Annals of Case Reports
Srinivas BC, et al. Ann Case Rep: 11: 102521
www.doi.org/10.29011/2574-7754.102521
www.gavinpublishers.com

OPEN ACCESS

GAVIN PUBLISHERS

Case Report

Metastatic Pancreatic Adenocarcinoma with Germline BLM and Somatic ATM Mutations: A Case Report and Review of DNA Damage Response

Bhargavram Channagiri Srinivas[1], Sai Sri Hari Paruchuri[2], Wei Zhang[3], Prasad Dandawate[4], Subhrajit Saha[5], Ravi Paluri[6], Ashish Manne[7], Anup Kasi[8*]

[1]Department of Internal Medicine, Gadag Institute of Medical Sciences, Gadag, Karnataka, India

[2]Department of Internal Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Gannavaram Mandal, Andhra Pradesh, India

[3]Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS 66205, USA

[4]Department of Medical Oncology, University of Kansas Medical Center, Kansas City, USA

[5]Department of Cancer Biology, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS, 66160, USA

[6]Department of Hematology and Oncology, Wake Forest School of Medicine, Winston-Salem, NC, USA

[7]Department of Internal Medicine, Division of Medical Oncology at the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, The Ohio State University Comprehensive Cancer Center, Columbus, OH, United States

[8]Department of Medical Oncology, University of Kansas Cancer Center, Kansas City, KS 66205, USA

***Corresponding Author:** Anup Kasi, Department of Medical Oncology, University of Kansas Cancer Center, Kansas City, KS 66205, USA

Citation: Srinivas BC, Parachuri SSH, Zhang W, Dandawate P, Saha S, et al. (2026). Metastatic Pancreatic Adenocarcinoma with Germline BLM and Somatic ATM Mutations: A Case Report and Review of DNA Damage Response. Ann Case Report. 11: 2521. DOI: 10.29011/2574-7754.102521

Received: 28 January 2026; **Accepted**: 04 February 2026; **Published**: 06 February 2026

Citation: Srinivas BC, Parachuri SSH, Zhang W, Dandawate P, Saha S, et al. (2026). Metastatic Pancreatic Adenocarcinoma with Germline BLM and Somatic ATM Mutations: A Case Report and Review of DNA Damage Response. Ann Case Report. 11: 2521. DOI: 10.29011/2574-7754.102521

Abstract

Introduction: Pancreatic adenocarcinoma (PDAC) is an aggressive malignancy with a poor prognosis. While germline mutations in BRCA1/2 are well-established risk factors, mutations in the BLM gene (associated with Bloom Syndrome) are rare in this context.

Case Presentation: We present a 73-year-old female with a recent history of small cell lung cancer (SCLC) who presented with metastatic pancreatic adenocarcinoma. Genetic profiling revealed a pathogenic germline BLM mutation and a somatic ATM mutation. The patient was treated with an oxaliplatin-based regimen (mFOLFOX6), modified due to comorbidities, achieving disease stabilization.

Discussion: This case highlights the complexity of managing metachronous malignancies and the utility of comprehensive genomic profiling. The presence of pathogenic variants in DNA damage response (DDR) genes (BLM and ATM) suggests a defect in homologous recombination, providing a rationale for platinum-based therapy. We discuss the implications of BLM mutations on therapeutic selection, potential immune checkpoint interactions, and the role of synthetic lethality in management.

Keywords: Pancreatic Adenocarcinoma; Metachronous Malignancies; BLM Mutations; Hyperlipidemia; Small Cell Lung Cancer.

Introduction

Pancreatic adenocarcinoma (PDAC) remains a leading cause of cancer-related mortality. While the majority of cases are sporadic, approximately 10% harbor a hereditary component involving genes such as BRCA1, BRCA2, PALB2, and ATM. The BLM gene encodes a RecQ DNA helicase essential for maintaining genomic stability. Biallelic mutations in BLM result in Bloom Syndrome, an autosomal recessive disorder characterized by short stature, photosensitivity, and a marked predisposition to early-onset malignancies. However, the contribution of monoallelic (heterozygous) BLM mutations to PDAC risk and treatment response is less defined.

Identifying defects in homologous recombination repair (HRR) is critical, as these tumors may exhibit synthetic lethality when exposed to DNA-damaging agents like platinum salts or PARP inhibitors. This report describes a patient with metastatic PDAC and a history of small cell lung cancer (SCLC) who harbored a germline BLM mutation and a somatic ATM mutation.

Case Presentation

A 73-year-old Caucasian female presented for surveillance following treatment for a prior malignancy. Her medical history was significant for limited-stage small cell lung cancer (SCLC) diagnosed 2 years ago, for which she completed four cycles of cisplatin and etoposide with concurrent radiation therapy. She had been without evidence of disease (NED) on recent imaging. Relevant comorbidities included type 2 diabetes, hypertension, hyperlipidemia, a recent acute lacunar cerebrovascular accident (CVA), and a 35-pack-year history of tobacco use (quit 2 years prior to presentation).

Her family history was notable for malignancy. Her father died of prostate cancer at age 93. Two sisters were diagnosed with breast cancer, one in her 50s and the other in her 60s. Additionally, the maternal grandmother had a cancer of unknown primary, which the family suspected was pancreatic in origin.

At presentation, surveillance imaging revealed a 2 cm nodule at the pancreatic head. Subsequent imaging a month later demonstrated rapid progression with new liver metastases, confirming Stage IV pancreatic adenocarcinoma. The patient developed obstructive jaundice, which was resolved via ERCP stenting.

Next-generation sequencing (NGS) was performed to guide therapy. Testing identified a pathogenic germline heterozygous variant in BLM (p.Q645*) and a pathogenic somatic mutation in ATM (p.R3008H), along with a somatic KRAS (p.G12D) mutation.

Clinical Course Due to the presence of DDR gene mutations (BLM and ATM), a platinum-based regimen was favored. The patient initiated first-line palliative chemotherapy with mFOLFOX6 (oxaliplatin 85 mg/m², fluorouracil 1800 mg/m², and leucovorin). Irinotecan was omitted from the standard FOLFIRINOX regimen due to the patient's severe baseline fatigue and recent stroke history.

Following the initiation of therapy, the patient tolerated the regimen with manageable toxicities. Due to persistent fatigue, a 20% dose reduction was implemented for subsequent cycles to preserve quality of life while maintaining platinum exposure. Follow-up evaluation showed stabilization of liver enzymes and stable disease on imaging, validating the decision to pursue a DNA-damaging strategy despite her complex medical history [1-3].

Discussion

This case illustrates the diagnostic and therapeutic nuances of treating PDAC in the context of hereditary cancer syndromes.

The patient's germline BLM mutation, combined with a somatic ATM mutation, likely compromised the tumor's homologous recombination repair capacity, rendering it susceptible to oxaliplatin.

The BLM gene functions as a "caretaker" of the genome. Loss of BLM function leads to increased sister chromatid exchanges and genomic instability. While Bloom Syndrome is rare, carriers of heterozygous BLM mutations may have an increased risk of colorectal and other cancers, though specific screening guidelines for PDAC in carriers are not yet established.

Regarding the tumor immune microenvironment, emerging research suggests a link between BLM expression and immune infiltration. High BLM expression has been regulated by the LINC01133/miR-30b-5p axis, which modulates immune cell infiltration in pancreatic cancer models. Consequently, BLM status may serve as a potential biomarker not only for chemotherapy sensitivity but also for determining the immunogenicity of the tumor, which could influence future immunotherapy strategies.

The molecular profile of this patient parallels other cases of HRR-deficient PDAC. Case reports involving somatic or germline ATM mutations have documented favorable responses to platinum-based chemotherapy and PARP inhibitors, similar to BRCA-mutated phenotypes. The stabilization of disease seen in this patient aligns with literature suggesting that defects in ATM and BLM confer a synthetic lethality vulnerability that can be exploited clinically.

Future management for this patient, should progression occur, may involve clinical trials targeting DNA damage response pathways, such as those utilizing ATR inhibitors or antibody-drug conjugates [4,5].

Conclusion

This case emphasizes the value of germline and somatic testing in pancreatic cancer. The identification of BLM and ATM mutations provided a clear rationale for optimizing platinum-based therapy in an elderly patient with significant comorbidities.

Funding

The NIH grant number for Subhrajith Saha (co-author) is NIAID 5U01AI138323-05, NIAID 5U01AI170036-02.

References

1. World Health Organization. (2019). Classification of tumours of the digestive system. 5th ed. Lyon: IARC. Available from online.
2. Tempero MA, Malafa MP, Al-Hawary M, Behrman SW, Benson AB, et al. (2023). National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: Pancreatic adenocarcinoma. Version 2. 19: 439-457.
3. Cunniff C, Bassetti JA, Ellis NA. (2017). Bloom's syndrome: Clinical spectrum, molecular pathogenesis, and cancer predisposition. Molecular Syndromology. 8:4–23.
4. Fares F, Fares B, Fares J, et al. (2022). LINC01133 regulates the miR-30b-5p/BLM axis to control pancreatic cancer progression and tumor immune infiltration. Cancer Cell International.
5. Golan T, Kanji ZS, Epelbaum R, Devaud N, Dagan E, et al. (2014). Overall survival and clinical characteristics of pancreatic cancer in BRCA mutation carriers. British Journal of Cancer. 111: 1132-1138.
6. Li Q, Zhang P, Zhang YN, Hu HX, Yan JF, et al. (2023). Aberrant expression of BLM correlates with malignant progression and immune infiltration in pancreatic adenocarcinoma. Cancer Screening and Prevention. 2: 14-29.