International Journal of Research in Medical Sciences
Rajkumar MB et al. Int J Res Med Sci. 2024 Sep;12(9):3412-3418
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20242623

Case Series

An insight into *Eikenella corrodens* infections in humans-experience from a tertiary care centre in South India

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Received: 04 July 2024
Revised: 19 August 2024
Accepted: 20 August 2024

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ABSTRACT

Eikenella corrodens is present in the natural microbial community of mucosal surfaces, but it can potentially cause illness in diverse medical contexts. We retrospectively analysed medical records of twelve cases of *E. corrodens* infection from 2020-23. Demographic characteristics, clinical manifestations and treatment outcomes of twelve patients were described. Seven of the twelve patients had carcinoma and they were treated with surgical drainage or abscess resection in addition to antibiotic administration. Only one patient died due to the infection. The most effective treatment often involves a combination of surgical drainage and antibiotics, tailored to the specific site of infection.

Keywords: *Eikenella corrodens*, Immunocompromised, Infection, Treatment

INTRODUCTION

Eikenella corrodens is a fastidious, facultative anaerobic gram-negative bacilli belonging to the genus Eikenella of the family Neisseriaceae. It is often grouped under the HACEK group of organisms, due to their tendency to cause infective endocarditis. Although it is considered a part of the normal human flora of the oral cavity, gastrointestinal tract, and also mucosa lining of the genital tract, *E. corrodens* can cause a wide range of infections in humans, including periodontal infections, endocarditis, bacteraemia, wound infections, and abscesses.[1] *E. corrodens* infections in humans are not considered to be novel. It is mainly a periodontal pathogen grouped under the "Red complex" which also includes *Porphyromonas gingivalis* and *Treponema denticola*.[2] The bacteria have been known to cause infections in humans for several decades, and it is well recognized for its ability to cause infections that are typically associated with mixed bacterial flora, such as oral abscesses, periodontal infections, and wound infections. It causes infections in both immunocompetent and immunocompromised individuals mainly in patients with underlying medical conditions, such as diabetes, cancer, or HIV/AIDS. Numerous case reports describe *E. corrodens* as a pathogen causing infections at different sites. However, there is lack of studies on the clinical-microbiological profile of infections caused by this bacterium. Understanding the risk factors and the pathogenesis of these infections may help in the early

diagnosis and treatment of these infections.[3] In this study we tried to analyse the clinical and microbiological characteristics of *E. corrodens* isolated from various sources.

Patient population

Computerized records from the clinical microbiology department were reviewed for cultures positive for *E. corrodens* during 2019-23. Fifteen cases were found and a review of medical records was possible only for 12 of these patients. As the identity of the patients was anonymized, obtaining consent from the patients was waived.

Cultural characteristics

For the samples submitted from the cases described below, a preliminary Gram stain was done for the presence of inflammatory cells and organisms and inoculated onto 5% sheep blood agar, Mac conkey agar, and incubated at 37℃ in the candle jar. Simultaneously enrichment broth like brain heart infusion (BHI) broth or Robertson cooked meat broth were also inoculated. Colonies of *E. corrodens* were non-haemolytic, grey moist with ill-defined edges and bleachy odour. Gram stain from the colonies revealed short, thin Gram-negative bacilli. (Figure 1) Biochemical characteristics were catalase-negative, oxidase-positive, and indole-negative. Colonies were identified as *E. corrodens* using the MALDI-TOF MS (VITEK MS, Version 3.2 Bio Merieux, France) system. Antimicrobial susceptibility testing is not typically done for *E. corrodens* in our centre as it is known to be sensitive to a wide range of antibiotics. The general clinical presentation, laboratory workup, treatment, and outcome are shown in Table 1.

CASE SERIES

Case 1

A laborer in their sixties with no known co-morbidities presented with complaints of lower abdominal pain of 3 days duration. The pain was sudden in onset and gradually progressive. It was of severe intensity and localized to the lower abdomen with no radiation. On examination, the patient was well-built and nourished. Per abdomen, tenderness on deep palpation with localized guarding was present in the right iliac fossa (RIF). Bowel sounds were present. Ultrasound examination (USG) revealed hypoechoic heterogeneous collection in the RIF. A provisional diagnosis of contained appendicular abscess was made and was given a trial of conservative management. However, the patient continued to have abdominal pain with marked guarding over the RIF. contrast-enhanced computed tomography (CECT) findings showed a well-defined thick-walled multiloculated collection with multiple air foci measuring 5×3.5×8 cm in the RIF. Right laterally collection was extended into the intramuscular plane of the rectus muscle and to the overlying subcutaneous plane with surrounding gross fat stranding and bowel thickening. Parietal wall incision and drainage along with intraperitoneal lavage was done. Intraoperatively 50 ml of frank pus was drained from the subcutaneous plane and sent for bacterial culture and sensitivity. The results of the pus culture showed polymicrobial infection of *E. coli*, *S. anginosus*, and *E. corrodens*. The patient was given injection cefoperazone sulbactam 2 gm IV 8th hourly for 5 days. The postoperative period was uneventful and the patient was discharged.

Case 2

An individual with no known co-morbidities presented with hoarseness of voice for 15 days associated with swelling over the anterior part of the neck, mild pain on swallowing and difficulty in breathing. An emergency tracheostomy was done, and a punch biopsy was taken from the mass involving the left aryepiglottic fold during direct laryngoscopy. The biopsy suggested squamous papilloma with mild dysplasia and was advised for close follow-up. The patient was discharged with a functioning tracheostomy.

After one month, the patient presented with complaints of increased neck swelling and was found to be febrile on examination. A repeat biopsy was done from the ulcer-proliferative growth over the right true cords. The biopsy sample was sent to the histopathology as well for culture and sensitivity. The patient was started on intravenous ampicillin 500 mg four times a day and continued for 3 days. The biopsy report was indicative of well-differentiated squamous cell carcinoma of true cords. The soft tissue from ulcer-proliferative growth was inoculated into 5% sheep blood agar (SBA) and Mac conkey agar and to robertson-cooked meat (RCM) broth for anaerobic enrichment. Though the primary plates revealed no growth after 48 hours of aerobic incubation, Sub-culture was done from turbid RCM which revealed minute colonies on SBA with a distinct bleach odor. The colonies were identified as *E. corrodens*. The patient was empirically started on Ampicillin before the culture was sent and continued for a total of 5 days and responded well.

Case 3

An adult with no known co-morbidities presented with complaints of right neck swelling of 1 week duration. He also gave a history of difficulty in swallowing and restricted mouth opening for the past 5 days. This was associated with high grade fever with chills and rigors. There was no history of trauma preceding the illness. On examination, there was an ill-defined swelling in the anterior aspect of the neck extending superiorly to the submandibular region, inferiorly up to the sternal notch, and laterally up to the posterior border of the sternocleidomastoid muscle. On examination, surrounding warmth, tenderness, and induration were

present with a 0.5 cm erupted area with active pus discharge. USG neck revealed a 2.9×3.9 cm collection in the intramuscular plane on the right side of the neck. CECT neck showed the right sternocleidomastoid muscle to be bulky with collection present in the right cervical space extending to the para pharyngeal space with great vessels pushed posteriorly. Incision and drainage of the abscess was done 20 ml of frank pus was drained and was sent for culture and sensitivity. The patient was started on an injection of cloxacillin 500 mg IV 6th hourly and injection gentamicin 160 mg IV 12th hourly for 5 days. The results of the pus culture showed pure growth of *E. corrodens*. The post-operative period was uneventful and the patient was discharged on POD-3.

Case 4

A middle-aged individual with history of multiple live births presented with complaints of white discharge per vagina for 2 months. There was history of loss of weight and loss of appetite. There is no history of bleeding per vagina, increased frequency, or burning micturition. The patient was diagnosed as a case of carcinoma cervix IV B with liver metastasis and referred to our hospital for further management. On per vaginal examination, 3×1.5 cm ulcer-proliferative growth was seen on the right lip and lower part of the cervix extending to the lower part of the vagina. Pus discharge was present in the cervical canal. CECT abdomen and pelvis showed significantly enhancing lesions in the cervix predominantly involving the right lateral wall with bladder invasion with heterogeneously enhancing lesions in the right lobe of the liver. Pus sample was collected from the cervical canal and sent for culture and sensitivity. The results of the pus culture showed pure growth of *E. corrodens*. The patient was started on Inj. cloxacillin 500 mg IV 6th hourly for 5 days. Radical external beam radiotherapy was given for carcinoma cervix. Repeat culture from the cervical canal showed no growth and the patient was discharged with the advice of regular follow-up for carcinoma cervix management.

Case 5

An elderly laborer, known case of type 2 diabetes mellitus and hypertension presented to the with complaints of weakness of left upper and lower limbs for the past 4 days and fever and headache for 2 days. No history of trauma or vomiting. On examination, the patient was conscious, and obeying commands but appeared disoriented with irrelevant talk. Glasgow Coma scale was found to be E4V5M6 and there was decreased muscle power in the left side of the body. A provisional diagnosis of intracranial space-occupying lesion was made. CECT showed a right high parietal ring-enhancing lesion. Right parietal craniotomy and evacuation was done. Pus sample collected was sent for bacterial and fungal culture and sensitivity. Postoperatively, the patient was started empirically on injection ceftriaxone 2 grams IV 12th hourly and injection voriconazole 240 mg IV 12th hourly. During the immediate postoperative period, patient was afebrile, conscious but continued to be tachypneic with a respiratory rate of 56/min and oxygen saturation of 95% with 6 liters of oxygen via facemask and tachycardia of 150 beats/min. On POD 2, his laboratory parameters showed thrombocytopenia, deranged coagulation profile, and renal parameters, and 4 units of fresh frozen plasma were transfused suspecting disseminated intravascular coagulation (DIC). The results of the pus culture showed pure growth of *E. corrodens* and the patient was started on Injection meropenem 1 gm IV 8th hourly. He was intubated and put on ventilatory support in view of persisted tachypnoea with laboured breathing and tachycardia. The patient expired on POD 5 due to septic shock and multiorgan dysfunction syndrome.

Case 6

A middle-aged individual, known alcoholic and smoker for the past 20 years, with no known co-morbidities presented with complaints of cough with sputum production and weight loss for the past 1 year. CECT thorax showed ill-defined enhancing lesions with areas of necrosis in the right hilar region with right mild pleural effusion. Cytological analysis of the pleural fluid and biopsy from the lesion were suggestive of neuroendocrine tumor grade 2. Robotic-assisted right lower bi-lobectomy was done. Intraoperative findings are as follows- dense adhesions were noted with parietal pleura and between the lobes with obliteration of the tissue and purulent discharge was seen from the collapsed lung bronchus. The pus sample was aspirated intraoperatively and was sent for culture and sensitivity. The immediate post-operative period was uneventful. On POD-7 purulent discharge was noted from the post-operative wound site. A Pus sample was sent for culture and sensitivity. Pus samples collected both intraoperatively and from the wound site on POD-7 showed pure growth of *E. corrodens*. The patient was managed conservatively by the drainage of the pus without starting any antibiotics and was discharged when the pus gradually decreased from the wound site.

Case 7

An elderly person with no known co-morbidities presented with complaints of difficulty in swallowing of one month duration. Initially, there was difficulty in swallowing solids, which gradually progressed to semisolids and liquids. He also gave a history of loss of weight and loss of appetite. Upper GI endoscopy revealed an ulcer-proliferative growth starting at 20 cm from incisors. Contrast-enhanced Computed tomography (CECT) findings are circumferential wall thickening of the upper thoracic esophagus measuring 5.7 cm in length and 1.5 mm thickness extending from T2 to T5 vertebral body level. Biopsy from the ulcero proliferative growth revealed moderately differentiated squamous cell carcinoma. A provisional diagnosis of squamous cell

carcinoma of the upper esophagus was made and planned for feeding jejunostomy with neoadjuvant chemotherapy. Patient was found to be febrile on POD-2 with pus discharge at the feeding jejunostomy site. Pus swab was taken and sent for bacterial culture and sensitivity. The results of the pus culture showed pure growth of *E. corrodens*. The patient was started on ceftriaxone 1 gram IV 12th hourly, continued for 5 days, and discharged.

Table 1: General clinical presentation, laboratory workup, treatment, and outcome of 12 patients.

Patient	1	2	3	4	5	6	7	8	9	10	11	12
Co-morbidity	Nil	Nil	Nil	Nil	DM/HTN	HTN	Nil	DM/HTN	Nil	Nil/PLHA	Nil	Nil
Carcinoma	Nil	SCC of true cords	Nil	Carcinoma cervix	Nil	Neuroendocrine tumor of the right lower lobe	Squamous cell carcinoma of the esophagus	Adenocarcinoma of stomach	Adenocarcinoma of stomach	Squamous cell carcinoma of the cervix	Nil	Nil
Site of infection	Gastro intestinal	Respiratory system	Respiratory system	Genitourinary system	Central nervous system	Respiratory system	Gastrointestinal	Gastrointestinal	Gastrointestinal	Genitourinary system	Head and neck	Head and neck
Provisional diagnosis	Ruptured appendicular abscess		Parapharyngeal abscess		Right Parietal abscess	Surgical site infection			Perisplenic abscess	Regional node recurrence of carcinoma		Left peritonsillar abscess
Specimen	Pus aspirate	Soft tissue	Pus	Pus aspirate	Pus aspirate	Pus	Pus swab	Pus	Pus	Pus	Pus	Pus
Mixed infection	Yes	No	No	No	No	No	No	Yes	Yes	No	No	No
	E.corrodens/ Streptococcus anginosus	-	-	-	-	-	-	*Enterobacter cloacae* and *E. corrodens*	*Escherichia coli* and *E. corrodens*	-	-	-
Treatment given	Surgical drainage+ antibiotics	Antibiotics	Surgical drainag+ antibiotics	Antibiotics	Surgical drainage+antibiotics	Surgical drainage	Antibiotics	Antibiotics	Surgical drainage+ antibiotics	Antibiotics	Surgical drainage +antibiotics	Antibiotics
Antibiotics given	Cefoperazone sulbactam	Ampicillin	Cloxacillin + Gentamicin	Cloxacillin	Meropenem	Nil	Ceftriaxone	Ceftriaxone	Cefoperazone-sulbactam	Amoxicillin-clavulanate	Cloxacillin	Ceftriaxone+ Metronidazole
Duration of antibiotic therapy	5 days	5 days	5 days	5 days	Patient died on 3rd day of therapy	Not applicable	5 days	5 days	7 days	7 days	5 days	6 days
Outcome	Discharged	Discharged	Discharged	Discharged	Expired	Discharged	Discharged	Discharged	Discharged	Discharged	Discharged	Discharged

Case 8

An elderly individual with history of chronic hypertension and diabetes for nearly a decade, under consistent medical treatment presented with complaints of abdominal pain of two months duration. The pain was insidious in onset, located in the epigastric region and radiating to the back. No history of fever, jaundice, hematemesis, melena, the patient was evaluated outside

where endoscopy showed antral gastric ulcer. Histopathological examination of the lesion was suggestive of moderately differentiated adenocarcinoma and referred to our hospital for further management. The patient was started on neoadjuvant chemotherapy followed by open subtotal gastrectomy, D2 lymphadenectomy, and Roux en Y gastrojejunostomy. The immediate post-operative period was uneventful. On post-op day 15, the patient presented with high-grade fever with chills. On examination, purulent discharge was present at the drain site. 60-80 ml of frank pus was aspirated and was sent for bacterial culture and sensitivity. Culture grew *Enterobacter cloacae* and *E. corrodens.* The patient was started on injection ceftriaxone 1g IV 12th hourly for 5 days. The fever subsided, and the patient was discharged when symptomatically improved.

Case 9

A middle-aged agricultural worker, known case of carcinoma stomach, post subtotal gastrectomy and gastrojejunostomy, post adjuvant chemotherapy, and defaulted radiotherapy presented with complaints of abdominal pain and vomiting for 10 days and chest pain for 2 days. The pain was on the left side of the abdomen which increased on food intake and radiating to the back. Vomiting was non-bilious, non-projectile and immediately after intake of solid food. There was no history of hematemesis, melena or decreased urine output. Patient had a history of splenic artery aneurysm for which he underwent embolization 2 months after subtotal gastrectomy.

On abdomen examination, tenderness was present in the left hypochondriac region. CECT was done for further evaluation which revealed the presence of localized collection around the peri splenic region. It was aspirated under USG guidance and sent for bacterial culture. The results of the pus culture showed dual infection of *Escherichia coli* and *E. corrodens*. The individual was empirically started on cefoperazone-sulbactam for 7 days. Collection persisted despite repeated aspirations. So NCCT abdomen was done which revealed residual collection in the perisplenic region and a pigtail was inserted which drained 50 ml of pus. The patient was discharged with the pigtail in situ and was under radiation oncology follow-up for adjuvant radiotherapy and chemotherapy.

Case 10

An individual in their late forties, known case of squamous cell carcinoma of cervix stage II A on radical radiotherapy, Human immunodeficiency virus infection for the past 10 years, and on antiretroviral therapy since then presented with swelling on the right groin for the past 1 month. It was painless and small to start with which gradually increased in size and ulcerated which sought medical attention now.

On examination, she was thin-built and nourished. Pallor was present. On local examination, an ulcerated lesion measuring 3×3 cm present over the right inguinal region with minimal pus discharge. Pus sample was collected and sent for bacterial culture and sensitivity. The patient was started empirically on a cap. Amoxicillin-clavulanic acid 625 mg thrice a day for 7 days. Gram stain from the pus sample showed plenty of pus cells but no bacteria. After 48 hours of incubation of culture plates, pure growth of *E. corrodens* was reported. The patient responded with healing of the lesion.

Case 11

A young child presented to the pediatric emergency room with complaints of high-grade fever associated with chills and rigors for 6 days, and swelling on the left side of the neck for the past 5 days. The swelling was small initially which progressed to the size of around 4-5 cm over 5 days. The patient also gave a history of difficulty in swallowing associated with pain. Pain also aggravates on touching the neck and turning to the left side. There is no history of weight loss or contact with tuberculosis patients. The child had similar episodes a few months back for which incision and drainage was done.

On examination, the kid was active and alert. Head was tilted to the right side. Multiple lymph nodes were present bilaterally of varying sizes with largest node on the left side below the angle of the mandible measuring 1.5×2 cm. On examination of the neck, 5x5cm tender, fluctuant, mobile swelling was present with signs of inflammation. USG neck showed a large ill-defined irregular heterogenous hypoechoic mass measuring 4.4×2.7×3.5 cm with thick internal echoes noted in the midline and the left side of the neck extending to another hypoechoic area in the skin through a tract of length 2 cm thickness corresponding to the external swelling. Thyroid, salivary glands, and great vessels were found to be normal. Since the swelling was fluctuant and tender, incision and drainage were done and pus was sent for bacterial culture and sensitivity and CBNAAT to rule out tuberculosis. The child was started empirically on cap. cloxacillin 500 mg thrice a day. Pus culture grew *E. corrodens* after 48 hours of incubation of the culture plates. The child improved clinically with cloxacillin and the same was continued for 5 days.

Case 12

A young child presented with complaints of high-grade, continuous fever associated with chills and rigors of 5 days duration. The kid also had difficulty and pain during swallowing for the past 4 days. On examination, the child was febrile but active. On examination of the throat, the left tonsillar bulge with uvula pushed to the right present. Grade 2 enlargement of the right tonsil was present. Bilateral tender enlarged cervical lymph nodes were present. Laryngeal crepitus was present with no stridor. A provisional diagnosis of left peritonsillar abscess was

made and wide bore aspiration followed by drainage was done. 3-4 ml of frank pus was drained which was sent for bacterial culture and sensitivity. The patient was started empirically on Inj. ceftriaxone 500 mg 12th hourly and Inj. metronidazole 200 mg 8th hourly. Gram stain from the pus sample showed plenty of pus cells but no bacteria. After 48 hours of incubation of culture plates, pure growth of *E. corrodens* was reported. The child improved clinically with ceftriaxone which was continued for 6 days.

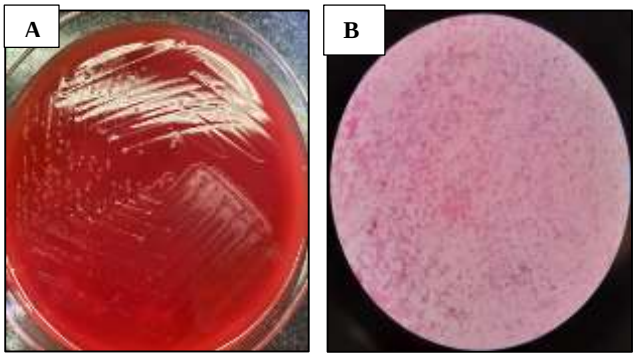

Figure 1 (A and B): Colony morphology and gram staining of *E. corrodens*.

DISCUSSION

E. corrodens, a normal inhabitant of dental plaques, has been recognized as an emerging pathogen, especially in individuals with compromised immune systems. Though relatively rare, infections due to *E. corrodens* can occur in different parts of the body with head and infections being the most common due to the typical location of the organism in the oropharynx as the normal commensal.[4] The most common type of infection is skin and soft tissue infections, in the form of cellulitis, abscesses, and wound infections especially in human bite infections.[5] Other types of infections include joint infections, central nervous system infections in the form of brain abscesses or meningitis especially in immunocompromised patients, gastrointestinal infections in the form of appendicitis and sinusitis, pneumonia in patients with underlying lung disorders, genitourinary infections in the form of chorioamnionitis leading to preterm delivery and neonatal sepsis, urinary tract infections and tubo-ovarian abscess.[6-9] The other rare forms of infections reported include pericarditis, liver abscess, intramuscular abscess formation, osteomyelitis intrauterine and neonatal sepsis.[10-12] However, one must recognize that the spectrum of cases identified through a literature search may reflect a selection bias since only rare manifestations or severe cases are more likely to be reported.

In our reports, 10 were adult patients and 2 were of the paediatric population. Pediatric infections due to *E. corrodens* are less common. Sheng et al reported that around 60-70% of the patients with invasive *E. corrodens* infections had an underlying medical illness in the form of malignancy and diabetes mellitus. 1 In our reports, two out of 12 patients had type 2 diabetes mellitus with systemic hypertension. Six patients had underlying malignancy with two patients having malignancy of the head and neck region. Multiple studies have revealed a strong association between *E. corrodens* infections in both adult and paediatric populations with malignancy of the head and neck region.[1,13] Malignancies in other parts of the body like the gastrointestinal tract which was the majority in our study group may lead to a generalized immunosuppressed state with alteration of the microbiome and dysbiosis. According to the study conducted by Danzinger et al, *E. corrodens* can be an important pathogen in intra-abdominal infections with appendicular abscess being the most common type of infection.[14] In our reports, out of 12, only one patient had appendicular abscess which ruptured into the intra-abdominal cavity.

Infections due to *E. corrodens* are often polymicrobial, found concomitantly with other organisms. However, in our reports, *E. corrodens* was the sole pathogen in 9 out of 12 cases. This depicts the true pathogenic potential of the organism in the absence of other organisms.

The literature search revealed a strong association of *E. corrodens* with *Streptococcus anginosus* complex in case of mixed infections probably due to the following reasons. Both these organisms are present in the oral cavity, respiratory tract, and gastrointestinal system and are often found in the infectious process where the host defense mechanism is compromised, and disruption of the mucosal barrier leads to deeper invasion.[15] In our cases, there was only one case of appendicular abscess where *E. corrodens* was isolated along with *Streptococcus anginosus*. Co-aggregation and growth stimulation that occurs between these species may be relevant for establishing mixed infections since co-aggregated cells are more resistant to phagocytosis and death by neutrophils than individual cells.

Though the exact pathogenesis of extra-oral infections caused by *E. corrodens* is not well studied, the various virulence factors postulated to play a role are the lipopolysaccharides, type IV pili, enzymatic activities like proline aminopeptidases and hemolysin, aggregation, and interaction with other species and lastly colonial diversity. The presence of genetically distinct clones in the same patient may be highly significant in understanding the pathogenesis of *E. corrodens* infections as some strains may be virulent whereas the others may be relatively innocuous and are part of the normal microbial consortium.

The organism is known to be sensitive to a wide range of antibiotics including beta-lactam antibiotics, aminoglycosides, fluoroquinolones, trimethoprim-sulfamethoxazole, and tetracyclines. It is typically resistant to clindamycin and metronidazole. In some

cases, mere surgical drainage of the collection without concomitant antibiotic therapy will eradicate the organism.[16,17] In our cases, most of the patients were started on empirical antibiotics based on the clinical diagnosis and they responded well with clinical improvement except a patient with a brain abscess who expired despite starting antibiotics. In the majority of the cases, antibiotics chosen for empirical therapy are based on the common organism profile in the hospital and do not consider *E. corrodens* as a serious pathogen. Patients were continued on the same antibiotics as *E. corrodens* being a fastidious and slow-growing pathogen, we could give the reports to the clinicians only after 48-72 hours of incubation of the primary plates.

CONCLUSION

This case series shows that *E. corrodens* is a serious pathogen in children and adolescents. Depending upon the location of the infection, combination of surgical drainage and antibiotics often give the best results. Despite its clinical significance, the epidemiology and virulence factors of this pathogen are not well understood, and future research is needed in this context.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Rajkumar MB, Kumaresan M, Olavera H, Jamir I, Sistla S, Raja K, et al. An insight into *Eikenella corrodens* infections in humans-experience from a tertiary care centre in South India. Int J Res Med Sci 2024;12:3412-8.