Journal of Infection and Public Health 12 (2019) 282–284

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: http://www.elsevier.com/locate/jiph

Premature labor and neonatal sepsis caused by *Actinomyces neuii*

Fahad Alsohime[a], Rasha A. Assiri[b], Fatimah Al-Shahrani[c], Hind Bakeet[a], Malak Elhazmi[b], Ali M. Somily[a,*]

[a] Department of Pediatric, College of Medicine, King Saud University and King Saud University Medical City, Riyadh, Saudi Arabia
[b] Department of Pathology and Laboratory Medicine, College of Medicine, King Saud University and King Saud University Medical City, Riyadh, Saudi Arabia
[c] Department of Medicine, Division of Infectious Diseases, King Saud University and King Saud University Medical City, Riyadh, Saudi Arabia

ARTICLE INFO

Article history:
Received 22 January 2018
Received in revised form 28 March 2018
Accepted 8 April 2018

Keywords:
Actinomyces neuii
Newborn
Sepsis

ABSTRACT

Actinomycosis is a rare infection in patients younger than 10 years of age. It mainly affects the cervicofacial region, but many other sites of infection have been recognized. About 70% of infections are due to either *Actinomyces israelii* or *Actinomyces gerencseriae*.

Actinomyces neuii was first described in 1985 in two patients with post cataract endophthalmitis, *A. neuii* represents 17% of clinical *Actinomyces* isolates. Several reports indicated a well-known association between *Actinomyces* infections and Intrauterine devices (IUD).

We are reporting a case of neonatal sepsis due to *A. neuii* as a first case reported from Saudi Arabia. It was thought to be the cause of the premature labor and neonatal sepsis.

The prevalence of *Actinomyces* infection is likely underestimated and additional premature labors and abortions could have been caused by *Actinomyces* infections that were never detected. More studies are needed to confirm the association of maternal *Actinomyces* infections with preterm labor.

Introduction

Actinomycosis is a rare infection in patients younger than 10 years of age. It mainly affects the cervicofacial region, but many other sites of infection have been recognized [1]. Actinomycosis is mainly caused by *Actinomyces israelii*, a Gram-positive bacterium that colonizes the oral cavity and belonging to genus *Actinomyces*, they are typically aero-tolerant branching and filaments Gram-positive rods. In addition, they are usually catalase and urease negative and CAMP positive, non-pigmented and produce succinic and lactic acid as major end products of metabolism [2]. However, not all *Actinomyces* species share all of these characteristics; one of these *Actinomyces* is *Actinomyces neuii* which rarely causes disease in humans. First, was described in 1985 in two patients with post cataract endophthalmitis, *A. neuii* represents 17% of all clinical *Actinomyces* isolates, with some 132 cases of infection caused by this microorganism reported to date [3]. *Actinomyces* genus: *A. neuii* subsp. *neuii* and *A. neuii* subsp. *anitratus* "*neuii*" was chosen to honour Dr. Harold Neu, an infectious diseases physician [2].

In this report we are reporting a case *A. neuii* from a neonate with sepsis and respiratory distress as a first case reported from Saudi Arabia.

Case report

A twenty-six years old primigravida Saudi woman presented with lower abdominal pain and copious vaginal discharge, she was admitted for premature labor at 25 weeks of gestation. At presentation the cervix was closed and the membrane was intact. She was given IV Dexamethasone, 6 mg, however the contractions continued and she had normal spontaneous vaginal delivery.

She gave birth to a 1090 g female baby. At birth, Apgar scores were 7 at 1 min and 9 at 5 min. Immediately following that the patient developed respiratory distress and hypothermia without hemodynamic instability. The baby was then transferred to the NICU and CPAP was started for the neonate. A full septic work-up (including LP) was performed for her and empiric antibiotic coverage was started with ampicillin, 50 mg/kg/dose every 12 h and gentamycin 5 mg/kg/dose every 48 h to rule out early-onset sepsis.

The mother reported a history of recurrent lower abdominal pain in association with brownish vaginal discharge without associated fever 2 weeks before the delivery. The high vaginal swab, urine and blood cultures were all negative. No antibiotic was started for

* Corresponding author at: Department of Pathology and Laboratory Medicine/Microbiology (32), College of Medicine, King Saud University, King Saud University Medical City, PO Box 2925, Riyadh, 11461, Saudi Arabia.
E-mail address: somily@ksu.edu.sa (A.M. Somily).

https://doi.org/10.1016/j.jiph.2018.04.001

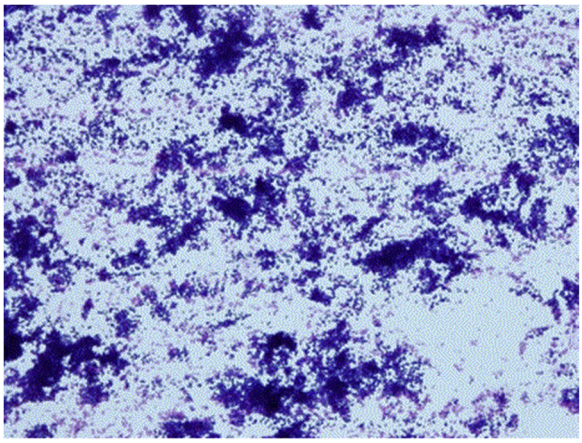

Fig. 1. Gram positive bacilli from primary blood culture.
Colonies of filamentous organisms. Their morphologic features and staining properties were consistent with those of *Actinomyces*. (Hematoxylin and eosin Gram stain and Modified Acid fast Stain).

Table 1
Index of sensitivity of *Actinomyces neuii* strains to different antimicrobial agents.

Antibiotic (MIC interpretive standard μg/ml)	MIC[a] μg/ml	Sensitivity
Vancomycin (≤2 = S[b])	.38	S
Penicillin (≤0.12 = S)	.012	S
Ceftrixon (≤1 = S)	.016	S
Meropenem (≤0.25 = S)	.006	S
Linezolid (≤2 = S)	.19	S

[a] Minimal inhibitor concentration.
[b] Sensitive.

the mother at that time and she received IV Dexamethasone only upon her arrival to the hospital for the delivery. There was no history of prolonged rupture of the membrane, no history of implanted IUD nor cerclage.

The laboratory investigations revealed sustained leukocytosis "maximum 48.5×10^9/l [Normal Range $6–18 \times 10^9$/l]" with predominance of neutrophils (70% [Normal Range 40–45%]). The CRP was 28 mg/dl [Normal Range 0–5 mg/dl] and the CXR finding was consistent with hyaline membrane disease.

Beside these positive inflammatory markers there was element of acute kidney injury initially with a maximum BUN level of 11.8 mmol/l [Normal Range 1.4–6.8 mmol/l] and hyperbilirubinemia "maximum direct bilirubin level 8.8 mcmol/l [Normal Range 0–3 mcmol/l]" which improved rapidly in the following days of starting the antibiotics.

On fifth day of life, the two blood cultures grew *A. neuii* species (Fig. 1). The CSF and urine cultures were both negative.

Following the results of index of sensitivity "see Table 1", the antibiotics were changed to IV penicillin 50,000 unit/kg/dose every 12 h for 6 weeks. The patient's health continued to improve gradually and we were able to wean the ventilator support by the CPAP to Nasal Canula then to room air. Similarly the inflammatory markers decreased progressively until it reached to the normal range. The repeated blood culture was negative on day 4 of starting the antibiotics.

Discussion

Actinomyces species used to be considered as normal flora of the oral cavity, gastrointestinal and female genital tracts. It has a low virulence potential and rarely cause infection in children younger than 10 years old [1]. Although, it can cause acute invasive pyogenic infection or more commonly chronic infections characterized by multiple abscesses and sinus tracts [2,4]. However, Actinomyosis is considered as uncommon disease and the current prevalence is unknown and the most common presentations are with skin and soft tissue infections or abscess [5].

Several reports indicated a well-known association between *Actinomyces* infections and intrauterine devices (IUD) [6,7] or other foreign bodies such as uterine cervical cerclage [8]. However, the pediatric cases of actinomyosis in much less frequent than in adults. Only 2 case report have reported neonatal sepsis with *Actinomyces* species and both of them were delivered prematurely.

In the first case reported by Mann et al. [9], the child was born prematurely at 27 weeks of gestational age and he developed sign of respiratory distress and circulatory compromise along with elevated white blood cell count. *A. neuii* was isolated from the residue of amniotic fluid in the ear canal, the gastric aspirate and from the blood culture. The newborn survived after prompt coverage by empiric antibiotic with ampicillin.

The second case of neonatal sepsis with *Actinomyces* was reported by Knee et al. [8] where the *Actinomyces* species were isolated from the blood sample, gastric and treacheal aspirate cultures. Similarly, this newborn was delivered prematurely at 29 weeks of gestational age but he developed severe sepsis with multi-organ failure (severe respiratory distress, DIC, anemia and acute renal failure). Unfortunately he passed away at day 35 of life.

This is the 3rd reported case in the literature of neonatal sepsis with *Actinomyces* species. In all the cases, the infants were prematurely delivered and the mothers presented with copious vaginal discharge. One of them only had emergent placement of uterine cervical cerclage. None of them had history of prolonged use of IUD. The severity of sepsis ranged from mild ARDs to multi-organ failure and death. Following these reports, we recommend to investigate for neonatal sepsis with *Actinomyces* species and start empiric treatment by ampicillin for any neonate delivered prematurely for a mother who presented with copious vaginal discharge. However we think that the actual prevalence of *Actinomyces* infection might be underestimated because in the majority of cases of premature labors and abortions that might be due to *Actinomyces* infection and no appropriate microbiological study has been carried out.

Abadi et al. suggested to perform screening of amniotic fluid for *Actinomyces* for any mother who present in preterm labor, particularly those who have history of miscarriages, pelvic infections, IUD use or vaginal discharge, as severe chorioamnionitis in these cases most likely contributed to the onset of preterm labor and treatment with ampicillin is effective to protect the patients from further morbidity and it is an effective treatment against *Actinomyces* [10]. However, more studies are needed to confirm the association of maternal *Actinomyces* infections with preterm labor.

Conclusion

A. neuii was isolated from the blood culture of a preterm neonate. It was thought to be the cause of the premature labor and neonatal sepsis. Screening for *Actinomyces* species should be performed for mothers and neonates who present in premature labor and prompt empiric antibiotics should be started.

Authors contributions

Fahad Alsohime: drafting the article, revising critical for important intellectual content, final approval of the version.

Rasha A. Assiri: drafting the article, final approval of the version.

Fatimah Al-Shahrani: drafting the article, final approval of the version.

Hind Bakeet: drafting the article, final approval of the version.

Malak Elhazmi: revising critical for important intellectual content, final approval of the version.

Ali Somily: drafting the article, revising critical for important intellectual content, final approval of the version.

Funding

No funding Sources.

Competing interests

None declared.

Ethical approval

Not required.

References

[1] Walther K, Bruder E, Goldenberger D, Mayr J, Schaad UB, Ritz N. *Actinomyces neuii* isolated from a 20-month-old girl with cervical lymphadenitis. J Pediatr Infect Dis Soc 2015;4(Suppl. 3):e32–7.

[2] Zelyas N, Gee S, Nilsson B, Bennett T, Rennie R. Infections caused by *Actinomyces neuii*: a case series and review of an unusual bacterium. Can J Infect Dis Med Microbiol 2016;2016:6017605.

[3] Gomez-Garces JL, Burillo A, Gil Y, Saez-Nieto JA. Soft tissue infections caused by *Actinomyces neuii*, a rare pathogen. J Clin Microbiol 2010;48(4):1508–9.

[4] Boyanova L, Kolarov R, Mateva L, Markovska R, Mitov I. Actinomycosis: a frequently forgotten disease. Future Microbiol 2015;10(4):613–28.

[5] Kononen E, Wade WG. *Actinomyces* and related organisms in human infections. Clin Microbiol Rev 2015;28(2):419–42.

[6] Fitzhugh VA, Pompeo L, Heller DS. Placental invasion by *Actinomyces* resulting in preterm delivery: a case report. J Reprod Med 2008;53(4):302–4.

[7] Westhoff C. IUDs and colonization or infection with *Actinomyces*. Contraception 2007;75(6):S48–50.

[8] Knee DS, Christ MJ, Gries DM, Thompson MW. *Actinomyces* species and cerclage placement in neonatal sepsis: a case report. J Perinatol 2004;24(6):389–91.

[9] Mann C, Dertinger S, Hartmann G, Schurz R, Simma B. *Actinomyces neuii* and neonatal sepsis. Infection 2002;30(3):178–80.

[10] Abadi MA, Abadi J. *Actinomyces* chorioamnionitis and preterm labor in a twin pregnancy: a case report. Am J Obstet Gynecol 1996;175(5):1391–2.