK, the incidence of neonatal HSV infection still remains very low. The reasons for this transatlantic difference remain uncertain.

Genital herpes infection in childhood is uncommon. Early case reports in children failed to speculate about its method of acquisition.^{15,16} Lazar in 1955¹⁷ described a 4 year old girl with primary herpetic vulvovaginitis whose mother had recurrent herpetic lesion on her fingers and suggested that the transmission was through nonvenereal contact with a virus shedding adult. Nahmias *et al* in 1968⁷ reported six cases, in five girls aged between 7-12 years and a boy aged 3 years, and observed that such infections in children can be transmitted either venereally or non-venereally. He demonstrated HSV1 from both the genital lesions and mouth of two of his cases. Although earlier reports suggested that HSV1 genital lesions could be assumed to be transmitted non-sexually, later case

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reports of HSV1 genital herpes in children with proven sexual transmission clearly demonstrated that detailed enquiry regarding sexual exposure is an essential part of the management of genital HSV infection, irrespective of the HSV type.¹⁸⁻²¹

The risk of acquiring STD by the victims of sexual abuse is related to prevalence of STDs among the adults in different populations. Lindsay in 1992²² reviewed the literature on reported STD among abused children and noted that the risk of acquiring a sexually transmitted disease (excluding ureaplasma, mycoplasma and bacterial vaginosis) varied between <1% and 20%. In all studies, HSV was rarely found. Gardner²³ could find only 1 case of HSV among 209 abused girls. Asymptomatic infection, said to be as high as 50% among adults,²⁴ may also occur in children. However, surveys based on type-specific serological assays in the USA has shown a low HSV2 seroprevalence rate of less than 0.3% in children below 15 years of age.⁴ Ano-rectal HSV infection in sexually abused boys has, so far, not been reported despite this being a common cause of non-gonococcal proctitis in sexually active homosexual males and male children being at higher risk of sexual abuse at a younger age than girls.^{25, 26}

Clinical features

The rare congenital HSV infection presents with widespread cutaneous HSV lesions and scarring at birth, usually with accompanying signs of damage to the central nervous system.⁸

Neonatal HSV infection can present with localised disease limited to skin, eyes and mouth (SEM) or life threatening disseminated disease involving multiple organs. Central nervous system involvement can be a part of the disseminated HSV infection, resulting from viraemia, or can occur in isolation relatively later in neonatal life when it is thought to be due to retrograde axonal transmission.²⁷

The presence of discrete vesicles is the hallmark of SEM. Lesions usually appear during the first week of life. Eye involvement, which can be the sole site of infection and be caused by both HSV1 and HSV2, can manifest with keratoconjunctivitis or, later, with chorio-retinitis. Gingivostomatitis is a rare presentation.⁸

Disseminated HSV disease can also be caused by both viral types and usually becomes evident about 7–10 days after birth. The neonate shows clinical features similar to those of bacterial sepsis with multi-organ involvement. When cutaneous vesicles are absent (in about 20% cases), clinical diagnosis can be very difficult. It is often fulminant, producing severe hepatitis, thrombocytopenia, intra-vascular coagulation and hypotension with or without meningo-encephalitis and pneumonia. Mortality in the absence of therapy exceeds 80%, the commonest cause of death being HSV pneumonitis and disseminated intra-vascular coagulopathy.

HSV encephalitis occurs later in neonatal life and is usually caused by HSV2. Initial

symptoms of fever, lethargy and poor feeding are followed within 24–48 hours by focal seizures which soon become generalised. The CSF can be normal or show elevated protein and lymphocytosis. Cutaneous evidence of HSV is frequently absent in this form of neonatal HSV. The mortality in untreated neonates is about 50% and is usually related to brain stem involvement. With rare exceptions, survivors are left with neurological impairment.

The maternal HSV immune status affects the rate and outcome of infection and the clinical manifestations in neonates exposed to HSV at delivery.²⁸ Sullender²⁹ found significantly low levels of the gG2 antibody in 17 neonates with neonatal HSV2 infection compared to those who were exposed but remained uninfected. Ashley³⁰ found no antibodies to gG2 in all four neonates who developed neonatal HSV in his study, compared to 83% of exposed neonates who remained uninfected. Further evidence for the importance of type-specific antibody status of the neonate comes from the finding by Brown *et al*³¹ that mothers who acquire HSV2 close to term and who are sero positive for HSV1, have a risk of transmitting to their neonates equal to that of seronegative mothers with primary HSV2 infection at term. The majority of infants with disseminated infection have no neutralising antibodies to the infecting or heterologous strain and have low levels of antibody-dependent cellular cytotoxicity.^{32, 33} In contrast, most infants with localised encephalitis have some detectable antibodies at the onset of disease, whilst those with SEM infection are in an intermediate category.

Other host factors are also important as the prognosis for neonatal HSV is poorer in premature infants than in full-term neonates.³⁴

Beyond the neonatal period, childhood genital herpes resembles the clinical presentation in adults. Symptoms of primary genital herpes infection appear after an incubation period of about 3–7 days and include fever, malaise, abdominal pain and groin pain due to lymphadenopathy. Prior to the development of vesicular eruptions, non specific genital symptoms such as pain, pruritus, vaginal discharge and urinary symptoms may be present for 24–48 hours. The herpetic lesions initially appear as erythematous papules which soon become painful vesicles. They may coalesce into larger pustular or ulcerative lesions and persist for up to 14 days. Urinary retention is the presenting symptom in a large proportion of children, particularly the very young.^{17, 18} In boys the lesions are commonly limited to the shaft of penis. Concomitant herpetic gingivostomatitis may be present.⁷ In older children nervous system complications are commonly due to HSV1 originating from the oropharynx and rare following genital HSV2 infection.³⁵

Recurrent cutaneous HSV lesions in survivors of neonatal HSV infection occurring in later infancy and early childhood has been recognised since early 1950s.³⁶ Such cutaneous

neous recurrences tended to be progressively less severe both in the number of vesicles and length of time for resolution.³⁷ Recurrent HSV encephalitis as a result of periodic activation of latent virus results in progressive neurological and developmental damage.^{38,39} There are no data regarding the rate of recurrences among older children, probably because of the small number of diagnosed cases; however there is no reason to believe it is any different from the pattern found in the adults.

Differential diagnosis

Early recognition of HSV infection is essential. The rising proportion of SEM cases amongst those with neonatal herpes reported in the USA is due to increased physician awareness and earlier recognition of the characteristic vesicular lesions.^{8,40} Other conditions causing skin rashes in neonates should be excluded and these include varicella zoster virus infection, enteroviral disease and disseminated CMV disease. Disseminated HSV infection can be difficult to differentiate from bacterial sepsis which can occur concurrently.

In older paediatric age groups, both non-sexually transmitted diseases such as aphthous ulcer, impetigo, erythema multiforme, candidiasis, varicella, as well as sexually transmitted diseases namely primary and secondary syphilis, chancroid, granuloma inguinale and lymphogranuloma venereum, come into the differential diagnosis.

Diagnosis

Virus isolation remains the gold standard for the diagnosis of HSV infection. In neonates, besides skin vesicles, the virus can be isolated from the oropharynx, conjunctivae, urine, stool and CSF. High risk newborns should have swabs taken at 24 to 36 hours of age from eyes and pharynx for HSV cultures.⁴¹ In HSV encephalitis, HSV is rarely detectable from these sites although in a small proportion of neonates with accompanying meningitis, CSF may yield the virus in culture or by polymerase chain reaction techniques. Brain biopsy is usually needed for a firm diagnosis. The classic temporal lobe lesion seen in older children and adults with HSV encephalitis is unusual in neonatal HSV encephalitis. Evidence of clinical HSV disease and/or virus isolation from genital tract of the mother may support the diagnosis of neonatal disease.

Tissue culture diagnosis from cytopathic changes may take several days. A rapid diagnosis, so important in neonatal disease, can be made using antigen detection methods on cell culture 24–48 hours after the specimen inoculation; however the sensitivity of this method is poor. Tzanck smears of vesicular lesions prepared at the bedside can demonstrate multinucleated giant cells suggestive of HSV infection in 50% of cases.⁴²

In older children the virus isolation should be followed by HSV typing and, if possible, type specific serological assay in view of possible medicolegal implications. The guidelines

prepared by the Working Party of the Royal College of Physicians of London on physical signs of sexual abuse in children, should be strictly adhered to when examining every child with genital herpes infection.⁴³

Management

The family Feelings of guilt are frequently observed in parents of children with neonatal HSV infection. The family of a sexually abused child with HSV infection suffers from feelings of failed responsibility in protection of the child, especially when the abuse is intrafamilial. Surviving children who are handicapped by the long term complications related to the eye and CNS, often place additional stresses on the entire family. Parents may require support from psychologists, marriage counsellors, family physicians and friends. Many neonates with HSV infection are born to mothers who have never had symptomatic HSV infection, who will need counselling with particular emphasis on future pregnancies.

Treatment of the child Neonates exposed to active HSV lesions from first episode HSV infection at delivery, should have viral cultures performed on specimens obtained from their conjunctivae, oropharynx and skin as well as specimens of urine, stool and CSF. Positive culture from any of these specimens in neonates older than 48 hours or abnormal CSF findings, are indications for initiating therapy with specific anti-viral drugs.⁴⁴

All neonatal infections must be treated with intra-venous antiviral drugs. Acyclovir is the drug of choice; vidarabine is equally effective but more toxic. The mortality of all forms of neonatal HSV is reduced with treatment, the highest reduction being in SEM disease and the least in disseminated disease. Severe neurological impairment following SEM disease is also reduced by treatment.^{45,46} As in adults, antiviral treatment has little or no effect on latency. A small number of neonates successfully treated with acyclovir or vidarabine, develop recrudescence of infection shortly after completion of therapy.^{38,47} Beyond the neonatal period, the treatment of the condition is similar to that of adults with oral acyclovir therapy, management of urinary symptoms and treatment of super-infections. Particular attention must be paid to the diagnosis of other STD in abused children which may precede or follow an attack of HSV.¹⁹

Although a thymidine-kinase deficient acyclovir-resistant HSV strain was isolated from an immunocompromised 7 year old child treated with three courses of acyclovir,⁴⁸ antiviral resistance is rare in immunocompetent children.^{47,49,50} Acyclovir suppression may be used in children with very frequent recurrences. The use of topical therapy in recurrences is of questionable value. The value of suppressive therapy in children with visceral recurrences remains uncertain.

Follow up Long term follow up of affected children is essential in order to monitor the possible neurological, developmental and

ocular complications of neonatal HSV. The cutaneous lesions of recurrent disease are a potential reservoir for HSV transmission to other children and adults. Parental education aimed at the early recognition of lesions in order that hygienic precautions can be encouraged may help to prevent such transmission. In older abused children, recurrences may have adverse psychological sequelae. Recurring systemic symptoms and local pain associated with outbreaks may cause despair and helplessness with secondary effects on education, quality of life and future sexual relationships. Children affected in this way need long term follow up, additional counselling and help from psychologists.

Prevention Careful clinical examination at the onset of labour to detect mothers with herpetic lesions will help prevent a minority of cases of neonatal herpes. Detection of asymptomatic shedders at term is difficult and cannot be predicted from those with asymptomatic shedding during the last trimester. Screening of mothers with a history of genital herpes by sequential HSV cultures in late gestation is not indicated unless cultures are employed to document cessation of virus excretion after clinical recurrence. Caesarean section is indicated for mothers with active first episodes at term. This method of delivery should not, however, be used as a prophylactic measure in women with a history of recurrent genital herpes unless they have active lesions present at the onset of labour. The clinical benefit of obtaining specimens for culture from mothers without lesions to help identify exposed infants has not yet been established. There are current studies which are investigating acyclovir suppression of genital herpes in late pregnancy in mothers with frequent recurrences, but this cannot be generally recommended with the limited published information presently available.

Prevention of transmission in sexually active older paediatric population, in the current absence of an effective, safe vaccine, can be achieved only through adequate counselling and health education.

Cytomegalovirus

An historical overview

Cytomegalovirus was first isolated in the 1950s, although its causal relationship to devastating neonatal disease had been recognised 40 years earlier.⁵¹ Since the advent of rubella immunisation, CMV has become the commonest viral cause of intrauterine foetal damage. Post-transfusion CMV syndrome, first described by Kreel in 1960, was reported initially in patients receiving multiple blood transfusions after open heart surgery.⁵²⁻⁵⁴ The devastating effects of opportunistic CMV disease have since become apparent in post-transplant patients, those on immunosuppressive drugs and, more recently, in AIDS.

Epidemiology

In most Western countries, CMV infection

occurs in two age groups; early infancy and early adult life. Stern⁵⁵ reported that in London about 10% of children had acquired CMV complement fixation (CF) antibodies by the age of one year. In the USA, 36–56% of infants were found to have CMV viruria.⁵⁶

Infection of infants may be transmitted during intra-uterine life, during delivery from the infected cervix, and in the post-natal period from ingestion of infected breast milk, from other children in nurseries, day care centres and, probably, from other family members. Transplacental transmission is more likely to occur following primary CMV infection during pregnancy; in the USA, this is reported in about 1% of deliveries. The risk of developing symptomatic disease in neonates is higher with primary infection during pregnancy than with reactivated infection, especially in the first half of pregnancy. Stern also reported that about 1–2% of pregnant women in London acquired primary CMV infection and that 50% of their foetuses were infected at birth.

Beyond infancy, little further infection occurs up to the age of 15 years in most western countries. In countries with crowded living conditions, about 80–90% of children are infected by the age of 5 years.

The second peak of transmission, particularly in population with high proportion of susceptible sero-negative adolescents, occurs between 15–30 years of age and is related to sexual activity. The absence of any attributable symptoms or signs at the portal of entry of CMV have made it difficult to demonstrate the sexual route of transmission. Carefully analysed epidemiological data, as well as DNA restriction enzyme finger-printing of CMV isolates, have clearly documented the sexual transmission of CMV in both heterosexual and homosexual population in young adults.⁵⁷⁻⁶¹ CMV is not routinely screened for during investigation of abused children and there are no reports of CMV mononucleosis occurring as a result of such abuse.

Clinical presentation

The consequences of intra-uterine infection range from asymptomatic infection to rapidly fatal neonatal cytomegalic inclusion disease. CMV inclusion disease presents at birth or shortly afterwards, with jaundice, thrombocytopenic purpura, haemolytic anaemia, hepato-splenomegaly, pneumonitis and often evidence of neurological damage. It is often fatal and surviving neonates frequently have residual brain damage. Minor infections with transient clinical features during the neonatal period may also occur and the residual mild brain damage may not be apparent for months or until school age.

Infections in older children generally go unrecognised. A small proportion of children develop CMV mononucleosis presenting with malaise, fever, pharyngitis, hepato-splenomegaly and, occasionally, rash. This syndrome is also accompanied by transient atypical lymphocytosis and hepatitis. Although mental retardation as a result of

CMV infection in this age group has not been reported, chronic CMV infection has been suggested as a cause of non-febrile seizure in children.⁶²

CMV in immunosuppression

Latent virus, probably maintained within leucocytes, may be reactivated in immunosuppressed individuals causing recurrent symptomatic CMV infection.⁶³ In the 3–4 months after transplantation, mononucleosis, unexplained leucopenia, pneumonia and/or hepatitis often occur as a result of CMV reactivation. At a later stage retinitis and, less commonly, encephalitis can develop. In HIV infected children, Frenkel⁶⁴ reported active CMV infection in about 45% of those with symptomatic disease. CMV retinitis is the most frequent cause of sight threatening disease in the corresponding adult population, however the incidence of blindness in paediatric AIDS is reportedly low.⁶⁵

Diagnosis

Isolation of CMV from urine, saliva, semen and cervical secretion is insufficient to ascribe a causative role for CMV to the clinical features under investigation. Detection of CMV in the urine of a newborn within the first week of life establishes congenital infection, but does not distinguish symptomatic from asymptomatic infants. Isolation of the virus from buffy coat leucocytes, however, has been found to have a high correlation with the presence of CMV disease.⁶⁶ Active infection is strongly suggested by seroconversion and the demonstration of CMV specific IgM antibody. The presence of typical cytomegalic inclusion cells in biopsy specimens is also indicative of an ongoing tissue infection. Prenatal diagnosis of CMV infection can be made on amniotic fluid culture; however, the sensitivity of this diagnostic method is unknown.⁶⁷

Treatment

Treatments for CMV infection in children of unproven value have previously included floxuridine, idoxuridine and cytarabine.⁶⁸ Vidarabine and acyclovir have also been used, but without satisfactory effect. Ganciclovir and foscarnet are currently the two drugs in use for treatment of both AIDS-related and AIDS-unrelated CMV disease. Recurrence of CMV disease in immunosuppressed individuals is common and maintenance therapy with these drugs is essential. Children with a high risk of developing CMV disease, such as after transplantation, are usually given prophylactic therapy. Acyclovir has been reported to be useful for prevention of CMV disease in bone marrow allograft recipients in whom ganciclovir and foscarnet carry a high mortality. In renal transplant patients, acyclovir prophylaxis is also reported to be effective. Concomitant administration of immune globulin may additionally limit serious CMV disease in these situations.⁶⁹

Prevention

Prevention of neonatal CMV disease will be

directly related to prevention of primary CMV disease during pregnancy. In the West, the number of girls reaching child bearing age with CMV seronegative status has steadily increased, making them vulnerable to primary disease at pregnancy. Two attenuated live virus vaccines are being tested for use in women of child bearing age.⁷⁰ Among healthy seronegative volunteers, over 95% had shown seroconversion with these vaccines and infants born to immunised mothers had no detectable CMV infection. Further studies are needed regarding the safety and effectiveness of these vaccines.

Hepatitis b

An historical overview

During the early twentieth century, jaundice was frequently encountered as a complication of intravenous arsenical injections for syphilis.^{71 72} During this same period, plasma administration for immunoprophylaxis in measles and mumps, as well as administration of vaccines containing human serum, such as for yellow fever, and blood transfusions were also noted to be complicated by the development of jaundice.^{73 74} After observing that intravenous drugs were given using inadequately sterilised syringes and needles between patients, Bigger⁷¹ suggested that the jaundice might be due to transmission of a virus from patient to patient. Most of these cases were undoubtedly due to Hepatitis B virus (HBV). It was the discovery of Australia antigen by Blumberg in 1965⁷⁵ and its eventual association with serum hepatitis that made positive diagnosis of this condition possible.

Epidemiology

HBV infection occurs throughout the world with widely varying prevalence rates. It is endemic in most developing countries where about 95% of the 300 million worldwide chronic HBV carriers live.⁷⁶ The prime reason for the persistence of high rates of chronic HBV infection in these populations, is the acquisition of infection during early childhood.⁷⁷ The risk of persistent HBV infection in children is inversely related to the age of initial infection; the reported risk is 70–90%, 60% and 10% when the infection is transmitted perinatally, during the second year of life, and at 6 years of age, respectively.^{78–80}

Intra-uterine transmission is the route of infection in only 5%–10% of neonatal HBV infections.⁸¹ The vast majority of neonatal HBV infections are a consequence of transmission at delivery or during the early postpartum period. The rate of transmission from mother to infant depends upon maternal infectivity; it is approximately 85% if she is e antigen (HBeAg) positive and 31% if HBeAg negative.⁸² In South-east Asia, perinatal infection is more common because of the larger proportion of HBeAg positive parturient women, as compared with Africa, Middle East and Arctic where fewer than 20% of HBsAg positive mothers are also HBeAg positive.^{83–85} In high and intermediate endemic

areas, substantial transmission also occurs during the early childhood period from infected family members, at schools and in institutions.⁸²⁻⁸⁸ Beasley⁸³ reported that in Taiwan, 10.6% of preschool children seroconverted during a 2 year follow up. A significant correlation between the frequency of injections, particularly those administered in rural hospitals, and the incidence of HBV infections in children has also been reported, indicating that contaminated needles is another source of infection. Similarly, ear piercing and scarification in children had been related to HBV transmission in parts of Africa.⁸⁶

In most developed countries, the prevalence of chronic HBV is less than 2% and transmission occurs primarily among adults. Only 1–3% of all HBV infection in these countries occur in children under 5 years of age; however, they account for 20–30% of all chronic infections.⁷⁷ In the USA, sexual transmission of HBV is the route of infection in 50% of teenage children who present with acute HBV infection. Reviewing the STD in rape victims, Glaser in 1989⁸⁹ could find no reported cases of CMV or HBV infection in children known to have been sexually abused. However, the risk is likely to be significant in high endemic areas.

Clinical presentation

In over 90% of neonates and young children, HBV infection is asymptomatic. Beasley⁸³ found no cases of clinical hepatitis among the 1,110 Chinese children studied in Taiwan. Neonates and young children often remain HBsAg positive for life. Studies in Japan, Taiwan and other endemic areas had shown that most children, in spite of showing persistent antigenemia, thrive and show no clinical evidence of hepatic disease. Schweitzer⁹⁰⁻⁹¹ reported that many children, however, show variable elevated levels of transaminases and histological evidence of persistent mild hepatitis. The mild persistent hepatitis is not always clinically stable, as some children followed up for a long term, will develop chronic liver disease.⁹²⁻⁹³ Neonatal HBV infection with persistent antigenemia can also progress to cirrhosis and hepato-cellular carcinoma.

Those neonates who develop overt hepatitis generally do so as the passive immunity wanes 2–3 months after birth. The severity of infection ranges from mild hepatitis with rapid recovery to fulminant hepatitis. Fulminant hepatitis B is rare, but carries a high mortality and high risk of cirrhosis development in survivors.⁹⁴⁻⁹⁵

Diagnosis

Sero-diagnosis in HBV infection is reliable, sensitive and specific. Detection of HBsAg, a positive anti-HBc IgM fraction and a rising anti-HBc titre are indicative of acute infection. In some patients, HBsAg is undetectable at clinical presentation. Presence of anti-HBs and anti-HBc antibodies without HBsAg or anti-HBc IgM, is consistent with past infection. Persistence of HBsAg and a high titre of

anti-HBc is indicative of chronic infection.

Treatment

In chronic hepatitis B infection, treatment with interferon-alpha has been reported to result in seroconversion from HBeAg to Anti-HBe status with loss of serum HBV DNA, in 30–50% of patients.⁹⁶ The effect of this therapy on the occurrence of cirrhosis and malignancy is not known. Many other therapeutic agents, both antiviral and immunomodulators, have shown disappointing results; other trial drugs are being assessed for their effectiveness in chronic Hepatitis B infection.

Prevention

Prevention of transmission, identification of at-risk populations, and protection through effective vaccination should be the basis for effective control of this infection.

Most infants born to HBV infected mothers are HBV negative at birth, but become positive within the first three months of life. Immunoprophylaxis, therefore, should be effective in preventing neonatal infection and hence reduce the size of HBV carrier population. Stevens⁹⁷ demonstrated that use of both Hepatitis B immunoglobulin and Hepatitis B vaccine at birth in “at risk” children reduced the carrier rate from 85% to 14.2%. Both the plasma-derived and recombinant DNA vaccines are safe and have been demonstrated to be effective in over 95% of immunocompetent people.⁹⁸ Current recommendations for the prevention of neonatal HBV infection are to give both active and passive immunisation at birth. Countries with high endemic HBV infection are developing strategies for the effective use of hepatitis B vaccine. In low endemic countries, such as the UK, the vaccination programmes are generally limited to identified, mainly adult, risk populations.

Molluscum contagiosum

An historical overview

There have been descriptions of molluscum contagiosum (MC) in the medical literature since 1817.⁹⁹ The transmissible nature of material from lesions, earlier called Henderson-Patterson bodies, has been known since the early 19th century; however, the MCs have also been described as epitheliomas and parasitic nodules. In 1905, Juliusburg established their viral nature by transmitting the disease using a filtrate of MC fluid. Recently, restriction endonuclease analysis of molluscum contagiosum virus (MCV) DNA has revealed the existence of two viral subtypes namely MCV1 and MCV11.

Epidemiology

MC is prevalent worldwide and affects two different age groups; children and young adults. Childhood MC is particularly common in Papua New Guinea, Fiji and certain parts of Africa.¹⁰⁰⁻¹⁰¹ In these countries the disease is most commonly seen in

children aged less than 5 years and, in some geographical regions, a prevalence rate approaching 25% has been reported. Adolescent MC is commonly seen in STD clinic attenders.

The infection is commonly acquired through close skin to skin contact; fomites, swimming pools, public baths, towels, gymnasium equipment and benches have been implicated.⁹⁹ Skin contact associated with sexual intercourse is the mode of transmission in young adults. The MCV type 1 is much more prevalent than MCV type 11 but neither subtype is exclusively associated with genital or non-genital lesions.¹⁰²⁻¹⁰⁴ However, MCV type 11 is rare in children below 15 years of age.

Clinical features

MC is a localised proliferative skin lesion which is confined to the epidermis. The lesions are smooth, firm, raised and flesh coloured nodules measuring about 2–5 mm in diameter which often show a typical central depression. In children, the lesions are more often found in the face, trunk and limbs whereas in young adults they are commonly found around the genital area. They can also occur on the eye-lids and may infect the conjunctiva, but they are rare on the palms and soles. The number of lesions can vary greatly and lesions in their hundreds have been described in children from endemic areas. In atopic dermatitis and immunosuppressed conditions including AIDS, multiple, widespread, persistent and disfiguring lesions can occur especially in the face.¹⁰⁵⁻¹⁰⁷ The MCs can coalesce to form plaques of confluent lesions.^{108 109} Development of profuse lesions of MCs may be the presenting feature of other underlying systemic diseases associated with immune suppression.¹¹⁰

Most patients with MC lesions are asymptomatic. A few patients may have pruritus and tenderness. "Molluscum dermatitis", an eczematous area around MC lesions has been described in about 10% of patients.^{111 112} Individual lesions may become inflamed and resemble furuncles.

Diagnosis

MC is usually diagnosed clinically, based on the classic appearance of the lesions; additional diagnostic procedures are seldom needed. Atypical MC lesions or typical MC lesions in unusual anatomic sites can be shown histologically or cytologically to contain molluscum bodies. Other laboratory methods used to confirm the diagnosis include electron microscopy of fixed material from a lesion and MC specific antigen detection by fluorescent antibody technique. In AIDS, cutaneous cryptococcal lesions, when presenting in large numbers, can resemble MC and histologic examination will be necessary for a definitive diagnosis.^{113 114}

Treatment

In immunocompetent individuals, MC lesions often resolve spontaneously if left

untreated; each lesion may persist for about two months.¹¹⁵ The lesions, however, especially in immunosuppressed states, may continue to erupt and persist in spite of treatment. The prognosis is generally determined by the underlying condition. In children with hundreds of lesions and who are otherwise well, the treatment may have to be carried out under general anaesthesia for cosmetic reasons as well as to prevent autoinoculation, superinfection and transmission.¹¹⁶

Treatment of MCs involves mechanical removal of virus containing material. This is usually carried out by breaking the MC lesion and cauterising the open skin using either chemical irritants, such as phenol, or electrocauterisation. Cryotherapy with liquid nitrogen is also effective. There are no reports of any effective systemic therapy for this condition.

Future developments

Success in the control of viral STDs in general will depend on the prevention of transmission of infection, reduction of "carrier population" and improved awareness among the public and health profession. Just as the development of vaccination now permits prevention programmes against hepatitis B in neonates, there is a clear need to develop effective vaccines against the herpes viruses, especially HSV and CMV. An effective vaccine against HSV is still a distant prospect and health education of the general public is likely to have only limited impact. Improved methods for rapid diagnosis of neonatal herpes and new antiviral drugs which combine the wide therapeutic index of acyclovir with increased efficacy and less frequent dosing intervals are needed. The wider availability of serological assays for type specific antibodies to HSV is essential to promote better understanding of local prevalence and help identify mothers who may be at increased risk of acquiring HSV during pregnancy.

In CMV infection, prospects for an effective vaccine are possibly nearer, but there is an urgent need for more effective, less toxic drugs for treatment of active disease. Oral preparations of ganciclovir currently on trials in adults would be an advance but is unlikely to answer all the problems of management of immunocompromised children.

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