ISSN: 2584-0355
DOI: doi.org/10.51219/MCCRJ/Nayab-Mustansar/135

URF PUBLISHERS
connect with research world

Medical & Clinical Case Reports Journal

https://urfpublishers.com/journal/case-reports

Vol: 2 & Iss: 4

Case Report

Case Report: Neuroendocrine Tumour of the Gallbladder: An Extremely Rare Malignancy

Nayab Mustansar[1]*, Ashfa Ameer Khan[2], Maimoona Afsar[2], Brig Aslam Channa[3], Maj Adnan[4] and Maj Rizwan Rafi[5]

[1]Resident, Radiology Department, FC Teaching Hospital, Pakistan

[2]Consultant Radiologist, FC Teaching Hospital, Pakistan

[3]Commdant, FC Teaching Hospital, Peshwar, Paksitan

[4]Surgeon, FCTH, Peshawar, Paksitan

[5]DADMS FC NORTH KPK, Fort Balahisar, Pakistan

Citation: Mustansar N, Khan AA, Afsar M, et al., Neuroendocrine Tumour of the Gallbladder: An Extremely Rare Malignancy. *Medi Clin Case Rep J* 2024;2(4):507-509. DOI: doi.org/10.51219/MCCRJ/Nayab-Mustansar/135

Received: 24 September, 2024; **Accepted:** 15 October, 2024; **Published:** 17 October, 2024

***Corresponding author:** Dr Mustansar N, Resident, Radiology Department, FC Teaching Hospital, Pakistan, Email: drnayabmustansar@gmail.com

ABSTRACT

Neuroendocrine tumours (NETs) of the gallbladder are rare and represent a challenging clinical scenario due to their aggressive nature and late presentation. We report a case of a 60-year-old female diagnosed with a stage 4B neuroendocrine tumour of the gallbladder. This case underscores the importance of early recognition and the complexities associated with managing advanced-stage neuroendocrine tumour.

Keywords: Neuroendocrine tumour; Gallbladder; Neuroendocrine cells

Introduction

Neuroendocrine tumors (NETs) are neoplasms arising from neuroendocrine cells, which are distributed throughout various organs, including the gastrointestinal tract. NETs of the gallbladder are exceptionally rare, with fewer than 100 cases reported in the literature. These tumors can be highly aggressive and often present at an advanced stage. The prognosis for stage 4B neuroendocrine tumors is generally poor, making early diagnosis and effective management critical.

Case Presentation

A 60-year-old female presented to the Frontier Corp Teaching Hospital on 13th August 2024 with worsening right upper quadrant pain and palpable swelling over the past 4 months. Her past medical history was notable for hypertension and type 2 diabetes mellitus, with no previous history of gallbladder disease. Physical examination revealed non tender firm palpable mass in the right upper quadrant rest of the systemic examination was unremarkable. Laboratory tests showed deranged CBC and raised fasting blood glucose as shown in (**Tables 1,2**).

Imaging studies included an abdominal ultrasound, which revealed a large heterogenous mass infiltrating the liver parenchyma mostly involving the segment IV and VI with perilesional lymphadenopathy. A subsequent contrast-enhanced computed tomography (CT) scan confirmed a large contour deforming mass of gall bladder fossa with extensive liver

infiltration, extension into anterior abdominal wall, pancreas and lymphadenopathy, consistent with stage 4B disease according to the American Joint Committee on Cancer (AJCC) staging system as shown below (**Figure 1**).

Table 1: Complete Blood Picture.

Parameters	Value	Reference Range
Hb	7.6	13.5 – 16.5 g/dL
RBC	3.67	3.80 – 5.80 x 10^{12}/ L
TLC	27.42	4.0 - 10.0 x 10^{9}/ L
Platelets	606	150 - 400 x 10^{9}/ L
ALT	42	upto 42 U/ L
Creatinine	79	62-106 umol/L

Table 2: Raised Fasting Blood Glucose.

Parameters	Result
CRP	1.6
Fasting blood Glucose	342
Hepatitis B	Negative
Hepatitis C	Negative
SARS-COV2	Negative

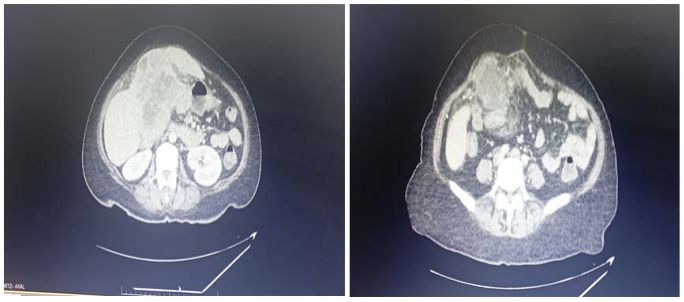

Figure 1: CECT abdomen and pelvis showing NET-GB Stage-IV.

A successful TRU-CU biopsy was done without any complications in radiology department of Frontier Corp Teaching Hospital and sample was sent for histopathology. The biopsy report of the gallbladder mass revealed a well-differentiated neuroendocrine tumour (NET) with high mitotic activity, indicative of a higher-grade neuroendocrine carcinoma. Immunohistochemical staining was positive for CK7 and CK19 with pleomorphic hyperchromatic nuclei and eosinophilic cytoplasm, supporting the neuroendocrine origin of the tumour. As the tumour was surgically irresectable the patient was referred to oncologist for further work up.

Discussion

Neuroendocrine tumors of the gallbladder are exceptionally rare, comprising less than 1% of all gallbladder tumors. They are often diagnosed at an advanced stage due to their nonspecific symptoms and late presentation. The most common symptoms, such as abdominal pain, jaundice and weight loss are often attributed to more common conditions, leading to delays in diagnosis.

Stage 4B NETs are characterized by extensive local and distant metastasis, which significantly impacts treatment options and prognosis. The prognosis for stage 4B NETs of the gallbladder is generally poor, with a median overall survival often less than 12 months. The treatment approach typically involves a combination of surgical resection, if feasible and systemic therapies including chemotherapy, targeted therapy and somatostatin analogs[1].

In our case, the advanced stage of the disease precluded surgical intervention. The patient was initiated on a regimen of cisplatin and etoposide, which is a standard treatment for high-grade neuroendocrine carcinomas. Additionally, she was started on octreotide, a somatostatin analog, to manage symptoms associated with carcinoid syndrome and potentially slow tumor progression.

Neuroendocrine tumours (NETs) of the gallbladder are exceedingly rare and are usually diagnosed at a late stage due to their nonspecific symptoms and the absence of routine screening protocols. The rarity of these tumours contributes to the limited understanding of their optimal management and prognosis[2].

The clinical presentation of gallbladder NETs often overlaps with other gallbladder pathologies, such as cholecystitis or gallbladder cancer, which can delay diagnosis. Symptoms like abdominal pain, jaundice and weight loss are common and can be mistaken for more prevalent conditions. The diagnosis is often made through imaging studies, but confirmation typically requires histopathological examination. The advanced stage of the disease at presentation reflects the indolent nature of symptom development and the lack of specific early warning signs.

Gallbladder NETs can vary in their histological features, but they are generally characterized by the expression of neuroendocrine markers such as chromogranin A, synaptophysin and CD56. Histological grading, based on the mitotic index and Ki-67 proliferation index, helps classify the tumors into well-differentiated or poorly differentiated categories. This grading is crucial for determining prognosis and guiding treatment.

The AJCC staging system is used to categorize neuroendocrine tumors based on their extent of disease. Stage 4B is indicative of extensive metastasis, including distant sites and extensive local lymph nodes, which significantly complicates management. The presence of liver metastases, as observed in this case, often necessitates systemic therapy as surgical resection alone is not feasible or curative[3].

For advanced-stage NETs, especially stage 4B, treatment typically involves a multimodal approach. The use of chemotherapy remains a cornerstone in managing high-grade neuroendocrine tumors. Regimens such as cisplatin and etoposide are frequently employed due to their efficacy in reducing tumor burden and controlling disease progression. However, the response can be variable and treatment-related side effects need to be managed carefully.

Somatostatin analogs like octreotide and lanreotide are used to alleviate symptoms associated with carcinoid syndrome and may also have antiproliferative effects. Their role in the management of gallbladder NETs is supported by their efficacy in controlling hormone-related symptoms and potentially slowing tumor growth.

Emerging therapies such as tyrosine kinase inhibitors and mTOR inhibitors are showing promise in clinical trials. These therapies target specific pathways involved in tumor growth

and proliferation. Although their use in gallbladder NETs is less established, they represent a hopeful area for future treatment options.

While not a primary treatment for NETs, radiotherapy can be considered for palliative care, particularly for symptomatic relief from local disease progression or in cases where metastases cause pain or dysfunction.

The prognosis for stage 4B neuroendocrine tumors of the gallbladder is generally poor, with median survival times often limited to months. Factors influencing prognosis include the tumor grade, the extent of metastasis, and the patient's overall health and response to treatment.

Recent advancements in genomic and molecular research offer new insights into NET biology and potential therapeutic targets. Comprehensive genomic profiling of NETs could lead to personalized treatment approaches, allowing for targeted therapies that are more effective and less toxic than conventional chemotherapy. The development of novel agents and combinations of existing therapies holds promise for improving patient outcomes[4].

Ongoing research and clinical trials are essential to advance the understanding and treatment of neuroendocrine tumors. Trials investigating novel drugs, combinations of therapies and new treatment paradigms are crucial for discovering more effective strategies for managing advanced-stage NETs. Participation in clinical trials should be considered for eligible patients, as these studies often provide access to cutting-edge treatments and contribute to the broader understanding of NETs.

Recent advances in molecular targeted therapies and immunotherapies have shown promise in the management of neuroendocrine tumors, though their efficacy in gallbladder NETs remains under investigation. Research into novel agents and combination therapies continues to evolve, aiming to improve outcomes for patients with advanced neuroendocrine tumors[5].

Conclusion

This case highlights the challenges associated with diagnosing and managing neuroendocrine tumors of the gallbladder, particularly at advanced stages. The rarity of these tumors necessitates a high index of suspicion for early diagnosis. Despite aggressive treatment strategies, the prognosis for stage 4B neuroendocrine tumors remains guarded. Continued research and clinical trials are essential to develop more effective therapies and improve survival outcomes for patients with these rare and challenging malignancies.

Neuroendocrine tumors of the gallbladder are rare and present significant diagnostic and therapeutic challenges. Advanced-stage NETs, such as stage 4B, require a multidisciplinary approach to management, including systemic therapy, symptomatic relief and supportive care. Although the prognosis remains poor, ongoing research and clinical trials offer hope for improved outcomes through novel therapies and personalized treatment strategies. Early diagnosis and tailored management are key to improving survival and quality of life for patients with this rare and complex malignancy.

References

1. Janson JB, Krenning EP. Neuroendocrine Tumors of the Gallbladder. Gastroenterology Clin of North America 2010;39(3):405-418.
2. Worrell SG, Kauffman EL. Gallbladder Neuroendocrine Tumors: A Review of Pathology and Management. World Journal of Gastroenterology 2018;24(29):3327-3335.
3. Falconi M, Eriksson B. Neuroendocrine Tumors of the Gallbladder and Biliary Tract: Clinical Features and Management. Endocrine Reviews 2016;37(4):589-610.
4. Kim HR, Kim Y. Advanced Neuroendocrine Tumors of the Gallbladder: Current Perspectives and Future Directions. Cancer Research and Treatment 2017;49(3):759-766.
5. Rinke A, Mueller M. Treatment Options for Advanced Neuroendocrine Tumors: A Focus on Somatostatin Analogs and Targeted Therapies. Journal of Clin Oncology 2014;32(6):623-634.