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CASE REPORT

Oral Melioidosis in Odontogenic Keratocyst of Mandible

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Abstract Melioidosis is a potentially fatal, life-threatening infection caused by the gram-negative saprophytic organism Burkholderia. It is a disease endemic to Southeast Asia and Northern Australia. This infection transmits through direct contact, cutaneous inoculation, inhalation, or ingestion, and patients clinically exhibit abscesses in single or multiple organs. It is clinically under-reported due to a low index of suspicion, lack of diagnostic facilities, and misdiagnosis as tuberculosis. Infections of the musculoskeletal system are exceedingly rare, and clinical presentation may vary from the involvement of femoral bone, palmar tenosynovitis, and parietal bone osteomyelitis secondary to central nervous system involvement. The rarity of the melioidosis to secondarily infect a developmental odontogenic cyst leading to focal osteomyelitis of mandible prompts the clinician toward thorough evaluation for early diagnosis and treatment.

Keywords Odontogenic keratocyst · Burkholderia · Melioidosis

Background

Infections of the Maxillofacial region may range from an early dental infection due to necrosed pulpal tissue producing a localized periapical infection to severe life-threatening infections of the head and neck with resulting sepsis and airway compromise. Intrabony cysts of the maxilla-mandibular complex usually have a relatively better prognosis, but they can be secondarily infected from oral flora. These infections can occur from dental biofilm, trauma to the overlying tissues, or related to iatrogenic inoculation. In the chronic osteomyelitis associated with previous odontogenic infections, mixed infections predominate oral anaerobes, particularly genera *Fusobacterium*, *Porphyromonas*, *Prevotella*, *Parvimonas*, and *Eikenella*, frequently associated with actinomycetes and staphylococci were detected.[1] In an otherwise immunocompetent patient, we present a rare case of a Melioidotic abscess of the mandible due to secondary infection of recurrent developmental odontogenic keratocyst. Infection by Burkholderia is potentially life-threatening due to its ability to disseminate systemically and the associated high mortality rate as high as 95% even after appropriate antibiotic therapy.[2] Early recognition of symptoms and prompt treatment improve the overall outcome and likelihood of survival.

Case Presentation

A 46 year-old male patient reported to the Department of Dentistry and Oral and Maxillofacial Surgery of AIIMS Raipur, with a chief complaint of altered sensation of the right side of lower lip along with the mobility of lower right back teeth for the past 20 days. The patient gave a history of swelling along the outer right angle of the mandible region for the same duration. The swelling was self-limiting and resolved spontaneously with episodes of trivial recurrence. There was no associated pus drainage. The patient was previously operated on for Odontogenic Keratocyst (OKC) in the right posterior mandible ten years

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back, for which enucleation, curettage, and removal of mandibular third molar was done.

A month ago, the patient started developing pain in the right third molar region and visited a local dentist. Radiological examinations were done and revealed an intra-bony radiolucent defect. Aspiration of the lesion was done by the same dentist a month ago that yielded about 20 ml of pus-like fluid. Aspiration was performed at regular intervals over 2–3 days as it recurred from time to time. The patient then developed pain radiating to the right ear and temporal region over time. The patient had no systemic comorbidities except that he had recovered from a COVID-19 viral infection six months ago, which might hamper the host immune response.

On examination, the patient had no obvious asymmetry of the lower half of the face; however, pain on mouth opening beyond 30 mm was elicited. A firm and tender palpable buccal mass on the right pre-masseteric region about an inch in greatest diameter was found on extra-oral palpation. Intraorally, there was a diffuse erythematous appearance of the right retromolar region with medial bulge and obliteration of pterygomandibular raphae. (Figs. 1, 2) Also, there were clinically missing second and third lower molars of the right side with normal-appearing overlying alveolar ridge mucosa with no color change was noted. There was grade two mobility of right mandibular first molar and paresthesia in the right mental nerve distribution, which was confirmed by pinprick test and two-point discrimination.

Aspiration of pterygomandibular space with wide bore needle yielded cheesy keratinaceous turbid fluid with a foul smell. (Fig. 3).

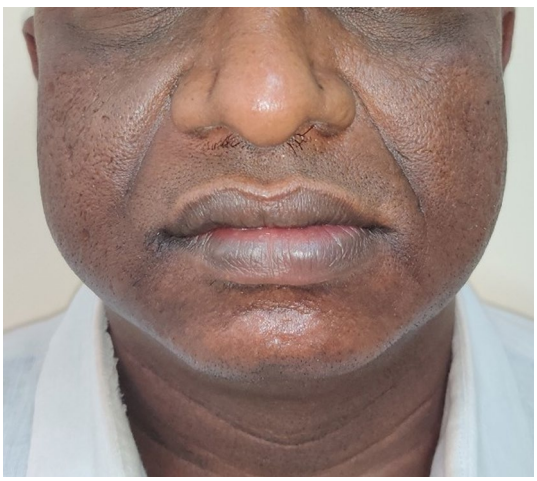

Fig. 1 Frontal view showing no gross facial asymmetry at the time of presentation

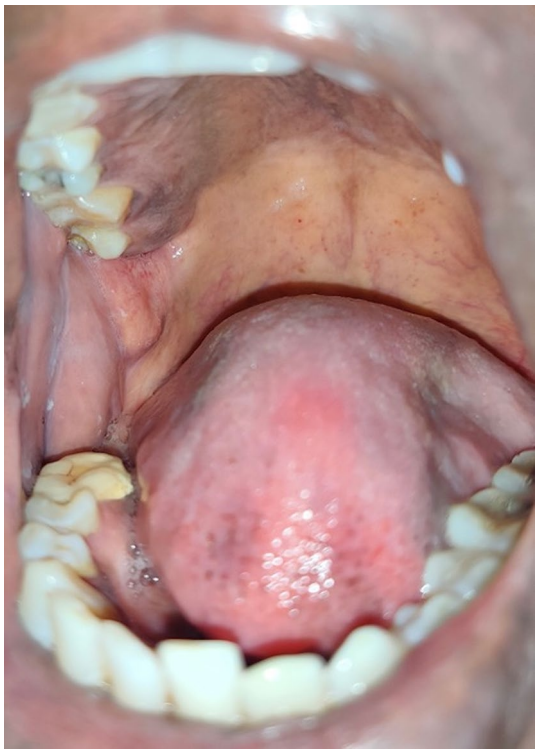

Fig. 2 Intraoral examination revealing the erythematous appearance of right retromolar region with medial bulge and obliteration of pterygomandibular raphae

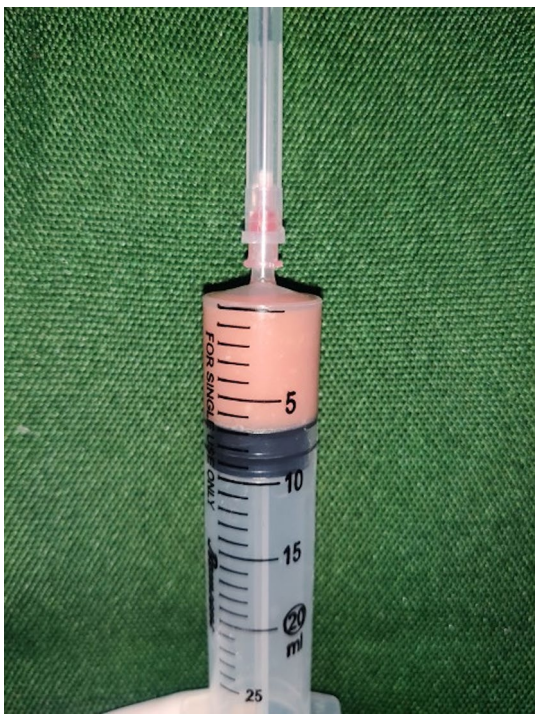

Fig. 3 Cheesy keratinaceous turbid fluid on aspiration from pterygomandibular space

Investigations

Orthopantomogram (OPG) revealed multilocular soap bubble appearance of right mandibular ramus extending up to coronoid process superiorly and extending up to alveolar process in the body of mandible asserting the working diagnosis. (Fig. 4) Computed tomography findings revealed a cystic non-enhancing expansile lytic lesion measuring about $3.6 \times 1.3 \times 4.2$ cm (AP × TR × CC) in the ramus, coronoid process of right mandible with resulting cortical thinning with erosive changes in the overlying bone. (Figs. 5 and 6).

Pus culture after 24 h of aerobic incubation showed growth of Burkholderia cepacia with intrinsic resistance to various Beta-lactam antibiotics. The growth of Burkholderia is sporadic in the maxillofacial region with no possible etiology of inoculation. Further investigation to analyze the diagnosis of melioidosis due to Burkholderia species revealed that the overwrought patient had started gargling with cow's urine (Gomutra) every day for over ten days before the initial presentation to our department. Considering the high mortality associated with Burkholderia requires serial blood cultures to early diagnose sepsis and chest radiographs to detect pulmonary involvement, if any. This case did not yield any significant signs of disseminated infection. (Fig. 7).

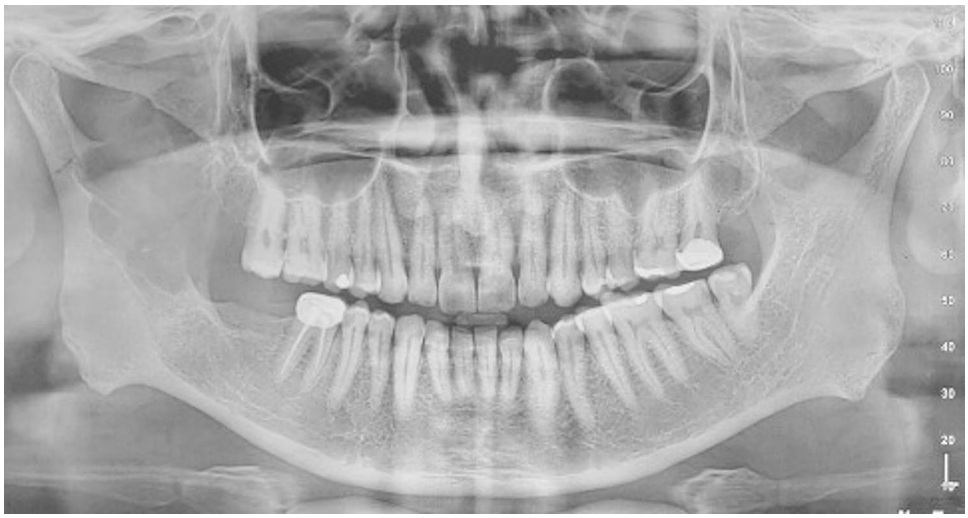

Fig. 4 Orthopantamogram showing multilocular soap bubble appearance of right mandibular ramus involving coronoid process and body of the mandible

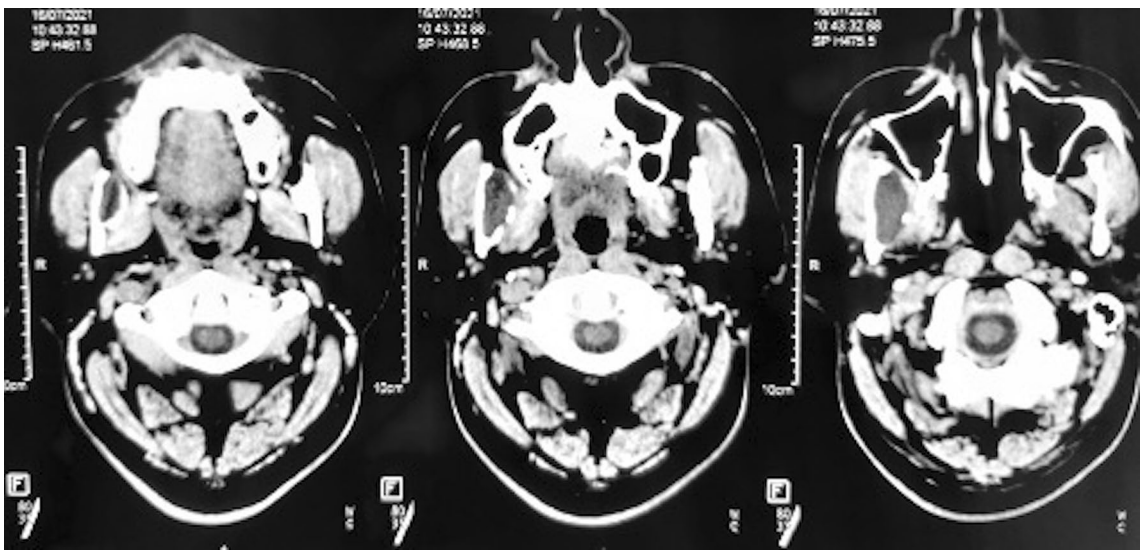

Fig. 5 Axial section of contrast-enhanced CT images showing a cystic non-enhancing expansile lytic lesion in the ramus, coronoid process of right mandible with resulting cortical thinning and erosive changes

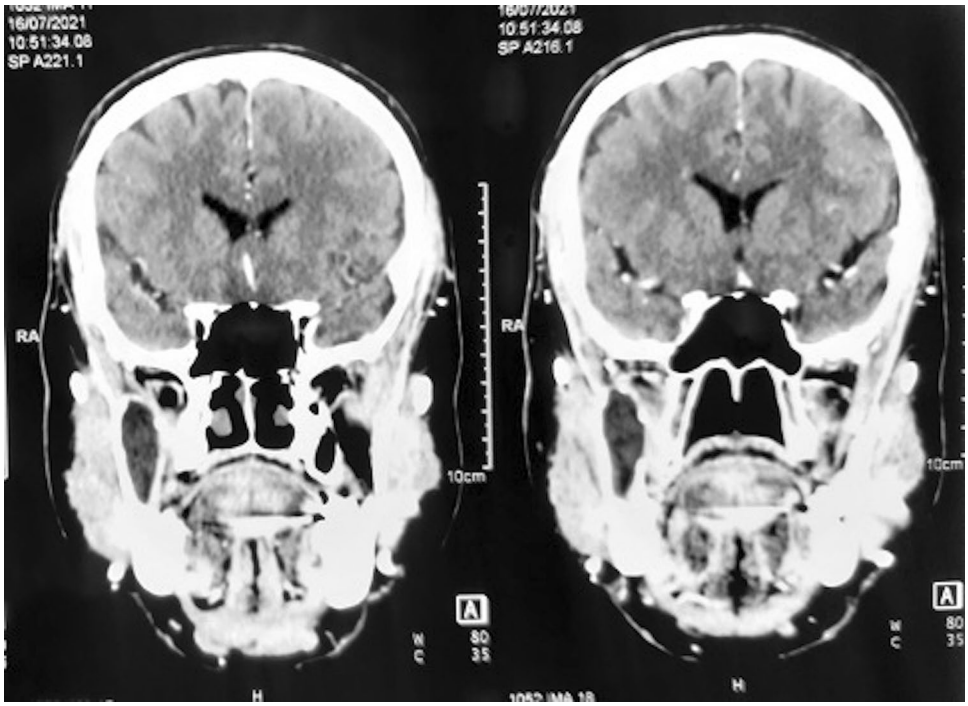

Fig. 6 Coronall section of contrast-enhanced CT images showing a cystic non-enhancing expansile lytic lesion in the ramus, coronoid process of right mandible with resulting cortical thinning and erosive changes

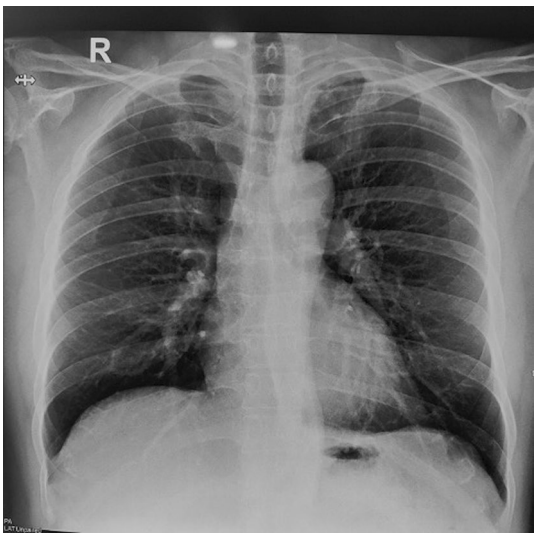

Fig. 7 Chest PA radiograph to rule out dissemination of infection and early pulmonary changes

Differential Diagnosis *if Relevant*

A working diagnosis of secondary infection of pterygomandibular space in a patient with recurrent odontogenic keratocyst was established because of OKC's highly associated recurrence rate and turbid keratin-filled aspirate presence. Odontogenic keratocyst usually does not involve the epineurium of the inferior alveolar nerve and is well preserved. A differential diagnosis of central bony squamous cell carcinoma or osteosarcoma of posterior mandible due to paresthesia was plausible but ostensible.

Treatment

As a plan of management, the patient was started on intensive antibiotic therapy with Ceftazidime 1 g IV 12 hourly and Meropenem 1g IV 8 hourly for over two months, along with serial aspirate cultures from the right pterygomandibular space until negative and symptom-free.

After two months, the cystic lining was enucleated in-toto using anterior ramal incision, and peripheral ostectomy was performed, followed by a 5-Fluorouracil pack application for 24 h within intrabony defect. (Figs. 8, 9 and 10).

Outcome and Follow-Up

Postoperatively patient developed dehiscence intraorally after one week, which was thoroughly irrigated and allowed for secondary healing for over four months with regular dressing and an acrylic plug. The continuous phase of antibiotic therapy with Cotrimoxazole was strictly adhered to during the healing of surgical wound to prevent the development of recurrent and refractory melioidosis.

In the follow-up phase after one year, the intraoral wound healed satisfactorily, and the orthopantomogram showed an uncomplicated post-surgical bony defect that had continued to regenerate over time. (Figs. 11 and 12).

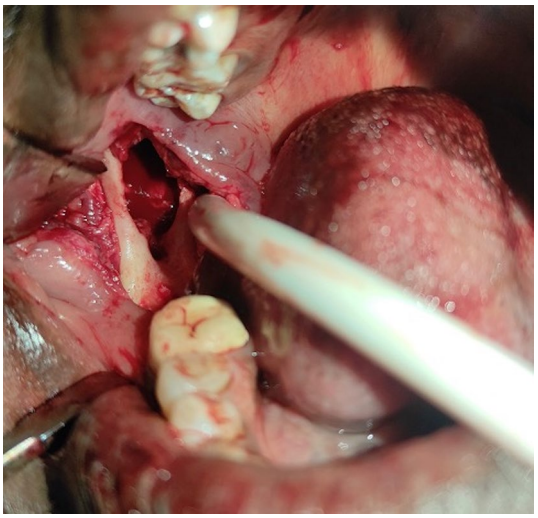

Fig. 8 Peroperative picture showing the resulting intrabony defect after cystic enucleation

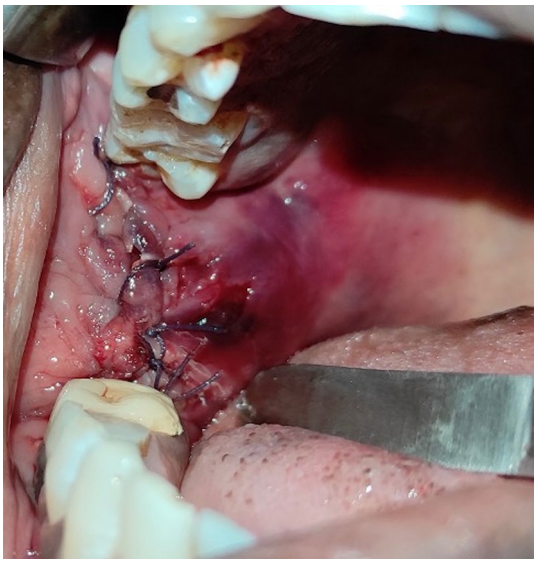

Fig. 9 Primary closure of defect

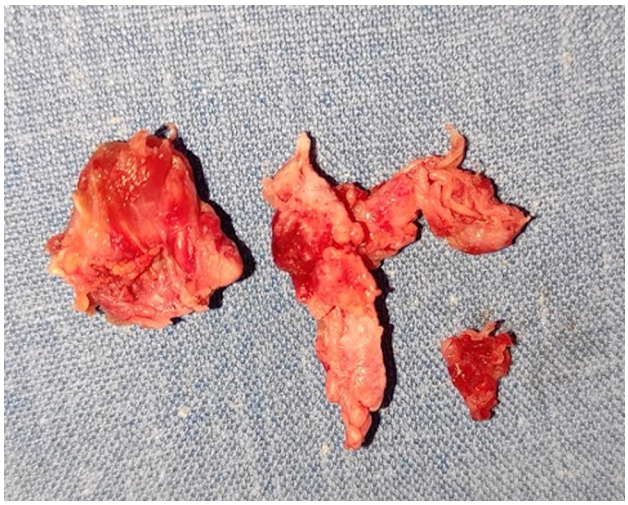

Fig. 10 Specimen of lining excised

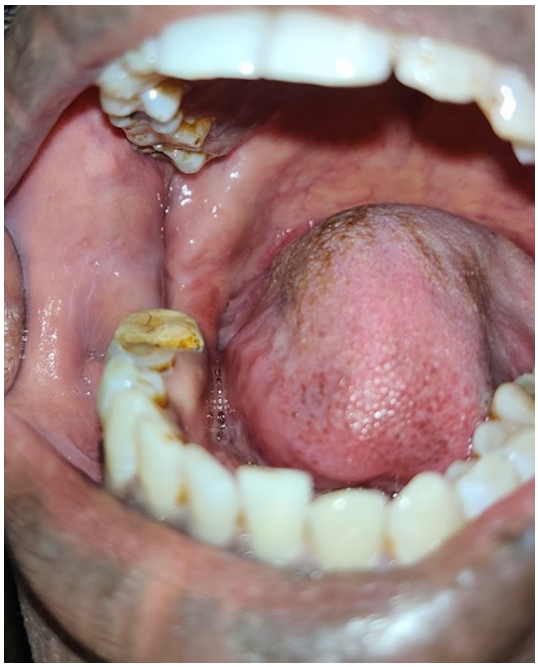

Fig. 11 Follow-up images at one year showing the well-healed surgical site in the retromolar region

Discussion

Among all forms of life-threatening bacterial infections, the ones caused by Burkholderia species, namely *Burkholderia mallei*, *Burkholderia pseudomallei* and *Burkholderia cepacia*, are scarce and warrants extensive and rigorous treatment methods. *Burkholderia cepacia* causes disease in patients with cystic fibrosis, especially pneumonia, bacteremia, urinary tract infections and septic arthritis. Whereas *Burkholderia pseudomallei* causes melioidosis and can be used as bioterrorism agents.[3].

Infections from these organisms may be initially asymptomatic and later give into various clinical manifestations that include multiple localized abscesses, chronic disseminated infection or even septic shock. Hence, timely diagnosis and targeting with correct antimicrobials form the mainstream of treatment to avoid the high morbidity and mortality related to the disease.

The prevalence of the disease is more in south-east Asia (especially Thailand, Malaysia region) and northern

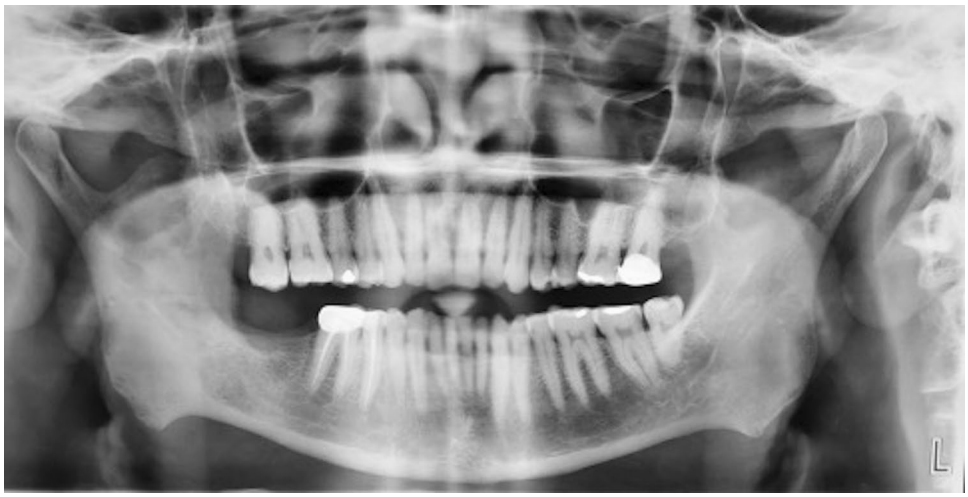

Fig. 12 OPG revealed regenerated bony defect of the posterior mandible

Australia. The disease is endemic in this region, responsible for 20% of all community-acquired bacteraemia, and causes death in 40% of diagnosed individuals.[4].

There have not been many reports of the infection in the head and neck region. Lim et al.[5] reported four cases of melioidosis in the head and neck region, presenting in various forms as parotid abscess, acute sinusitis, acute suppurative lymphadenitis and otitis media. A literature review reveals strange clinical manifestations in each case. Loh et al.[6] reported right-sided facial soft tissue infection, mastoid effusion and temporal lobe cerebritis. Since the usual manifestations are widely varied, Lim et al. has classified the presentation in four classes: asymptomatic carrier in the latent period, prolonged fever without any apparent site of infection, localized infection and fulminant septicaemia.

In our case report, the patient had no signs and symptoms of systemic toxicity, and the infection was more localized. There have been reports of facial nerve palsy in cases of melioidosis with parotid abscess.[7] The patient had subjective symptoms of mental nerve paresthesia in our case, suggesting the organism's invasive nature over the nerve sheath. The cases reported with facial palsy didn't regain the facial nerve function, the same as in our patient who has no subjective signs of normal sensation in the lower lip of the right side.

Head and neck infections with Burkholderia can be challenging to diagnose and manage because of variations in duration of infection, ranging from acute to chronic, lasting even up to three months. Our patient was also having the infection for a more extended period for about two months, despite the targeted antibiotics for the same and required almost daily aspiration of pus for about 10–20 ml per day from the same region, which is not usual in another type of bacterial infections.

Microbiological culture is a gold standard for such a type of diagnosis. Since the disease itself is rare and is limited to specified regions, expertise in diagnosing in such a rare species is crucial not to undermine the diagnosis and instead help start the medication at the earliest and limit the morbidity and mortality to a great extent.[8].

Treatment for melioidosis can be divided into two phases: the initial acute phase and then the second is eradication phase.[9] The acute phase needs an antibiotic to prevent complications and further dissemination. Surgical drainage usually is reserved for macro abscesses. Our patient needed both, and when the infection was totally subtle, the surgical removal of the infected cystic lining was carried out, followed by peripheral ostectomy and chemical cauterization with 5-Fluorouracil.

The antibiotic of choice is Ceftazidime because of its high efficacy against *Burkholderia pseudomallei*. Dutta et al.[10] reported all 20 isolated *Burkholderia pseudomallei* to be uniformly sensitive to Ceftazidime. However, Ahmed et al. found that one isolate was resistant to Ceftazidime. Alternate antibiotics like meropenem are recommended as second-line drugs. The infections, in general, are resistant to usual antibiotics like ciprofloxacin, gentamycin and amikacin.

Cotrimoxazole monotherapy is a treatment of choice in the eradication phase, and in isolates resistant to Cotrimoxazole, drugs like co-amoxiclav can be given. Our patient was initially started with Ceftazidime and later was added with meropenem as the infection was in the acute phase for more than two weeks. The total duration of antibiotics given in the active phase was for two months. It was followed by Cotrimoxazole during the healing phase after the surgical intervention.

Inoculation of the Burkholderia species in our patient seemed to be due to cow urine (Gomutra) rinses after the initial aspirations done by the local dentist. The cow urine therapy forms a traditional practice of Indian medicine, which believes the ability of the cow urine to treat various forms of infections and varied diseases,[11] which the

Allopathic system does not approves off. Our patient had mixed two forms of treatment due to his anxious nature to get rid of the pain caused by the swelling in his lower jaw. Burkholderia species is predominantly found in cow dung and urine and rinsing for more than ten days orally after a series of wide-bore aspirations had led to inoculation of the microorganism, causing a form of localized melioidosis which was diagnosed promptly and was adequately treated with proper antibiotics and followed up for one year until good healing.

Learning Points/Take Home Messages

- The unusual presentation of the lower lip sensation can mislead the diagnostician to speculate a more aggressive central bony tumor with intrinsic malignant potential.
- Identifying the etiology of secondary infection is challenging as the organism is a saprophytic gram-negative bacterium. The possibility of inoculation from cow urine rinses (Goumutra) is the only plausible explanation leading to an intrabony mandibular Melioidotic abscess.
- Infection with COVID- 19 is an additional risk factor influencing the pathogenesis of melioidosis in an otherwise immunocompetent patient.

The treatment warrants intensive antibiotic therapy and control of osteomyelitis of mandible to arrest the disease process. Resection, although is the ideal treatment option to avoid recurrence of OKC, the invasive therapy may facilitate the dissemination of infection via the hematogenous route and increase mortality. Local debridement of the lesion by enucleation and topical 5-fluorouracil combined with systemic antibiotic therapy reduced the infective load leading to resolution of active infection.

Declarations

Conflict of interest None of the authors have any financial or personal interest associated with this article. No funding has been received by any author in relation to this study.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent: A written informed consent was obtained from all individual participants included in the study.

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