

CASE IMAGE

Imatinib associated temporal bone osteonecrosis

Dominic McKenna  | Ekambar Reddy

Craigavon Area Hospital (Southern Health and Social Care Trust), Portadown, UK

Correspondence

Dominic McKenna, ENT Speciality doctor, Craigavon Area Hospital (Southern Health and Social Care Trust), Portadown, UK.
Email: dommckenna2011@gmail.com

Key Clinical Message

Tyrosine kinase inhibitors have substantially improved survival in patients with gastrointestinal stromal tumors (GIST) and chronic myeloid leukemia (CML). We report the first association between long-term imatinib use and temporal bone osteonecrosis, highlighting the importance of prompt ENT evaluation of such patients with new otological symptoms.

KEYWORDS

chronic infection, CML, ear canal, ear discharge, ear pain, erosion, GIST, imatinib, osteonecrosis, otalgia, otology, otorrhea, temporal bone

1 | CASE

A 75-year-old man presented with a 4-month history of bilateral ear pain and otorrhea, both more severe on the right. He has a background of recurrent gastrointestinal stromal tumor (GIST), initially treated with distal pancreatectomy, splenectomy, and partial gastrectomy. Retroperitoneal recurrence required further surgery. He has been on continuous adjuvant imatinib therapy, 400 mg daily, for 10 years without macroscopic recurrence.

He has no history of diabetes, previous radiotherapy, or bisphosphonate use.

On examination, bilateral bony erosion and necrosis on the floor of both external auditory canals (EAC) were observed, with infected debris (Figure 1A). This was confirmed on CT imaging (Figure 1B,C). Inflammatory markers, bone profile, microbiology cultures, vasculitis, and autoimmune screens were all normal. Histology confirmed osteonecrosis and excluded neoplastic or granulomatous causes (Figure 1D).

He underwent local anesthetic debridement of necrotic debris and was commenced on a 6-month course of oral ciprofloxacin along with 2 weeks of topical gentamycin, successfully resolving his symptoms without imatinib

cessation. He remains under follow-up for regular aural toiletry.

2 | QUESTION

What are the important differentials in a patient with suspected temporal bone osteonecrosis?

- Skull base osteomyelitis
- Malignancy
- Cholesteatoma
- Keratosis obturans
- Osteoradionecrosis
- Benign necrotizing otitis externa
- Medication related

3 | DISCUSSION

Gastrointestinal stromal tumors (GIST) are mesenchymal sarcomas thought to arise from myenteric plexus precursor cells, predominantly found in the stomach or small intestine.¹

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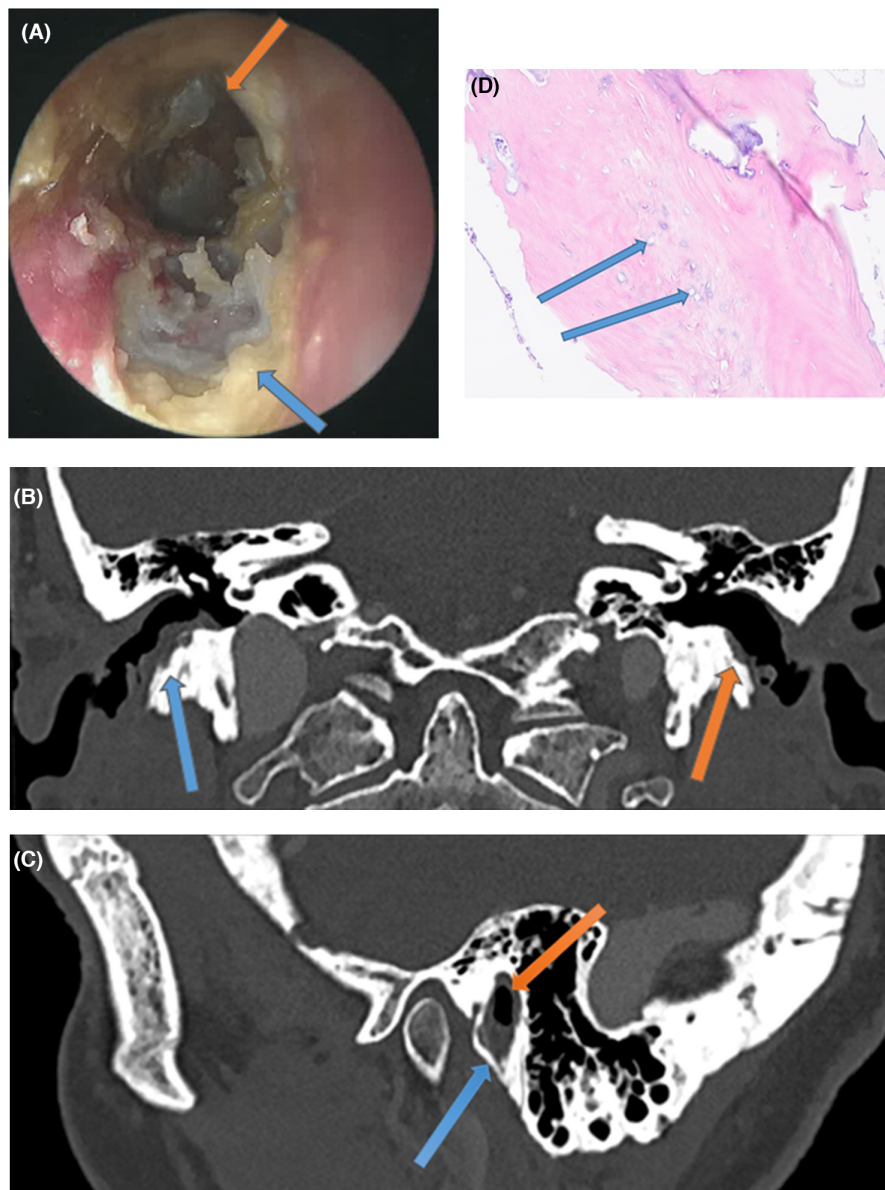


FIGURE 1 (A) Endoscopic image of right ear canal. Blue arrow—bony erosion of canal floor. Orange arrow—tympanic membrane. (B) CT scan of temporal bones (coronal plane). Blue arrow—bony erosion of the right external auditory canal. Orange arrow—bony erosion of the left external auditory canal. (C) CT scan of temporal bones (Sagittal plane). Blue arrow—bony erosion of right external auditory canal. Orange arrow—air in the ear canal. (D) Right external auditory canal bony specimen. Arrows—Empty lacunae indicating bony necrosis.

Pathogenetically, they are defined by KIT tyrosine kinase positivity, allowing utilization of the tyrosine kinase inhibitors (TKI) imatinib or sunitinib as targeted therapy. Their use has led to dramatic increases in survival when used adjuvantly or neoadjuvantly in combination with surgery.¹ In metastatic disease, lifelong imatinib is recommended.

Although most patients on long-term adjuvant imatinib for GIST report side effects, these are generally mild and well tolerated. Grade 3–4 side effects occur in 19%.² The most frequent hematological side effects were anemia and granulocytopenia. Non-hematological side effects included oedema, fatigue, nausea, diarrhea, and muscle spasms.

Aggressive management of side effects is vital to avoid treatment interruptions, which can be associated with rapid tumor regrowth.¹

Medication related ear canal osteonecrosis is rare, with case reports linking its development to bisphosphonates,³ denosumab,⁴ and sunitinib.⁵ It can range from asymptomatic to requiring extensive surgical debridement.

Imatinib is known to affect bone metabolism, with cases of TKI-related jaw osteonecrosis also described.⁶ Our patient represents the first published instance of imatinib related ear canal osteonecrosis. The successful treatment of this condition, allowing maintenance of full dose imatinib, highlights the importance of prompt ENT intervention in the presence of new otological symptoms in patients on long-term imatinib therapy.

AUTHOR CONTRIBUTIONS

Dominic McKenna: Conceptualization; data curation; validation; visualization; writing – original draft; writing

– review and editing. **Ekambar Reddy**: Conceptualization; data curation; supervision; writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

None declared.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed.

ORCID

Dominic McKenna  <https://orcid.org/0000-0002-0251-123X>

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