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Neonatal stridor in association with herpes simplex infection of the larynx

H. R. Sharp, F.R.C.S., S. P. A. Blaney, F.R.C.S., G. A. J. Morrison, F.R.C.S.

Abstract

Herpes simplex virus (HSV) infection in the neonatal period may be confined to the eyes, skin and upper aerodigestive tract or may be widely disseminated to other organs, with particular recognition of involvement of the central nervous system (CNS) causing herpes encephalitis (Whitley *et al.*, 1980a, b; Andersen, 1987).

Primary laryngeal HSV infection is extremely uncommon. We present a case of acute neonatal stridor secondary to such localized disease and discuss its management.

Key words: Respiratory sounds; Neonatal; Herpes simplex; Acyclovir

Case report

A 13-day-old boy was admitted to hospital with a 48-hour history of worsening stridor, difficulty in feeding and vomiting. He had had a coryzal type illness for five days prior to his presentation. He was born at 39 weeks via a normal vaginal delivery, and had had no other neonatal problems. At initial assessment, he was afebrile, with mild biphasic stridor and bilateral widespread rhonchi on chest auscultation. There was no mucocutaneous vesicular eruption. Chest X-ray and white cell count were normal, a provisional diagnosis of 'viral tracheobronchitis' was made and he was commenced on intravenous cefotaxime and benzylpenicillin. Hours later he deteriorated markedly, with worsening stridor, respiratory distress and the development of tracheal tug and intercostal recession. He became increasingly cyanosed and bradycardic, and despite adrenaline nebulizers and systemic steroids suffered a respiratory arrest. He was resuscitated, intubated and transferred to the Intensive Care Unit. Intravenous erythromycin was added to his therapeutic regime, and over the next 24 hours his ventilatory requirements decreased to a point where extubation was attempted. He quickly developed further stridor, but oxygen saturations were maintained on 30 per cent oxygen. An echocardiogram at this stage showed no evidence of cardiac or aortic arch anomalies, and no evidence of a vascular ring.

Microlaryngoscopy and bronchoscopy was carried out, which demonstrated areas of patchy oedema and ulceration over the laryngeal surface of the epiglottis and both vocal folds, extending into the subglottis (Figures 1 and 2). Biopsies and culture swabs were taken, a presumptive diagnosis of viral or fungal infection made and treatment with intravenous acyclovir, nystatin and fluconazole instituted. Herpes simplex type 2 virus was confirmed via the polymerase chain reaction three days later.

After seven days of acyclovir therapy he was well enough to be discharged, breast feeding normally and with no remaining airway noise. On direct questioning both parents did suffer with intermittent oral herpetic vesicles, but neither had had clinical or symptomatic evidence of active infection over the infant's life. Subsequent vaginal swabs taken from the mother were negative for HSV. Follow up at three and six months revealed no further episodes of airway compromise and otherwise normal infantile development.

Discussion

Isolated HSV infection of the upper respiratory tract is extremely uncommon as compared to mucocutaneous or disseminated, and in particular CNS, involvement.

Whitley *et al.* (1980a) studied the presenting features and likely aetiology of 56 infants with HSV infection. Fifty per cent of the infants had gestations ending in premature labour and 70 per cent of the mothers were asymptomatic and clinically free from infection at the time of delivery. Twenty-eight per cent of the group had had a bacterial infection predating their HSV infection. Seventy-one per cent had skin vesicles as their mode of presentation and of

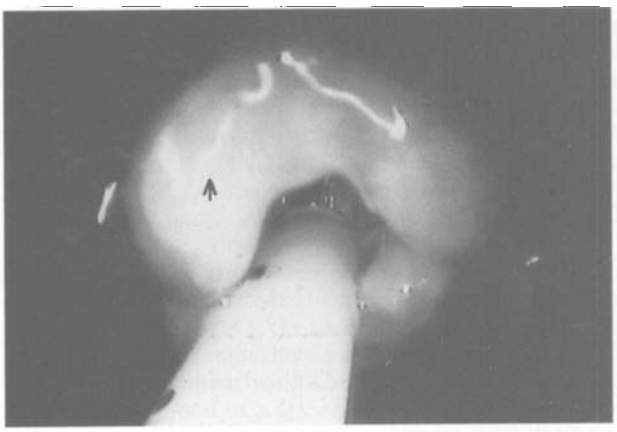

Fig. 1
Ulceration on laryngeal surface of epiglottis (arrow).

From the Department of Otorhinolaryngology/Head and Neck Surgery, Guy's and St Thomas' Hospitals, London, UK.
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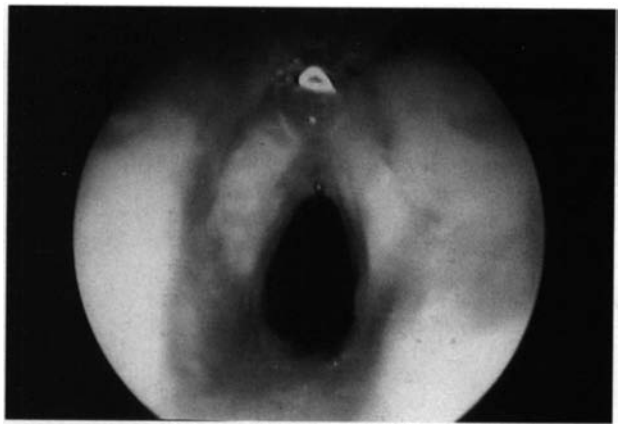

FIG. 2
Diffuse oedema and ulceration of both true and false folds.

these 70 per cent progressed to more severe infection. None of this group presented with respiratory tract symptoms. Andersen (1987) described three cases of neonatal HSV infection presenting with a febrile illness and predominantly lower respiratory tract symptoms. This occurred without mucocutaneous involvement or clinical evidence of maternal infection. Arvin *et al.* (1982) suggested that disseminated HSV infection and HSV encephalitis may occur in up to 70 per cent of infected infants without prior development of mucocutaneous lesions.

Whitley *et al.* (1980b) recorded that vidarabine therapy caused 50 per cent of babies to cease shedding virus by day four, and 100 per cent ceased viral shedding by day 10. However, while significantly reducing mortality in severe CNS HSV infection, vidarabine had more dubious efficacy with more superficial involvement, and they suggested that its use in such cases warranted larger studies.

Nyquist *et al.* (1994) described a case of HSV type 2 infection of the upper airway that was resistant to treatment by both acyclovir and foscarnet. They postulated that this was due to rapid selection of resistant strains among the HSV pool by antiviral therapy, or by direct transmission of resistant virus. Others have suggested that the disease responds rapidly to acyclovir, as in the case presented by us. Nadel *et al.* (1992) presented two patients with HSV infection of the upper airway that resolved with acyclovir therapy, including one case in which large doses of corticosteroids were employed before the diagnosis was made. They suggested, however, that the steroids may have prolonged the period of infection and recommended that such treatment should be withheld from all neonates under one month of age until HSV infection has been excluded. They also postulated that HSV infection of the upper aerodigestive tract may be caused by over-vigorous suctioning of the airway during the period of delivery facilitating the entry of vaginal HSV into the areas of mucosal injury. Wackym *et al.* (1986) suggested a similar aetiology in adults whereby intubation trauma may be the cause of herpes zoster infection in the adult larynx. They went so far as to suggest indirect laryngoscopy in every patient following intubation.

In summary, HSV infection of the upper airway should be considered in the stridulous neonate even if skin and other disseminated disease is not clinically evident. Diagnosis is made via endoscopy with patchy erythema, oedema and shallow ulceration being the characteristic features. Confirmation of the infection is achieved with polymerase chain reaction techniques via a very small biopsy specimen. There may be a 48-hour period before a positive result is achieved, but we recommend early institution of acyclovir therapy as soon as there is sufficient clinical suspicion of HSV.

Fourteen days of therapy is standard in disseminated involvement although we found that 10 days of treatment resulted in resolution of laryngeal infection. It must be borne in mind that failure to respond may suggest viral resistance.

References

Andersen, R. D. Herpes simplex virus infection of the neonatal respiratory tract. *American Journal of Diseases of Children* **141:** 274–276.

Arvin, A. M., Yeager, A. S., Bruhn, F. W., Grossman, M. (1982) Neonatal herpes simplex infection in the absence of mucocutaneous lesions. *Journal of Pediatrics* **100:** 715–721.

Nadel, S., Offit, P. A., Hodinka, R. L. Gesser, R. M., Bell, L. M. (1992) Upper airway obstruction in association with perinatally acquired herpes simplex virus infection. *Journal of Pediatrics* **120:** 127–129.

Nyquist, A.-C., Rotbart, H. A., Robinson, C., Weinberg, A., Hayward, A. R., Berens, R. L., Levin, M. J. (1994) Acyclovir-resistant neonatal herpes simplex virus infection of the larynx. *Journal of Pediatrics* **124:** 967–971.

Wackym, P., Gray, G., Avant, G. (1986) Herpes zoster of the larynx after intubation trauma. *Journal of Laryngology and Otology* **100:** 839–841.

Whitley, R. J., Nahmias, A. J., Visintine, A. M., Fleming, C. L., Alford, C. A. (1980a) The natural history of herpes simplex virus infection of mother and newborn. *Pediatrics* **66:** 489–494.

Whitley, R. J., Nahmias, A. J., Galasso, G. G., Fleming, C. L., Alford, C. A. (1980b) Vidarabine therapy of neonatal herpes simplex virus infection. *Pediatrics* **66:** 495–501.

Address for correspondence:
Mr H. R. Sharp, F.R.C.S.,
Department of Otorhinolaryngology – Head and Neck Surgery,
Guy's and St Thomas' Hospitals,
Lambeth Palace Road,
London SE1 7EH.