International Journal of Otorhinolaryngology and Head and Neck Surgery
Krishna VB et al. Int J Otorhinolaryngol Head Neck Surg. 2025 Aug;11(4):431-434
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20252255

Case Report

Gastrointestinal stromal tumour of larynx: a case report

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Received: 28 April 2025
Accepted: 19 June 2025

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ABSTRACT

Gastrointestinal stromal tumour (GITs) are the most common mesenchymal tumours of GI tract and occur mostly in stomach, small intestine and rarely in omentum, mesentery, retroperitoneum. These tumours arise from interstitial cells of cajal due to mutations in KIT (CD117) or PDGFRA. GIST most commonly present in the stomach (60%) or small intestine (20 to 30%) and may rarely occur extra gastro intestinally like omentum, mesentery or retro peritoneum. The 30% of GIST are malignant and common metastatic sites are liver, mesentery and omentum, lung, lymph node, bone, pancreas, colon are less common metastatic sites. Ultrasound, magnetic resonance imaging (MRI), CT, PET CT, endoscopy, endoscopy guided fine needle aspiration (FNA) or core biopsy are used modalities for diagnosis. GISTs are diagnosed by immunohistochemical methods. Surgical resection (open/ laparoscopic/ combined laparoscopic-endoscopic) is the main curative treatment. Most recurrences occurred within first 5yrs and a close follow up is required for early detection of relapses. Imatinib mesylate showed better response in advanced cases and recurrent cases. So far, there has been one publication found regarding gastointestinal stromal tumours occurring in vocal cords and one literature GIST of rectum with larynx metastasis. This current case report is regarding GIST occurring in vocal cords and its management. Further studies need to be conducted for better management options and to know the prognosis in such cases.

Keywords: Gastrointestinal stromal tumour, Larynx, True vocal cord, Mutation analysis

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most prevalent mesenchymal tumors of the GI tract, accounting for approximately 80% of all such tumors and representing 0.1% to 3% of all GI malignancies. GISTs are most commonly located in the stomach (60%) and small intestine (20-30%), but they can also be found in extra- GI locations such as the omentum, mesentery, or retroperitoneum. Common metastatic sites include the liver, mesentery, and omentum, while metastasis to the lungs, lymph nodes, bones, pancreas, and colon is less frequent. There are only two documented cases of GISTs occurring in the larynx, based on a PubMed database search.[1,2]

CASE REPORT

A 48-year-old male with a history of bidi smoking and chronic tobacco chewing for 22 years presented to the ENT department with an 11-month history of hoarseness. The hoarseness was gradual in onset, persistent, and progressively worsened over time. The patient did not report any breathing difficulties. Fiber-optic laryngoscopy revealed an ulcerative growth on the left true vocal cord (TVC), leading to microlaryngoscopy and biopsy. Histopathological examination (HPE) of the

biopsy initially suggested a leiomyoma, but immunohistochemistry (IHC) confirmed the diagnosis as a GIST. The patient was subsequently lost to follow-up but returned six months later with a recurrence of similar symptoms.

Upon re-evaluation with fiber-optic laryngoscopy, a proliferative growth was observed on the left TVC at the junction of the anterior one-third and posterior two-thirds, extending inferiorly into the subglottic region by 5-10 mm (Figure 1). A contrast-enhanced CT (CECT) scan of the neck revealed an ill-defined, heterogeneously enhancing lesion measuring 18×8×12 mm in the anterior half of the left TVC, with lateral abutment of the thyroid cartilage. The anterior commissure and false vocal cord were free of the lesion (Figure 2).

A whole-body PET scan was performed to rule out abdominal metastasis and showed an ill-defined lesion measuring 1.6×1.0×1.2 cm in the anterior half of the left TVC, with a maximum standardized uptake value (SUV max) of 7.81. No abdominal metastasis was identified. The patient was diagnosed with recurrent GIST of the left TVC and underwent micro laryngoscopy with tumor excision (Figure 3).

Histopathological and immunohistochemical findings

Microscopic examination revealed a poorly circumscribed spindle cell tumor arranged in intersecting fascicles, with accompanying mast cells and lymphocytes. The tumor cells were plump spindles with pleomorphic oval to elongated nuclei, open chromatin, conspicuous nucleoli, and moderate pale eosinophilic cytoplasm. Many tumor cells exhibited paranuclear cytoplasmic vacuolations. The mitotic count was 1-2 per high-power field (HPF), with no evidence of necrosis (Figure 4).

Immunohistochemical analysis showed that the tumor cells were positive for vimentin (cytoplasmic), CD117 (moderately intense, membranous), and DOG1 (dim and cytoplasmic). The cells were negative for SMA, S100p, CD34, and CK. The Ki67 proliferative index was 30%.

Molecular analysis

KIT mutational analysis revealed wild-type status for Exons 9, 11, 13, and 17. PDGFRA mutational analysis also showed wild-type status for Exons 12, 14, and 18. Both KIT and PDGFRA mutational analyses were negative.

Follow-up and management

At a one-month postoperative follow-up, the patient was asymptomatic, and fiber-optic laryngoscopy revealed no evidence of new growth or lesions (Figure 5). The patient was referred to oncology, where treatment with imatinib 300 mg once daily was initiated. The patient has since been under regular follow-up to monitor prognosis.

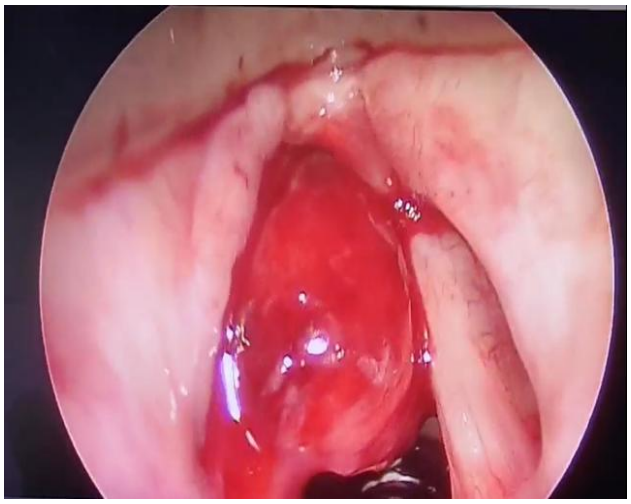

Figure 1: Pre-operative fibre optic laryngoscopy image.

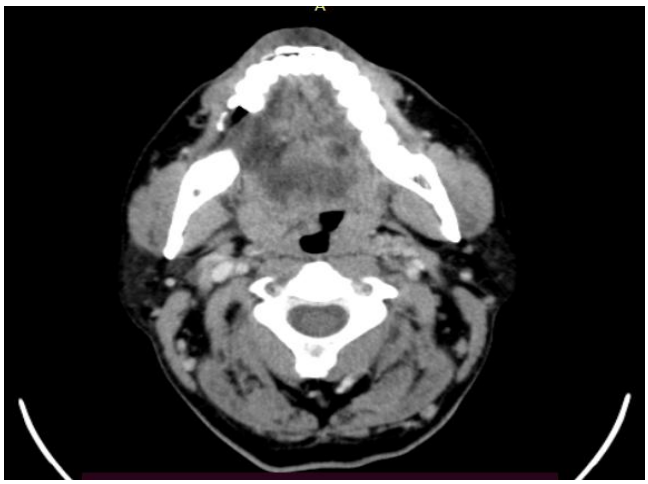

Figure 2: CECT of neck shows extension of tumour.

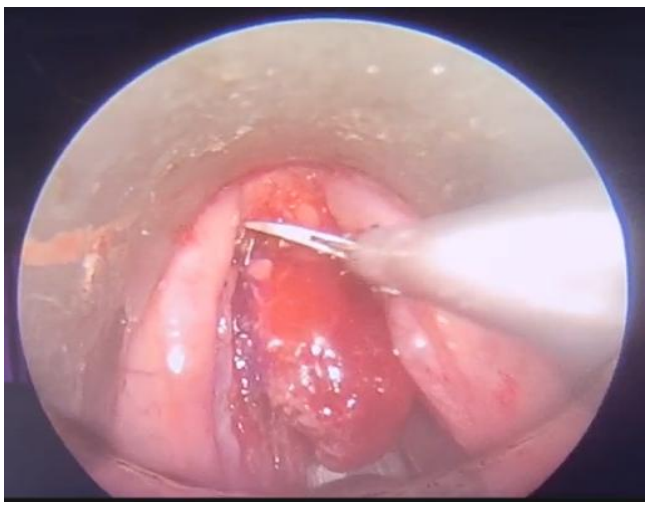

Figure 3: Intra-operative image GIST.

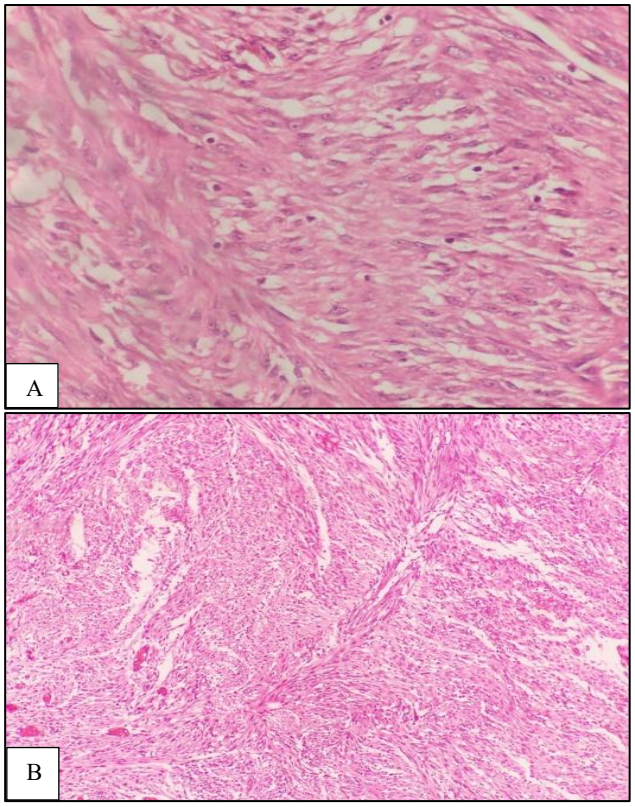

Figure 4 (A and B): HPE findings. A-low power intersecting fascicles of spindle cells and B-high power, Spindle cells with oval to elongated nuclei with nucleoli and open chromatin.

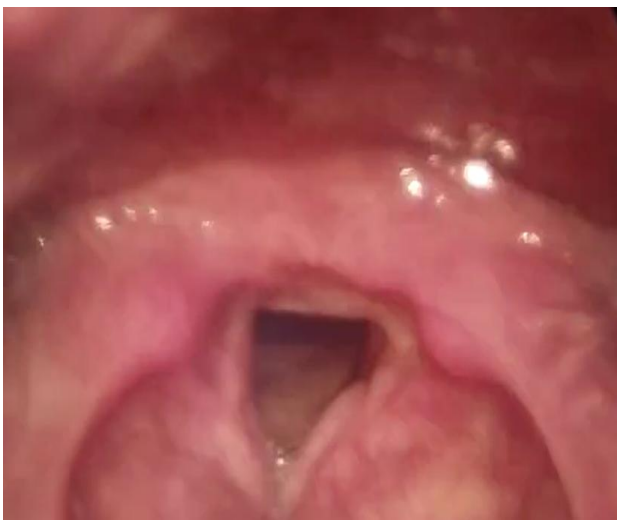

Figure 5: Post-operative image of GIST.

DISCUSSION

GISTs are the most common mesenchymal tumors of the GI tract, accounting for 0.1% to 3% of all GI malignancies. The annual incidence ranges from 6.8 to 19.7 cases per million worldwide. GISTs most commonly occur in the stomach (60%), followed by the small intestine (30%), duodenum (4-5%), colon (1-2%), rectum (2-4%), and esophagus. Rarely, they can be found in the omentum, mesentery, or retroperitoneum.[3,4]

GISTs affect men and women equally and are rare in patients under the age of 18, accounting for only 1-2% of cases. The median age at diagnosis is between the mid-50s and mid-60s, consistent with the age of our patient. GISTs originate from the interstitial cells of Cajal, which function as pacemakers for intestinal peristalsis. These tumors express a growth factor receptor with tyrosine kinase activity, known as KIT (CD117). Mutations in KIT or platelet-derived growth factor receptor alpha (PDGFRA) genes lead to constitutive activation of their encoded tyrosine kinase receptors, resulting in hyperplasia, resistance to apoptosis, and ultimately, neoplasia. Other mutations, such as those in NF1, BRAF, and HRAS, are associated with syndromes like neurofibromatosis type 1, the Carney triad (GIST, paraganglioma, and pulmonary chondroma), and Carney-Stratakis syndrome (GIST and paraganglioma).[5]

KIT and DOG1 surface protein mutations are common in GISTs. In cases where KIT is absent (5% of cases), PDGFRA mutations are often present. GISTs are diagnosed using imaging modalities like ultrasound, endoscopy-guided fine needle aspiration (FNA), magnetic resonance imaging (MRI), CT, PET-CT, and endoscopy. Immunohistochemical staining is crucial for diagnosis, with 95% of GISTs expressing CD117, DOG1, and PDGFRA mutations, and 70-80% expressing CD34 mutations. Tumors lacking KIT or PDGFRA mutations tend to have a more aggressive course and poorer prognosis.

GISTs are categorized by the national institutes of health (NIH) into four risk categories-very low, low, intermediate, and high-based on tumor size and mitotic count. The national comprehensive cancer network (NCCN) further assesses malignancy risk using tumor size, mitotic count, and tumor site. Surgical resection, whether open, laparoscopic, or combined laparoscopic-endoscopic, remains the mainstay of curative treatment. Most recurrences occur within the first five years, necessitating close follow-up for early detection and prompt management with tyrosine kinase inhibitors (TKIs) like Imatinib. The introduction of the KIT inhibitor Imatinib Mesylate has revolutionized the management of advanced GISTs.[6]

Despite advancements, ongoing challenges include the development of secondary mutations in KIT or PDGFRA, leading to tumor progression. Ripretinib, a novel switch-control TKI, inhibits both primary and secondary mutations in KIT and PDGFRA, addressing this challenge. In the pivotal INVICTUS Phase III trial, patients with advanced GIST who had progressed on imatinib, avapritinib, sunitinib, or regorafenib experienced significantly longer progression-free survival, improved overall survival, and better quality of life when treated with Ripretinib compared to placebo.

Ripretinib has since been approved for the treatment of advanced GIST in adults who have received three or more TKIs, including Imatinib.

Metastasis from GISTs commonly involves the liver, mesentery, and omentum, with less frequent metastasis to the lungs, lymph nodes, bones, pancreas, and colon. The incidence of secondary malignancies associated with GISTs varies from 4.5% to 33%, with most being GI tumors. Female genital tract tumors and sarcomas are much less common. Treatment options for metastatic GISTs include radiotherapy, chemotherapy, hepatic artery embolization, chemoembolization, and radiofrequency ablation.[7]

This case report describes the second documented case of GIST occurring in the vocal cords and its management. Further studies are needed to optimize treatment strategies and understand the prognosis for such rare cases.

CONCLUSION

GISTs predominantly occur in the GI tract, with the stomach being the most common site, followed by the small intestine, duodenum, colon, rectum, and esophagus. Metastasis frequently occurs in the liver, lungs, lymph nodes, bones, and pancreas. GISTs are diagnosed using imaging modalities and immunohistochemical methods to detect KIT/CD117, PDGFRA, or other mutations. Risk assessment is based on tumor size and mitotic count. Surgical resection is the primary curative treatment, with high-risk and advanced cases requiring adjuvant TKI therapy. Close follow-up is essential for early detection of recurrences and complications, leading to better management and prognosis. GIST of the vocal cords is an extremely rare occurrence, with only two other cases documented in the literature. Further research is needed to improve treatment and outcomes for such rare presentations.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Krishna VB, Sharma V, Das D, Kumar SH, Madakshira MG, Mulajker DS. Gastrointestinal stromal tumour of larynx: a case report. Int J Otorhinolaryngol Head Neck Surg 2025;11:431-4.