Noma Neonatorum From Multidrug-Resistant *Pseudomonas aeruginosa*: An Underestimated Threat?

Francesco Raimondi,1 Claudio Veropalumbo,1 Clara Coppola,1 Sergio Maddaluno,1 Teresa Ferrara,1 Giancarlo Cangiano,2 and Letizia Capasso1

Divisions of 1Neonatology, Department of Translational Medical Sciences; and 2Maxillofacial Surgery, Università “Federico II”, Naples, Italy

Corresponding Author: Francesco Raimondi, MD, PhD, Division of Neonatology, Department of Translational Medical Sciences, Università “Federico II”, Naples, Italy, via Pansini 5–80131 Napoli, Italy. E-mail: raimondi@unina.it.

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We present the case of an extremely low birth weight infant with diffuse gingival noma, initially misdiagnosed as thrush. Multidrug-resistant *Pseudomonas aeruginosa* strain was cultured and treated with systemic and local colistin with complete healing. Noma neonatorum from multidrug-resistant pathogens may appear in neonatal intensive care units. Old antibiotics may help.

Noma (*cancrum oris*) is a devastating gangrenous disease that leads to destruction of facial tissue with significant morbidity and mortality in children and young adults. Noma has virtually disappeared from Europe and North America, but it is still common among children and young adults in India, Africa, and South America [1]. Noma is a polymicrobial opportunistic infection related to malnutrition and immune dysfunction. In the neonate, a similar but distinct condition, known as “noma neonatorum” was described in 1977, in which gangrenous lesions involve the mucocutaneous junctions of oral, nasal, and anal area, and, occasionally, the eyelids and the scrotum. The neonatal disease has been linked to *Pseudomonas aeruginosa*, prematurity, and low birth weight. There is no established treatment, and mortality is almost inevitable in the few reported cases [2–10]. In this study, we present the first European case of noma neonatorum from a multidrug-resistant strain of *P. aeruginosa*.

Key words. colistin; newborn; noma; *Pseudomonas aeruginosa*.

**CASE REPORT**

A primiparous woman at 28 weeks of gestation with prolonged premature rupture of membrane of over 96 hours delivered a 990 g, appropriate-for-gestational age, female infant. The neonate was stabilized with continuous positive airway pressure (CPAP), received an Apgar score of 7 and 9 at 1 and 5 minutes after birth respectively, and was transferred to the neonatal intensive care unit (NICU). On the second day of life, the infant received an INSURE procedure with a single dose of surfactant (200 mg/kg Curosurf; Parma, Italy). In the following weeks, some feeding intolerance was noted while on mixed feeds and remaining on room air.

At 28 days of life, a white linear lesion was observed on the lower gingival mucosa and treated with oral nystatin. The lesion rapidly expanded to the upper gum appearing slightly ulcerated, hard, and sticky (Figure 1). Both sites were swabbed. At 30 days of life, the general conditions started to deteriorate and CPAP was reintroduced. Vancomycin and amikacin were started. A full sepsis work-up was run including complete blood count, C-reactive protein (CRP), blood, urine culture, and spinal tap. Swabs were taken from the pharynx, the rectum, and both eyes. We documented leucopenia (780 white blood cells/mm3), elevated CRP (6 mg/dL), while *P. aeruginosa* grew from the gingival specimen. The strain showed resistance to penicillins, carbapenems, aminoglycosides, sulfamethoxazole-trimethoprim, and nitrofurantoin while being sensitive to colistin with a very low minimal inhibitory concentration (<0.5 μg/mL). A regimen of intravenous (iv; 25 000 international units/kg for 2 times/day) and topical colistin was followed for 3 weeks. Pseudomonas was grown from all swabs but cultures were sterile.

The infant recovered promptly on room air and full feeds, and no sign of renal or other organ toxicity was
was resistant to gentamicin, amoxicillin-clavulanate, and amikacin, and clindamycin. Her destruction and survived after iv therapy with netilmicin, a 2350 grams. At the age of 7 months, the infant had a normal physical examination with a tooth erupted on an area previously affected on the lower gum.

DISCUSSION
In 1977, Ghosal et al [3, 4] described the only case series of premature infants fatally infected from P aeruginosa presenting with gangrenous lesions similar to cancrum oris in older children but extending also to other body sites. This condition, which they named noma neonatorum, was later sporadically reported in the literature, mostly from emerging countries, to underline its destructive sequelae on the few survivors. It is not always clear, at least in the original Ghosal et al [3, 4] series, whether patients were inborn or outborn and what therapy was given.

Our case has a different scenario: a level III European NICU, where our initial diagnosis was misled by the rarity of the condition. Yet, it is an environment where Pseudomonas colonization is a feared and not uncommon event [11], and neonatologists need to have an appropriate index of suspicion for noma to prevent its mortality or morbidity. Previous reports seldom included the antibiotic resistance pattern of the causative Pseudomonas strain. Nayak et al [12] recently described a 25-day-old Indian female infant that presented with significant facial tissue destruction and survived after iv therapy with netilmicin, amikacin, and clindamycin. Her Pseudomonas strain was resistant to gentamicin, amoxicillin-clavulanate, and lomefloxacin. Our resistance pattern was even wider (although other quinolones were not tested), and it forced us to consider an uncommon treatment option such as colistin. This polypeptide antibiotic was used since the 1950s, but it was gradually abandoned in the early 1980s because of the reported high incidence of nephrotoxicity [13]. In recent studies, the challenging occurrence of aggressive pathogens resistant to newer antibiotics has led to reconsider a role for iv colistin even in the NICU. In 2011, Jajoo et al [14] reported the safety of 21 courses of treatment in 18 neonates (8 preterm) treated with colistin for serious infections (pneumonia, blood stream infections, meningitis, and empyema thoracis). They achieved a favorable outcome in 76% of patients, and a significant increase in creatinine (>0.5 mg/dL over baseline) was documented in only 2 of the 5 patients who later died.

In conclusion, Western neonatologists need to be aware that a multidrug-resistant nosocomial pathogen such as P aeruginosa may present with a destructive oral lesion before the occurrence of systemic symptoms. The early use of an old antibiotic such as colistin may, as in our case, safely and completely heal a disease that had been often reported as fatal.

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References

