

Development of Undifferentiated Pleomorphic Sarcoma and Autoimmune Complications Following SARS-CoV-2 Infection: A Case Report

Authors: Authors: K Patel, N Olson, R Nadkarni, D Naidu, S Niar, A Patel, C Bogan, S Ramaswamy, E Gillespie, M Sullivan, A Kodali, N Clinton, R Lozano, N Anandpura, H Taylor, S Naidu, N Nathwani, A Gor, V Rabara

Institutions: Carolina Blood and Cancer Care Associates, No One Left Alone, Community Clinical Oncology Research Network

Abstract

We present a case of a 73-year-old woman who developed undifferentiated pleomorphic sarcoma, leukocytosis, and autoimmune complications following consecutive SARS-CoV-2 infections. Previously healthy, she experienced back-to-back COVID-19 infections in December 2022, followed by arthritis, psoriatic changes, chronic fever, leukocytosis, and weight loss—features consistent with Long COVID. Imaging later revealed large retroperitoneal masses, pathologically confirmed as high-grade undifferentiated pleomorphic sarcoma. Despite resection, the disease recurred with multifocal peritoneal spread requiring chemotherapy. She subsequently developed autoimmune ulcerative colitis. This case suggests a possible link between SARS-CoV-2, immune dysregulation, malignancy, and autoimmunity, underscoring the importance of close monitoring in post-COVID patients with persistent inflammation.

Introduction

Long COVID is increasingly linked to persistent inflammation and immune dysregulation, with emerging evidence suggesting it may trigger or exacerbate autoimmune diseases. There is also growing interest in the connection between chronic inflammation, viral infections, and cancer development. Undifferentiated pleomorphic sarcoma (UPS) is a rare, high-grade soft tissue sarcoma with unclear etiology, though chronic inflammation may play a role. This report describes a case of UPS, leukocytosis, and autoimmune manifestations developing after consecutive SARS-CoV-2 infections, raising the possibility of a link between COVID-19, autoimmunity, and malignancy.

Case Presentation

A 73-year-old female with a past medical history of hypertension, hypothyroidism, and previous sacrocolpopexy presented to our institution. The patient had been in excellent health until December 2022, when she experienced two consecutive SARS-CoV-2 infections. Following these infections, she developed features of arthritis and psoriasis, along with leukocytosis, chronic fever, and unintentional weight loss. In April 2023, approximately four months after her COVID-19 infections, the patient presented to the emergency department with worsening lower back pain, abdominal pain, nausea, early satiety, and an unintentional weight loss of approximately 8 pounds. She had no prior history of malignancy or significant family history of cancer. Of note, her husband had also developed cancer following COVID-19 infection.

Investigations

Laboratory studies revealed significant inflammatory markers:

C-Reactive Protein: 172 mg/L (reference range: 0-10 mg/L) Procalcitonin: 0.16 ng/mL (reference range: 0.00-0.08 ng/mL) Interleukin-6: 34.5 pg/mL (reference range: 0.0-13.0 pg/mL) D-Dimer: 1.41 mg/L FEU (reference range: 0.00-0.49 mg/L FEU)

Computed tomography (CT) of the abdomen and pelvis revealed a 12.9 × 10.4 cm heterogeneous mass in the right abdomen, closely associated with the second and third portions of the duodenum and abutting the inferior aspect of the pancreatic head. An additional adjacent similar-appearing lesion measuring 6.2 × 4.7 cm was also noted.

Multiple biopsies were obtained through endoscopic ultrasound and percutaneous core needle approaches. Fine-needle aspiration of the duodenal mass revealed a high-grade malignant neoplasm consistent with pleomorphic sarcoma.

Next-generation sequencing identified a BCL2-SIGLEC15 fusion. Germline testing detected variants of uncertain significance in NF1 and FANCE genes.

Staging studies showed no evidence of distant metastatic disease within the chest, abdomen, or pelvis.

Differential diagnosis

The initial differential diagnosis for the abdominal masses included gastrointestinal stromal tumor, pancreatic neuroendocrine tumor, and metastatic lymphadenopathy. Following pathological examination, the diagnosis of high-grade undifferentiated pleomorphic sarcoma was established. Liposarcoma was considered in the differential but not confirmed by pathology.

Treatment:

On May 31, 2023, the patient underwent extensive surgery including resection of a large retroperitoneal mass, en bloc right hemicolectomy, Whipple procedure, vein resection with reconstruction, and cholecystectomy. Postoperative recovery was complicated by a minor pancreaticojejunostomy leak. She was discharged on June 8, 2023, with a drain, steroid taper, and apixaban. One month later, CT imaging showed rapid disease progression with new bulky peritoneal metastases. She then began combination chemotherapy with cyclophosphamide, vincristine, doxorubicin, and dacarbazine.

Outcome and Follow-Up:

Serial CT scans showed a progressive partial response to chemotherapy. By 6 weeks, tumor sizes had decreased notably, with continued shrinkage over 5 and 9 months. As of March 2025, the right upper quadrant nodule measured 9 × 5 mm and the pelvic mass 16 × 13 mm. Despite the favorable treatment response, the patient developed autoimmune ulcerative colitis, contributing to her ongoing post-COVID immune-related complications.

Discussion:

This case illustrates a temporal association between COVID-19 and the subsequent development of undifferentiated pleomorphic sarcoma, persistent leukocytosis, and autoimmune conditions (psoriasis and ulcerative colitis). The interplay of these events suggests a shared pathogenic foundation potentially triggered by SARS-CoV-2. Emerging evidence supports multiple biological mechanisms:

- Chronic Inflammation and Oncogenesis SARS-CoV-2 initiates a sustained inflammatory response—marked in this patient by elevated CRP (172 mg/L), IL-6 (34.5 pg/mL), and procalcitonin (0.16 ng/mL)—that can persist for months post-infection. This pro-inflammatory microenvironment, involving IL-6, IL-1β, TNF-α, and NF-κB, fosters tumorigenesis via enhanced angiogenesis, reduced apoptosis, and uncontrolled cell proliferation.
- Viral Oncogenesis Though not classically oncogenic, SARS-CoV-2 may promote cancer through: Epigenetic alteration of host genes Chronic inflammation Impairment of tumor suppressor pathways This "hit-and-run" oncogenesis model could explain delayed sarcoma development in our patient.
- Autoimmune Activation via Molecular Mimicry SARS-CoV-2 proteins share molecular motifs with host antigens, causing cross-reactivity and loss of immune tolerance. This likely contributed to our patient's autoimmune features, including psoriatic skin lesions and ulcerative colitis. Studies show mimicry between the spike protein and human peptides central to immune regulation.
- Immune Dysregulation and Surveillance Failure COVID-19 leads to exhaustion and dysfunction of immune cells, impairing the body's ability to eliminate emerging tumor cells. Persistent immune activation resembles conditions seen in chronic infections and cancer, potentially explaining the rapid disease onset in this case.
- Epigenetic Reprogramming Long-term COVID-19 effects include stable epigenetic changes—DNA methylation shifts, histone modifications, and altered transcription factors—which may predispose individuals to both cancer and autoimmune disorders. These changes persisted in hematopoietic stem cells up to a year post-infection in recent studies.
- The Disease Continuum This case supports the concept of a disease continuum, where shared immune pathways can lead to either: Excessive activation (autoimmunity) Immune evasion (cancer) The BCL2-SIGLEC15 fusion in this tumor is of interest: BCL2 inhibits apoptosis, while SIGLEC15 promotes immune suppression, potentially enabling tumor escape in a post-inflammatory setting.
- Cytokine Storm Sequelae The cytokine storm of severe COVID-19 leaves long-term immunological scars. Elevated IL-6 and other cytokines may prime tissues for malignant transformation or autoimmune dysregulation, especially in genetically susceptible hosts.

Clinical Implications

Surveillance: Patients with prolonged inflammatory symptoms post-COVID may require regular monitoring for both cancer and autoimmune conditions.

Therapeutic Considerations: Tumors arising post-COVID may respond well to conventional chemotherapy, as seen here. Anti-inflammatory agents, including IL-6 inhibitors, may help mitigate long-term complications.

Environmental and Genetic Context: The concurrent cancer diagnosis in the patient's husband raises questions about shared environmental exposures or genetic predispositions (e.g., NF1, FANCE variants).

Future Directions

Mechanistic Studies: Clarify how SARS-CoV-2 contributes to tumorigenesis and immune dysregulation.

Biomarker Development: Identify inflammatory or genetic markers predictive of post-COVID malignancies.

Epidemiology: Quantify the true incidence of cancer and autoimmunity following COVID-19.

Therapeutic Trials: Evaluate preventive or early-intervention strategies for high-risk post-COVID populations.

Conclusion

While causality cannot be confirmed, this case underscores a biologically plausible link between COVID-19 and subsequent malignancy and autoimmunity. It highlights the need for vigilance, early detection, and deeper investigation into the long-term sequelae of SARS-CoV-2 infection—particularly as millions globally continue to live with its aftermath.

References

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