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Nocardiabrasiliensis as an Emerging Cause of Opportunistic Infection in Surgical Wards

Medical Science

KEYWORDS :

DrShivanand Reddy	Post Graduates in Dept.of General Surgery. JSS Medical college,mysore
DrVijayanand Reddy	Post Graduates in Dept.of General Surgery. JSS Medical college,mysore
DrManjunathShenoy	Professor and unit chief,Dept of Gen.Surgery JSS Medical college,mysore.

ABSTRACT

A 34-year-old female was admitted to the Surgery ward of JSS Hospital with multiple inflammatory nodules, Single keloidal scar and discharging sinuses over the thoracic wall right sided. Physical examination revealed a discharging area that occupied the entire right sided thoracic wall, extending up to the left shoulder and scapular region. There were numerous large sinuses discharging viscous yellow pus and serosanguinous material, often plugged with protuberant masses of granulation tissue.The PCR products were sequenced by using an ABI Prism 377 automated sequencer (PE Applied Biosystems)1.The strain was definitively identified as N. brasiliensis (ATCC 19296, accession number AY756544)2.The patient was medicated with imipenem-cilastatin (60 mg/kg/day i.v. q6h) for 8 weeks, with a good response (healing of most of the cutaneous lesions, improvement of general health, weight gain of 13 kg and Hb increased to 11.4 g/l) (Fig. 1B) and subsequently with trimethoprim and sulphamethoxazole (160 mg TMP/800 mg SMZ p.o. q12h) until complete eradication of the organism was documented2.Among the several species of Nocardia causing cutaneous infections, N. brasiliensis is the commonest species isolated . Recently, new species including N. mexicana and N. veterana were reported as causative agents of human mycetoma3. Cutaneous involvement with N. asteroides is usually secondary to haematogenous dissemination from a pulmonary focus. The commonest predisposing event in all the reported cases of primary cutaneous nocardiosis is a local trauma caused by thorns or splinters or, less commonly, insect bites and cat scratches3-4. It is most commonly caused by N. brasiliensis, typically affects immunocompetent individuals, and can be subdivided into 3 clinical entities, including: lymphocutaneous infection, mycetoma, and superficial skin infection, including ulceration, abscess, and cellulites 4. An intermediate form of the disease between mycetoma and superficial skin infection has been reported recently 5.We report here a case of an immunocompetent female patient with extensive and destructive primary cutaneous nocardiosisover the thoracic wall .

CASE REPORT.

A 34-year-old female was admitted to the Surgery ward of JSS Hospital with multiple inflammatory nodules, Single keloidal scar and discharging sinuses over the thoracic wall right sided. She gave no history of injury, and reported that the first lesion had appeared 4 years previously, over the right shoulder. She had subsequently developed a swelling, followed by multiple discharging sinuses with purulent and serosanguinous material. The lesions slowly expanded to the contiguous thoracic wall, eventually leading to deformity of both breasts. Over the previous year, she had complained of fever, intense anorexia with heavy weight loss (that she could not quantify) and dry cough. There was no history of chronic illness such as diabetes, tuberculosis or malignancy. She had first been observed at a local hospital in hassanand had unspecified treatment without improvement. As a consequence, she wasreffered to JSS, for aetiological investigation and treatment.

Physical examination revealed a discharging area that occupied the entire right sided thoracic wall, extending up to the left shoulder and scapular region. There were numerous large sinuses discharging viscous yellow pus and serosanguinous material, often plugged with protuberant masses of granulation tissue. Single keloidal scar could be seen over the entire area and severe deformity of both breasts was evident. Systemic examination of the patient showed that she was in bad general health, with emaciation, weighing 35 kg (body mass index 13.3). There was no palpable regional lymphadenopathy and no fever.

Among routine investigations, ESR was increased (114 mm) as was reactive C-protein (11 mg/dl). Her white blood count was normal, but she had a severe normocytic anaemia (Hb of 6.8 g/l), which warranted a blood transfusion. Serologies for HIV 1 and 2 were negative. Roentgenograms of the chest were normal. Computed tomography scan of the lungs and chest wall showed densification of the soft and breast tissues, with involvement of the part of the anterior mediastinum related to the internal mammary chains. Several blood cultures were performed, which were all negative. Histological study of the biopsy taken from the left breast revealed granulation tissue with neutrophilic abscesses containing basophilic grains with an eosinophilic rim, which was suggestive of mycetoma.

Sequential mycological and bacteriological studies were carried out on the exudate from discharging sinuses and from the dressings. The first bacteriological cultures revealed *S. aureus*.

Direct examination of samples stained with lactophenol blue for microscopic observation revealed white grains (mean diameter 0.5 mm); isolates consisting of orange-white colonies and a white mycelium were obtained from cultures at 24°C and 37°C (mycobiotic agar, Sabouraud dextrose agar and Brain Heart agar alone or supplied with 0.5/1000 w/w cloramphenicol), which were suggestive of Nocardia[6.]

A PCR assay was conducted to confirm phenotypic identification of the isolate 639.07 by genomic DNA extraction from pure culture using an achromopeptidase method and sequence analysis of the 16S rRNA gene6. Primers Noc-1 (5'-GCTTAACACATGCAAGTCG-3') and Noc-2 (5'-GAATTCCAGTCTCCCCTG-3') (position 46 to 64 and 663 to 680 fromE. coli numbering), which amplified a 606 bp segment were employed (12). After 40 cycles consisting of denaturation at 94°C for 60 sec, primer annealing at 58°C for 60 sec, and primer extension at 72°C for 60 sec, followed by a post-amplification extension at 72°C for 5 min. The PCR products were sequenced by using an ABI Prism 377 automated sequencer (PE Applied Biosystems)7.The strain was definitively identified as N. brasiliensis (ATCC 19296, accession number AY756544).

The patient was medicated with imipenem-cilastatin (60 mg/kg/day i.v. q6h) for 8 weeks, with a good response (healing of most of the cutaneous lesions, improvement of general health, weight gain of 13 kg and Hb increased to 11.4 g/l) (Fig. 1B) and subsequently with trimethoprim and sulphamethoxazole (160 mg TMP/800 mg SMZ p.o. q12h) until complete eradication of the organism was documented.

DISCUSSION :

Primary cutaneous nocardiosis remains a diagnostic challenge. None of the three types has any characteristic feature that would make a definitive clinical diagnosis possible . In the case described here the initial clinical differential diagnosis was made with diseases having a similar clinical presentation and included deep mycosis with high prevalence in African countries, actinomycetoma, cutaneous tuberculosis and atypical mycobacteriosis[4.]

It was not possible to elicit a history of trauma; this might be explained by a long incubation period because that of *Nocardia spp*. can vary from one week to several months Mycetoma is described as a chronic, indurated, progressively destructive, granulomatous infection of skin, subcutaneous and eventually deeper tissues following localized trauma, with multiple draining sinus tracts and elimination of grains (sulphur granules)[5]. It occurs most commonly on the extremities, especially the foot, but other locations have been reported .

Identification of the Nocardia species by culture is a tedious process and it is advisable to submit multiple clinical specimens for culture because smears and cultures are simultaneously positive in only one-third of infections. The organism is slow growing and it may take up to 2–3 weeks for isolation from a clinical specimen6. The small nocardial colonies are occasionally overgrown by other rapidly growing organisms, resulting in an initial negative culture report. Species identification is based on classical biochemical methods. These can be completed by Western blot assay, using monoclonal antibodies against 54-kDa circulating antigens of Nocardia, and species specific DNA probing help in the rapid and definitive diagnosis of nocardiosis. ELISA for serodiagnosis of nocardial infection is also useful 6.

An antibiogram is suggested for all species isolated because of the varied antibiotic sensitivity pattern .Sulphonamides have been the mainstay of antimicrobial therapy for human nocardiosis. Trimethoprim and sulphamethoxazole (TMP-SMZ) is used most commonly7. Other effective drugs include minocycline, dapsone, tetracycline, amikacin, amoxicillin-clavulanic acid, cefotaxime, imipenem, and rifampicin. Although the optimal duration of therapy is uncertain, suggestions range from 6 weeks to one year .

In our case, we chose to start intravenous antimicrobial therapy with imipenem-cilastatin because: (*i*) the patient was also infected with *S. aureus*; (*ii*) the cutaneous disease was extensive.

The clinical response to imipenem-cilastatin was impressive, with a rapid improvement not only from the cutaneous lesions but also from the anaemia and the emaciation. She stopped coughing 3 days after beginning antibiotic therapy.

After 8 weeks she was discharged and oral TMT-SMZ was started. She is being followed-up regularly in our outpatient clinic and will maintain this antimicrobial therapy scheme until control microbiological exams are consistently negative.

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