

Nocardiosis in Patients of Chronic Idiopathic Thrombocytopenic Purpura on Steroids

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Abstract

We present two cases of chronic idiopathic thrombocytopenic purpura (ITP) on prolonged steroid therapy who developed subcutaneous and brain abscesses due to *Nocardia asteroides*. The special diagnostic and therapeutic challenges encountered in the patients because of severe thrombocytopenia are being highlighted. ©

INTRODUCTION

Nocardiosis is an opportunistic infection caused by Gram-positive, weakly acid-fast filamentous aerobic organisms. *Nocardia asteroides* is the most common species to cause infection in man. Nocardiosis is a described infective complication in a setting of immunosuppression but is often missed. It has been rarely reported in a setting of chronic ITP,^{1,2} even though most patients are on prolonged steroid therapy. Management of nocardial brain abscess in a setting of thrombocytopenia is a challenge amidst a paucity of therapeutic guidelines in literature. The lesson learnt from the management of the reported cases, together with similar published reports, may help in the evolution of concrete guidelines for the management of nocardial abscesses in ITP.

CASE 1

A 42 years male, a known case of chronic idiopathic thrombocytopenic purpura for last 3 years, presented to us with the complaints of pyrexia (100-101°F), swelling on the back, weakness of the right lower limb with difficulty in walking for the last 5-6 days and increase in purpuric spots all over the body for the last 3-4 days. He had been on oral prednisolone 40-60 mg/day for last one year. Examination revealed an ill-looking, pyrexia (100-101°F) patient with gum bleeding and purpura. There was a right upper interscapular maroon-colored inflammatory abscess, 10 x 7 cms, warm, tender, with surrounding induration and with no regional lymphadenopathy. The patient had a right-sided hemiparesis (Right lower limb-grade I, Right upper limb-grade II) with right supranuclear facial palsy. The left upper and lower limb were normal. There was no other cranial nerve involvement. Pupils and fundus were within normal limits. There were no

signs of meningeal irritation. There was no organomegaly and the cardiovascular and respiratory systems were unremarkable.

Investigations revealed leukocytosis with thrombocytopenia (26000/cumm). Renal and liver function tests and urine examination were within normal limits. Bone marrow aspiration was suggestive of ITP. Serology for HIV 1 and 2 was negative. Pus aspirate from the abscess on the back revealed large number of polymorphonuclear cells with Gram positive and weakly acid fast bacilli (decolorized with 1% H₂SO₄) arranged in the form of multiple branching hyphae, with tendency to break up into rod shaped to coccoid forms, suggestive of *Nocardia* species (Fig. 1). Culture on appropriate media and biochemical tests revealed it to be *Nocardia asteroides*, sensitive to co-trimoxazole, ciprofloxacin, amikacin and IIIrd generation cephalosporins. CSF examination was normal. Contrast-enhanced computerized tomography and magnetic resonance imaging of the head revealed a parafalx space-occupying lesion with

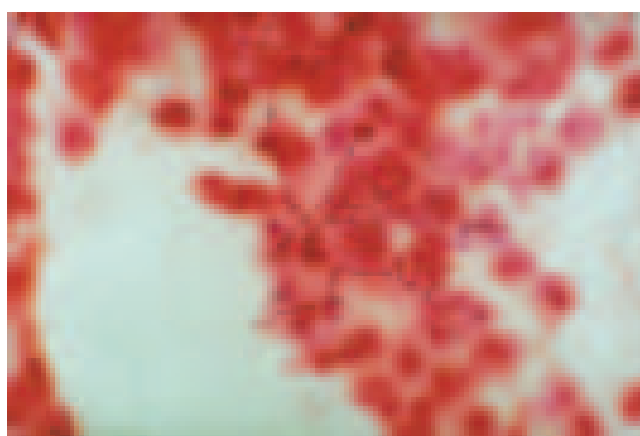


Fig. 1 : *Nocardia asteroides*

Gram positive branched filamentous bacilli that fragment into rod-shaped to coccoid forms with plenty of polymorphonuclear leukocytes in a direct smear of pus aspirated from subcutaneous abscess (x 100).

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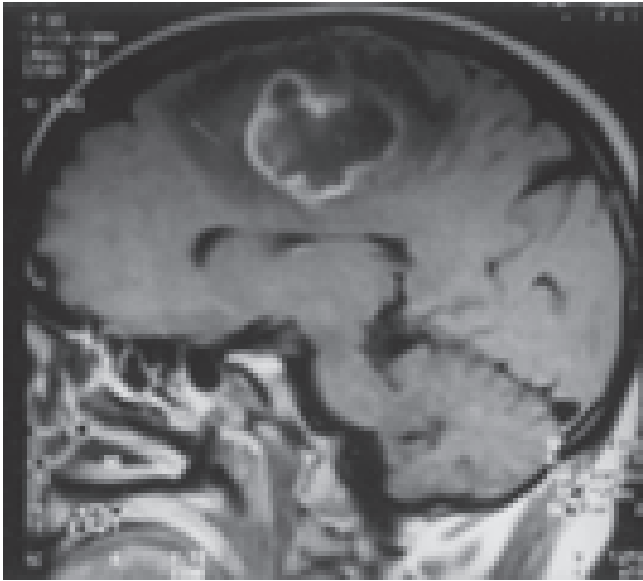


Fig. 2 : Post contrast T1 weighted axial and left para sagittal images showing a cystic mass (abscess) with rim enhancement, associated with perifocal oedema with mass effect on the ventricular system

surrounding edema? confluent brain abscess (Fig. 2). Pus was aspirated from the brain lesion, which revealed similar organism on microscopy as described earlier and grew *Nocardia asteroides*. Skiagram chest PA view was normal. Ultrasonography of the abdomen revealed cholelithiasis and no organ involvement or organomegaly.

The patient was started on oral co-trimoxazole, parenteral

ceftriaxone and amikacin, prophylactic phenytoin and decongestant measures. Steroids were tapered gradually and withdrawn. The patient improved, became afebrile and the power on the right side partially recovered. Attempts to increase the platelet counts with vincristine and anti-RhD failed.

While on conservative management, patient again deteriorated neurologically. Then the brain abscess was aspirated under intensive platelet support. Perioperative and postoperative periods were uneventful. Three days after the aspiration, the power on the right side started improving. Antibiotics were continued concurrently. Patient was able to tolerate extended 'platelet transfusion' free periods.

The patient has now been in our follow-up for the last 35 months, the initial 12 months being on mono drug therapy with co-trimoxazole subsequent to which co-trimoxazole was stopped. He has grade IV power on his right side. Repeat magnetic resonance imaging during the follow-up period have shown resolution of the abscess with remnant minimal perifocal edema.

CASE 2

A 51 years male, a diagnosed case of chronic idiopathic thrombocytopenic purpura, was on steroid therapy for the last five months. He presented with progressive pain and swelling in the left gluteal region and moderate grade fever for the last two weeks. There was no history of trauma to the left gluteal region, local injections or bleeding from any other site. There were no complaints referable to the respiratory or central nervous system. Examination revealed pyrexia (39°C) and a 10 x 12 cm erythematous, warm, tender, indurated and fluctuant area involving the gluteal region and lower back on the left side. Regional lymph nodes were not enlarged. Rest of the general and systemic examination was unremarkable. Investigations showed haemoglobin 11 gm%, total leukocyte count 9600/cumm, DLC P 76 L 24, platelet count of 63,000/cumm and normal liver and renal function tests. X-ray chest did not revealed any abnormality. Ultrasound of the left gluteal region revealed a 4 x 4.3 x 3.4 cm anechoic area. Patient was started on intravenous cloxacillin with a possibility of staphylococcal cellulitis and abscess, pending bacteriological examination and culture of the pus. However, there was no sign of resolution of the indurated area or a decrease in the size of the abscess. Pus aspirated from the gluteal abscess showed Gram positive and weakly acid fast, beaded, branching filamentous organisms suggestive of *Nocardia*. Culture of the pus grew *Nocardia asteroides* sensitive to trimethoprim/sulfamethoxazole, ceftriaxone, amikacin and ciprofloxacin. Patient was started on ceftriaxone and amikacin as there was a history of sensitivity to sulpha drugs. The abscess and the indurated area completely resolved in three weeks time.

DISCUSSION

Nocardia species are Gram positive, weakly acid fast aerobic actinomycets, characteristically arranged in the form of extensively branching hyphae that fragment into rod-

shaped to coccoid forms. Many species are known to be pathogenic in humans of which *Nocardia asteroides* is responsible for causing the disseminated form of disease, usually in immunocompromised patients. Involvement of the lung (75-80%) and the skin in the form of abscesses are the most common presentations, but virtually any organ system may be involved.¹⁻³ Brain abscesses are seen in 7% of the cases and are usually described in cases having pulmonary involvement but this was not so in our case who thus had an unusual clinical presentation.² Disseminated disease occurs in 25-40% cases, as was seen in one of our cases. Criteria for disseminated disease include involvement of two or more non-contiguous organs and/or CNS involvement. Diagnosis of nocardiosis depends on the demonstration of the bacterium by direct microscopy and culture. The predominance of PMN leukocytes in the pus and the frequent absence of regional lymphadenopathy are characteristic, as were seen in our cases.

A number of drugs have been advocated in the treatment of nocardiosis, but the drug of choice is co-trimoxazole,^{2,3} which can be used alone or in combination with one or more of the following antimicrobial drugs-imipenem, amikacin, ampicillin, IIIrd generation cephalosporins, fluoroquinolones or minocycline (intravenous administration in the case of cerebral nocardiosis).^{2,3} The selection of the drugs should be according to the culture sensitivity pattern of the organism. The value and need for combined chemotherapy is an unsettled issue but is usually used for disseminated disease, as we did in our case initially.^{2,4,6} The recommended duration of therapy ranges from 6-12 months. Exact role of surgery has not been well defined in nocardial brain abscesses, with variable results being obtained with conservative drug therapy alone, drug therapy with repeated stereotactic aspirations or excision of the abscess.²⁻⁴ Decision for surgical intervention needs to be individualized.²

There are only two previous reports on disseminated nocardiosis in patients with chronic ITP.^{1,2} Management of nocardial brain abscesses in a setting of ITP is a therapeutic challenge and needs a special approach, which is highlighted by our case. We initially resorted to conservative management, because of the fear of producing intractable intracranial bleed, especially since we had to withdraw steroids. Continuation of steroids has been shown to be associated with a poorer prognosis in nocardiosis. However, our approach was of

intensive combination chemotherapy.⁴⁻⁶ The patient showed an initial improvement but because of subsequent neurological deterioration, the brain abscess was aspirated under intensive platelet cover. This corroborates with the observation of others, that some form of surgical intervention is usually required in nocardial brain abscesses.^{2,5}

Poor prognostic criteria include acute infection (symptoms less than three weeks), continuation of steroids, immunocompromised status, disseminated disease and the presence of brain abscess. Even with the best of medical and surgical therapy, the overall mortality in disseminated disease amounts to 40-60%.³ Eventhough our patient with disseminated nocardiosis had a number of poor prognostic criteria in the background of ITP, he has done remarkably well so far on the protocol of management that we have followed.

Thus, there should be a high index of suspicion for nocardiosis in the appropriate clinical setting as described above. For disseminated disease with brain abscess, multidrug chemotherapy with surgical drainage is the management of choice. Thrombocytopenia should not be a deterring factor for aspiration/drainage of a brain abscess.

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