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Infections of the upper respiratory tract in cases of sudden infant death

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Abstract The nasal cavities were examined in 56 cases of sudden infant death syndrome (SIDS) and 26 control cases and the following criteria were compared: inflammatory infiltration of the nasal mucosa (SIDS 59% – controls 65%; $P = 0.577$), diapedesis of inflammatory cells (SIDS 38% – controls 42%; $P = 0.678$), epithelial desquamation (SIDS 62% – controls 85%; $P = 0.043$); hyperemia (SIDS 66% – controls 65%; $P = 0.951$) and hypersecretion of the seromucous glands (SIDS 55% – controls 69%; $P = 0.233$). Only epithelial desquamation was found significantly more often in the controls than in SIDS cases, but these alterations are unspecific and are influenced by the postmortem interval. The intensity of rhinitis was not different between the SIDS and control groups. The frequency of rhinitis is therefore not specific for the sudden infant death syndrome, and seems to be merely a result of the high incidence of upper respiratory tract infections in this age group. We speculate, however, that infections of the nose in conjunction with other factors, such as prone position, covering of the head, hyperthermia, parental smoking and immaturity of the central nervous system, could play a role in the pathogenesis of the sudden infant death syndrome.

Key words SIDS · Infection · Rhinitis · Upper respiratory tract

Introduction

A possible role of upper respiratory tract infections in the etiology of the sudden infant death syndrome has been discussed for many years (Bowden 1950; Wilske 1984; Zink et al. 1987; Entrup and Brinkmann 1990). Most of these studies focused on the morphology of lower respiratory tract and pulmonary infections. Examination of the nose and pharynx was only included in studies by Althoff (1977, 1986). Because Althoff's investigations did not include any or included only a few control cases, we used the method described by Gräff (1932, 1934) and Althoff (1977, 1986) to examine the nasal cavities in cases of sudden infant death syndrome and control cases.

Materials and methods

Thorough postmortem examinations were performed at the Department of Legal Medicine of the Hannover Medical School on 56 cases of sudden infant death syndrome (22 female, 34 male) and 26 controls, aged between 7 and 365 days. The average age in the SIDS group was 124 days, in the control group 163 days. Of the SIDS victims, 78.6% died during the first 6 months of life and 55.4% between the 2nd and 4th months. The autopsy included microbiological and immunological testing. The definition of sudden infant death syndrome used was that of Beckwith (1970), and slight illnesses such as mild infection of the upper respiratory tract, isolated middle ear infections, and positive bacteriological or virological results unanccompanied by morphological findings were

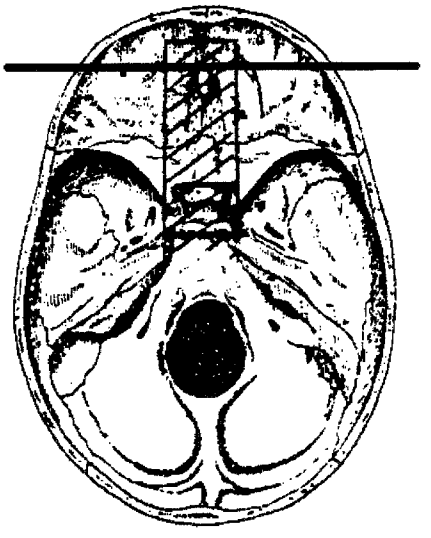

Fig. 1 View of the skull base and section line (modified after Althoff 1977)

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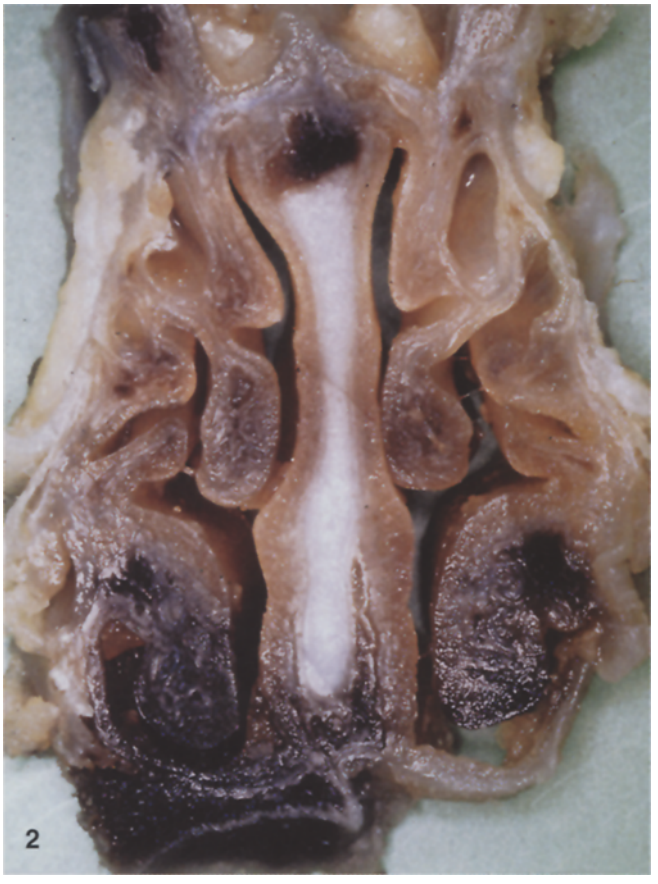
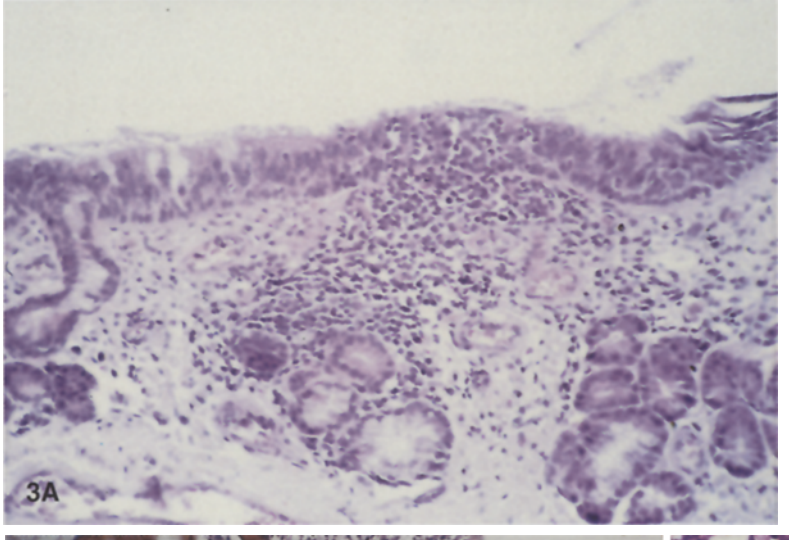


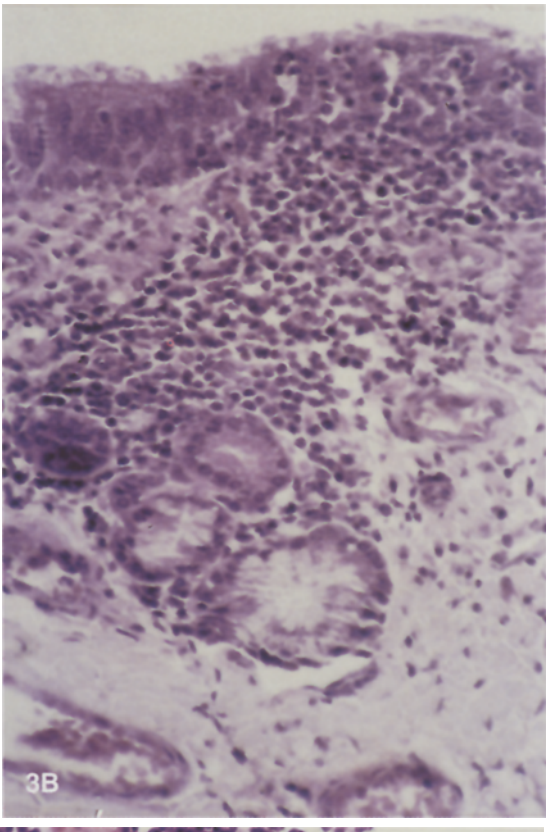
Fig. 2 Parafrontal section through the nose

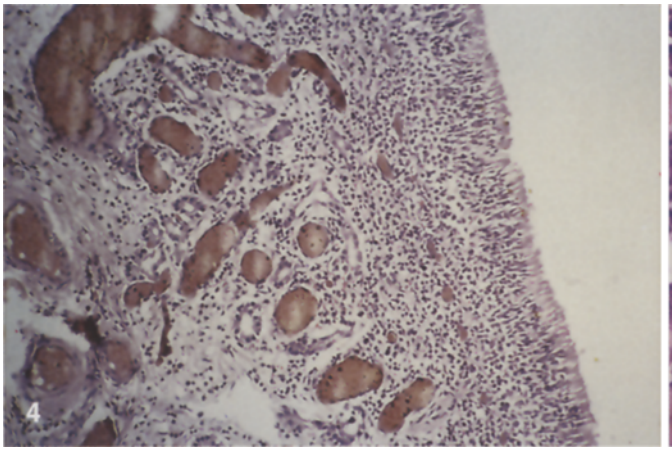
Fig. 3 **A** Overall view, **B** detail, of nasal mucosa: focal inflammatory cellular infiltration showing migration through the epithelium, hypersecretion. Hemalaun-eosin stain

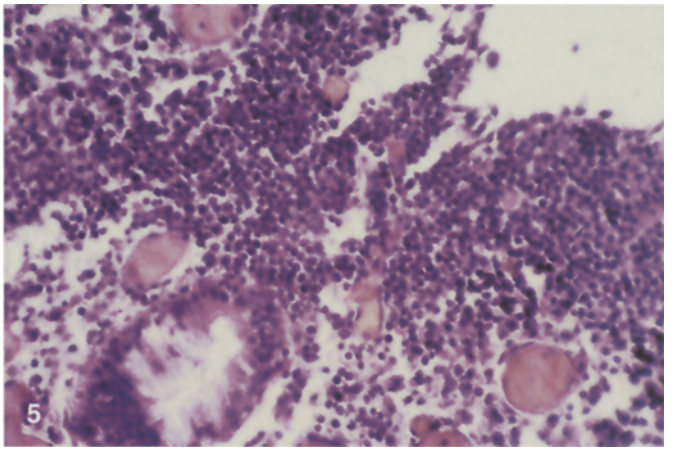
Fig. 4 Nasal mucosa: diffuse mononuclear infiltration, migration through the epithelium, hyperemia. Hemalaun-eosin stain

Fig. 5 Nasal mucosa: diffuse necrotizing rhinitis. Hemalaun-eosin stain









not considered to have been the cause of death. The control group encompassed 15 infants (7 female, 8 male) with traumatic causes of death, e.g. craniocerebral injuries ($n = 1$), CO poisoning ($n = 1$), suffocation or strangulation ($n = 11$), drowning ($n = 1$), blunt trauma injuries ($n = 1$) and 11 (6 female, 5 male) with natural causes of death, e.g. pneumonia ($n = 4$), enteritis ($n = 1$), encephalitis ($n = 1$), and congenital malformations ($n = 2$). All children with traumatic causes of death died shortly after the trauma, and none received medical care in hospital.

At autopsy an oscillating saw with a long, thin blade was used to remove blocks from the anterior base of the skull (Fig. 1). The nose blocks prepared by this procedure were decalcified using Althoff's method (personal communication). The blocks were incubated in 8% formic acid for 24 h and 20% formic acid for 3 × 1 h and parafrontal sections were made (Fig. 2). Hemalaun eosin (HE), Masson-Goldner, Giesons's elastica and PAS were used as stains and 2 examiners studied the specimens. For comparison of the frequencies, the variables were analyzed by the Chi-square test; the age distribution was verified by analysis of variance.

Results

The following histomorphological criteria were evaluated: inflammatory infiltration of the nasal mucosa, epithelial desquamation, hyperemia, diapedesis of inflammatory cells and hypersecretion of the seromucous glands. Only epithelial desquamation differed significantly between the two groups (Table 2). The criteria epithelial desquamation and hyperemia were further differentiated with respect to intensity (Tables 3 and 4). For a comprehensive evaluation of the inflammatory changes of the nasal mucosa, the classification according to Althoff (1977) given in Table 5 was chosen (Fig. 3–5). There were no significant differences in frequency of inflammatory changes between SIDS cases and the controls.

Table 1 Age distribution among SIDS cases and controls (analysis of variance: $P = 0.156$)

Age in days	SIDS $n = 56$	Traumatic death $n = 15$	Natural death $n = 11$	Total controls $n = 26$
7– 90	22	3	3	6
91–180	22	6	4	10
181–270	9	4	2	6
271–365	3	2	2	4

Discussion

A connection between the pathogenesis of the sudden infant death syndrome and infections of the respiratory tract has been postulated for a long time. An increased incidence of the sudden infant death syndrome during the cold winter months has been observed world-wide and the increased frequency of infections during these months makes a correlation of the two seem especially likely. Some authors have reported an association with viral epidemics (Marshall 1972; Nelson et al. 1975; Bonser et al. 1978). These findings were questioned by other groups (e.g. Ford et al. 1990). In Southern Australia, a common frequency peak of sudden infant death syndrome and hospital admissions of children due to bronchiolitis was observed between 1975 and 1981 (Beal 1986). A mild infection of the upper respiratory tract was often found to precede sudden infant death syndrome (Hoffmann et al. 1988). In 30–85% of the cases, histological proof of mild infection of the respiratory tract was found, and less commonly of the middle ear, gastrointestinal tract or other organs (Wilske 1984; Entrup and Brinkmann 1990; Berry 1992).

Morphological studies performed so far have not included analysis of the nasopharynx, even though this region plays an important part in the pathological mechanism especially in this age group. The only study which is comparable to ours is one by Althoff (1986), which includes a systematic examination of the nose and pharynx in 324 cases of sudden infant death syndrome and 6 control cases in the same age group. In the sudden infant death syndrome cases, he found normal results in 28% (89 cases), while 35% (113 cases) demonstrated focal and lo-

Table 2 Comparison of results according to histomorphological criteria in the SIDS and the control groups

	SIDS $n = 56$	Traumatic death $n = 15$	Natural death $n = 11$	Total controls $n = 26$	Chi-square test
Inflammatory infiltration of the nasal mucosa	59%	73%	55%	65%	$P = 0.577$
Diapedesis of inflammatory cells	38%	40%	46%	42%	$P = 0.678$
Epithelial desquamation	62%	87%	82%	85%	$P = 0.043$
Hyperemia of small nasal vessels	66%	73%	55%	65%	$P = 0.951$
Hypersecretion of seromucous glands	55%	67%	73%	69%	$P = 0.233$

Table 3 Epithelial desquamation in the SIDS and control cases according to severity

	SIDS $n = 56$	Traumatic death $n = 15$	Natural death $n = 11$	Total controls $n = 26$
Without epithelial detachment	37%	13%	18%	15%
Epithelial detachment up to one third of the nasal section	41%	53%	46%	50%
Epithelial detachment up to two thirds of the nasal section	17%	33%	36%	35%
Complete epithelial detachment	5%	0%	0%	0%

Table 4 Hyperemia in SIDS and control cases according to severity

	SIDS $n = 56$	Traumatic death $n = 15$	Natural death $n = 11$	Total controls $n = 26$
Without hyperemia	34%	27%	36%	31%
Strong hyperemia	32%	27%	27%	30%
Massive hyperemia	34%	47%	36%	42%

Table 5 Inflammatory changes in SIDS and controls according to severity

	SIDS $n = 56$	Traumatic death $n = 15$	Natural death $n = 11$	Total controls $n = 26$
Normal findings; only slight hyperemia	41%	27%	46%	35%
Mild focal rhinitis with inflammatory infiltration and without significant epithelial involvement	46%	53%	36%	46%
Acute diffuse rhinitis with epithelial desquamation and dissociation, diapedesis of lymphomonocytic inflammatory cells, mucous gland hypersecretion, hyperemia	11%	20%	18%	19%
Acute necrotizing rhinitis with complete round cell infiltration of the mucosa, complete epithelial loss, massive hyperemia with hemorrhages	2%	0%	0%	0%

calized changes, 33% (108 cases) revealed diffuse and 4% (14 cases) necrotizing rhinopharyngitis. As a comparison, he included 6 control cases with acute unnatural causes of death (e.g., CO intoxication, trauma to the central nervous system, external choking). In these cases, 4 infants showed normal findings and 2 revealed mild focal rhinopharyngitis. Diffuse or necrotizing inflammatory changes were not observed in these control cases.

In our study, 59% of the sudden infant death syndrome cases demonstrated rhinitis, which correlates with reports in the literature of the frequency of respiratory infections in the sudden infant death syndrome. However, almost the same frequency of infections was noticed in the control cases. These findings therefore confirm the frequency of infections as a common observation in this age group. We speculate, however, that infections of the nose combined with other factors could play a role in the sudden infant death syndrome. Since infants are obligate nose breathers and learn breathing through the mouth during the 1st year of life, even small infections of the nose can cause obstruction of the airway. A coincidental presence of other factors that increase the risk of sudden infant death syndrome, such as the prone and/or face-down position (Saternus 1985; Fleming et al. 1990; Jorch et al. 1991; Schäfer et al. 1991; Mitchel et al. 1992), covering of the head and soft bedding (Kemp and Thach 1991, 1993), hyperthermia (Gilbert et al. 1992; Ponsonby et al. 1993, Jorch et al. 1994), parental smoking or smoking during pregnancy (Poets et al. 1995) and individual disposition including variable competence of cellular and humoral immunological reactions in these infants can result in an individually varied reaction to a respiratory tract infection.

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