

Use of Gallium-67 in the Assessment of Response to Antibiotic Therapy in Malignant Otitis Externa - A Case Report

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ABSTRACT

Malignant Otitis Externa (MOE) can cause considerable morbidity and mortality in affected individuals. The outlook is now much improved with the use of ciprofloxacin, but it is important to ascertain that the infection has been completely eradicated before stopping treatment, as undertreatment may lead to a recurrence which is usually more resistant than the initial infection. Gallium-67 Single Photon Emission Computerised Tomography (SPECT) is a sensitive and cost effective tool in monitoring the disease activity of MOE, and should be used in the assessment of the response to antibiotic therapy.

Keywords: malignant otitis externa, Gallium-67 SPECT, assessment of response to antibiotic therapy

INTRODUCTION

Malignant otitis externa (MOE) is a progressive, debilitating and often fatal infection of the external auditory canal, the surrounding tissue and the base of the skull. Since Chandler's classic description, this disease has become recognised as an affliction which usually occurs in poorly controlled diabetics or the immunocompromised patient. The causative organism is almost always *Pseudomonas aeruginosa*⁽¹⁾.

The infection begins in the external auditory canal, and if untreated, will spread to invade the periauricular tissues, including the parotid gland, the temporomandibular joint and the soft tissues at the base of the skull. It then progresses along the skull base, causing a skull base osteomyelitis which may lead to paralysis of the VII, IX, X, and XII cranial nerves. This progressive cranial neuropathy is usually indicative of poor prognosis with impending meningitis and transverse sinus thrombosis. The diagnosis is usually based on clinical and pathological findings, supported by the isolation of *Pseudomonas aeruginosa*. However the extent of disease is not easy to determine. Initial evaluation is done with conventional X-rays and computerised tomographic (CT) scans, but these are rather insensitive to the presence and extent of cellulitis or early osteomyelitis^(2,3). ^{99m}Techetium Methylene Diphosphonate (MDP) and Gallium-67 SPECT have proven to be more sensitive and accurate in tracing

the extent of early MOE⁽²⁾. Magnetic Resonance Imaging (MRI) is now the most effective modality for evaluating the extent of soft tissue changes but it alone cannot be relied upon to determine physiologic response to therapy⁽⁴⁾.

Today, the recommended drug of choice in the treatment of MOE is ciprofloxacin, a fluoroquinolone, which has proven to be very effective⁽⁵⁾. It can be taken orally and so obviates long hospital stay. However, the response to treatment has to be monitored by a sensitive method so that the drug can be given for the correct duration. Gallium-67 SPECT has been shown to be a useful tool for this purpose. We report a case of MOE, where the disease activity monitored by Gallium-67 SPECT, has played an important role in the management of the patient.

CASE REPORT

A 58-year-old diabetic male presented with a history of left ear pain and discharge of 2 months' duration. He had earlier been treated conservatively with eardrops and analgesics without improvement. The pain had progressively worsened and 3 days prior to admission, he noted that his voice had become hoarse and he had difficulty swallowing. Otological examination revealed fleshy granulation tissue filling the external auditory canal together with some pus. Sensorineural deafness was detected on the left side and a neurological examination revealed left VII, IX, X, and XII cranial nerve palsies. An urgent CT scan of the temporal bone was requested and this showed a soft tissue mass in the left side of nasopharynx obliterating the left fossa of Rosenmuller and the parapharyngeal fat spaces. Parts of the clivus, the left petrous and the left pterygoid plates were eroded. There was also sclerosis of the left mastoid air cells. Biopsy of the fleshy external canal mass was done and this was reported as inflamed granulation tissue. Culture of the left ear discharge grew *Pseudomonas aeruginosa*. The diagnosis of malignant otitis externa with skull base osteomyelitis and multiple cranial nerve palsies was made.

^{99m}Techetium MDP planar and SPECT bone scintigraphy of the skull revealed increased activity in the left mastoid and petrous bone, with extension into the pterygoid and sphenoid bones. Gallium-67 SPECT images of the skull, 48 hours after injection

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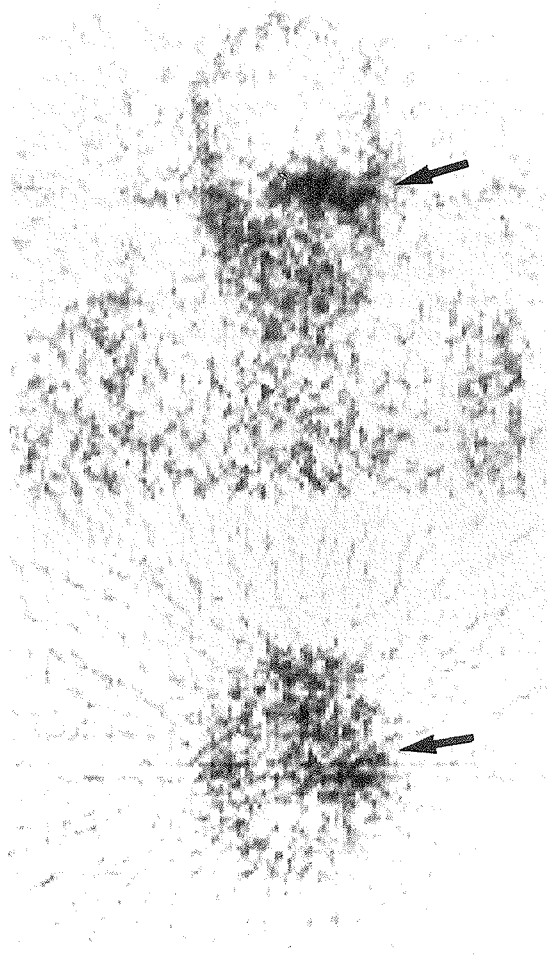


Fig 1 - Gallium-67 SPECT examination of the skull performed just before the commencement of therapy demonstrating increased activity in the regions of the left mastoid, petrous, pterygoid, and sphenoid bones consistent with acute sepsis. In comparison, the corresponding regions on the contralateral side showed normal distribution of uptake in bone, which is similar to that in the remainder of the skull.

of 5mCi of Gallium-67, showed accumulation of radionuclide in the regions of the left mastoid, petrous, pterygoid and sphenoid bones (Fig 1). These findings were indicative of sepsis with bony involvement in the affected areas.

The patient was started on intravenous ciprofloxacin for 2 weeks, and then continued with oral medication (ciprofloxacin) for 6 more weeks. At the end of 8 weeks therapy, a repeat bone scan was performed and this showed significant reduction of activity in the involved areas. This reduction in MDP activity reflects response to therapy with associated bone repair, but it does not necessarily indicate residual sepsis. As such, a Gallium-67 SPECT of the head was done a few days later and this showed minimal activity in the sphenoid region, with complete absence of activity in the petrous, pterygoid and mastoid regions. Based on these findings, antibiotic therapy was continued for another 4 weeks. The patient was scheduled for a repeat Gallium-67 SPECT examination upon completion of antibiotics, which

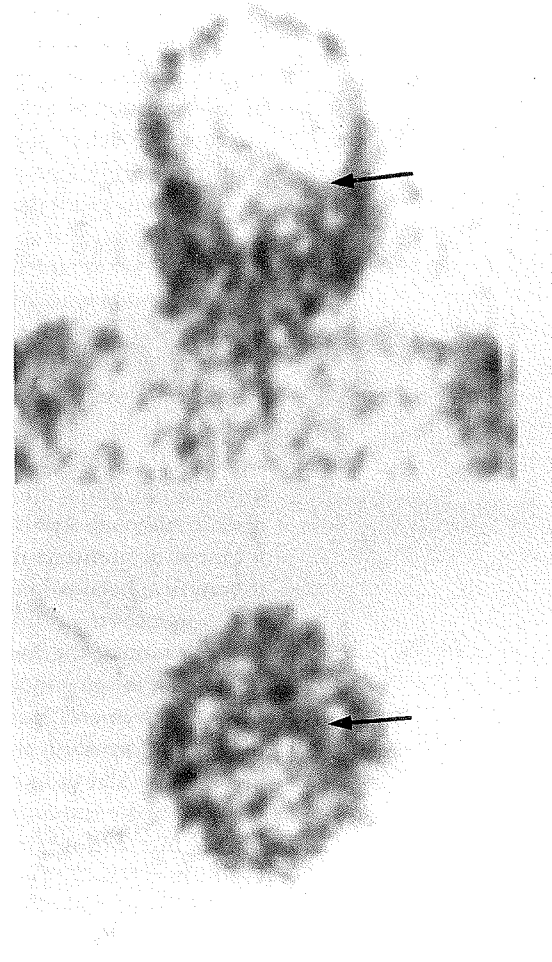


Fig 2 - Repeat Gallium-67 SPECT performed 7 months after completion of 12 weeks' therapy showing complete resolution of sepsis, as demonstrated by normal distribution and uptake in the previously affected areas. The gallium activity seen in the rest of the skull is physiological.

at that time, would have been given for a total of 12 weeks. Unfortunately, he defaulted follow-up as he was asymptomatic and only came back 7 months after the scheduled date of examination. Gallium-67 SPECT done then revealed complete resolution, with no evidence of residual sepsis or inflammation in the previously affected areas (Fig 2).

DISCUSSION

Following treatment with antibiotic therapy, the clinically observable infection in the external canal may clear while the deep seated infection in the skull base may persist. Therefore, the clinical picture alone is a poor indicator of disease activity and should not be used as a criterion for cessation of therapy, as this may lead to undertreatment. Failure to treat the infection adequately often results in recurrence of symptoms and a second infection that is more resistant than the first. The goal of treatment is therefore to cure the patient with one course of therapy and to prevent a relapse.

When gallium accumulation in malignant tissue was first described by Edwards and Hayes in 1969, it was hailed as a promising tumour-scanning agent. Following that, it was reported to accumulate at sites of inflammation as well, and this led to its use as an indicator of active sepsis. In the case of MOE, Gallium-67 SPECT provides valuable information of disease activity and is therefore the method of choice in the monitoring of patient's response to therapy. Sequential scans are recommended and therapy continued until a normal scan is obtained. At this stage, the bone scan may still remain positive, as seen in this patient, as it reflects bone repair that can continue even after the infection has been cleared. It is therefore not suitable to be used to monitor disease activity. Similarly, CT scan is also not suitable as it only gives information about the anatomical extent of the disease. Although it provides better spatial resolution, it cannot demonstrate disease activity. Furthermore, if bony demineralisation has occurred, the scan rarely, if ever, returns to normal. MRI has found its place in the evaluation of the disease, and has proven superior to all other imaging modalities in assessment of soft tissue involvement. However, like CT scan, it only provides information about the extent of structural involvement and cannot be relied upon to evaluate the physiologic response to antibiotic therapy⁽⁴⁾.

An interesting and potential substitute for Gallium-67 is ^{99m}Techetium or Indium-111 labelled white blood cell (WBC) scan. Its cost is similar to that of gallium, and is shown to be more sensitive in the detection of acute infection, while gallium is more sensitive in chronic infection. Further

work to compare the sensitivity and specificity of these two radionuclides needs to be done. Technetium labelled WBC has the advantage that it can be easily prepared from commercially available 'cold' kit, while preparation of Gallium-67 takes about 5 days to a week in most laboratories.

In conclusion, sequential Gallium-67 SPECT is a sensitive and useful method in the monitoring of disease activity in MOE. Taken in conjunction with clinical evidence, it can play an important role in ensuring that adequate treatment has been given and antibiotics can be discontinued. This will avoid undertreatment and prevent a recurrence. We recommend that Gallium-67 SPECT be done just before the commencement of therapy and at the end of the course, which is usually 8 weeks. A scan at mid-therapy might be useful, though not essential, to look at the response and predict the eventual outcome of disease.

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