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SMALL CELL LUNG CARCINOMA WITH CORONARY ARTERY DISEASE AND SUPERIOR VENA CAVA SYNDROME IN NON SMOKER, ELDERLY WOMAN PATIENT: A CASE REPORT

KARSINOMA SEL KECIL PARU-PARU DENGAN PENYAKIT ARTERI KORONER DAN SINDROM VENA KAVA SUPERIOR PADA PASIEN WANITA LANJUT USIA YANG TIDAK MEROKOK: LAPORAN KASUS

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ABSTRACT

Small cell lung carcinoma (SCLC) is an aggressive form of lung cancer typically associated with tobacco exposure; however, a subset of patients develops SCLC without a history of smoking. This case report describes an elderly non-smoking female with SCLC complicated by coronary artery disease and superior vena cava (SVC) syndrome treated at Wangaya General Hospital. The patient presented with progressive dyspnea, facial swelling, and productive cough. Thoracic computed tomography revealed a large right lung mass compressing both the superior and inferior vena cava, accompanied by pleural effusion. Histopathological examination confirmed SCLC. The patient also had underlying coronary artery disease and electrolyte disturbances. Clinical and imaging findings were consistent with advanced-stage disease (T4N3M1) complicated by SVC syndrome. This case highlights a non-smoker SCLC phenotype with vascular compression and cardiovascular comorbidity, suggesting potential oncogenic mechanisms beyond smoking exposure. The coexistence of coronary artery disease and SVC obstruction posed challenges in clinical management, emphasizing the importance of individualized treatment strategies. Non-smoker SCLC remains underrepresented in the literature despite its increasing incidence and distinct biological characteristics. In conclusion, non-smoking–related SCLC with concurrent cardiovascular disease and SVC syndrome presents significant diagnostic and therapeutic challenges, and further documentation is essential to improve clinical understanding and guide future management approaches.
***Keywords**: Small cell lung carcinoma, non-smoker risk factors, coronary artery disease, superior vena cava syndrome.*

ABSTRAK

Karsinoma sel kecil paru (SCLC) adalah bentuk kanker paru yang agresif yang umumnya dikaitkan dengan paparan tembakau; namun, sebagian kecil pasien mengalami SCLC tanpa riwayat merokok. Laporan kasus ini menguraikan seorang wanita lanjut usia non-perokok dengan SCLC yang disertai penyakit arteri koroner dan sindrom vena kava superior (SVC) yang dirawat di Rumah Sakit Umum Wangaya. Pasien datang dengan keluhan sesak napas yang semakin parah, pembengkakan wajah, dan batuk berdahak. Computed tomography (CT) toraks menunjukkan adanya massa besar di paru kanan yang menekan vena cava superior dan inferior, disertai efusi pleura. Pemeriksaan histopatologi mengonfirmasi SCLC. Pasien juga memiliki penyakit arteri koroner dan gangguan elektrolit. Temuan klinis dan pencitraan konsisten dengan penyakit stadium lanjut (T4N3M1) yang disertai sindrom vena cava superior. Kasus ini menyoroti fenotipe SCLC pada non-perokok dengan kompresi vaskular dan komorbiditas kardiovaskular, yang mengindikasikan mekanisme onkogenik potensial di luar paparan asap rokok. Koeksistensi penyakit arteri koroner dan obstruksi vena kava superior (SVC) menimbulkan tantangan dalam pengelolaan klinis, yang menekankan pentingnya strategi pengobatan yang disesuaikan secara individual. Karsinoma sel kecil (SCLC) pada non-perokok masih kurang terwakili dalam literatur meskipun insidensinya meningkat dan memiliki karakteristik biologis yang khas. Kesimpulannya, SCLC pada non-perokok yang disertai penyakit kardiovaskular dan sindrom vena kava superior (SVC) menghadirkan tantangan diagnostik dan terapeutik yang signifikan, dan dokumentasi lebih lanjut sangat penting untuk meningkatkan pemahaman klinis serta menjadi panduan bagi pendekatan pengelolaan di masa mendatang.

Kata kunci: Karsinoma sel kecil paru, faktor risiko pada non-perokok, penyakit arteri koroner, sindrom vena cava superior.

INTRODUCTION

Globally, lung carcinoma remains the primary driver of oncological mortality across both sexes, responsible for nearly 25% of all cancer-related fatalities (Siegel et al., 2024). Within Indonesia, it is the third most frequently diagnosed malignancy following breast and cervical cancers and stands as the leading cause of cancer mortality among the male population. Epidemiological data from 2020 reported 34,783 newly identified lung cancer cases in Indonesian men, comprising roughly 14.1% of the total cancer incidence (Globocan, 2020).

From a histopathological standpoint, pulmonary malignancies are broadly categorized into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). While NSCLC constitutes the majority of cases and encompasses subtypes like adenocarcinoma, squamous cell, and large cell carcinomas, SCLC makes up a narrower fraction of the disease burden but is distinguished by highly aggressive clinical behavior (Miller & Hanna, 2022).

The pathogenesis of SCLC is fundamentally tied to impaired DNA repair pathways. Frequent genetic aberrations include the loss of function in critical tumor suppressor genes, namely TP53 and RB1, alongside structural deletions on the short arm of chromosome 3 (3p) affecting the FHIT gene (George et al., 2015). Tobacco exposure is undeniably the most profound risk factor, contributing to roughly 85% of all documented SCLC cases (WHO, 2023).

Morphologically and clinically, SCLC typically arises within the central bronchial airways and demonstrates explosive proliferation, characterized by an elevated mitotic index and a brief tumor doubling time. Patients frequently experience a sudden onset of symptoms just 8 to 12 weeks prior to formal diagnosis. These clinical signs range from pulmonary issues like hemoptysis, chronic cough, and wheezing to manifestations of local mass effect, such as superior vena cava (SVC) syndrome. Furthermore, systemic complaints including severe fatigue, anorexia, pain, and neurological deficits are widely prevalent. At the time of initial presentation, approximately 60% of individuals already harbor distant metastases, predominantly affecting the liver, brain, bone marrow, adrenal glands, and skeletal system (Molina et al., 2008). Left untreated, the median life expectancy for this disease drops precipitously to just two to four months.

Notably, SCLC is recognized for its strong association with paraneoplastic syndromes. These conditions arise from immunomodulatory responses or the ectopic secretion of hormones by the solid tumor itself, frequently manifesting as the syndrome of inappropriate antidiuretic hormone secretion (SIADH), Lambert-Eaton myasthenic syndrome, or ectopic Cushing syndrome (Sabari et al., 2020).

Definitive diagnosis relies strictly on pathological or cytological evaluation of tissue samples, which are generally secured via bronchoscopy or CT-guided biopsies. Comprehensive clinical staging and therapeutic formulation necessitate a battery of investigations, including basic laboratory panels, conventional chest radiography, contrast-enhanced computed tomography (CT) of the chest and abdomen, positron emission tomography (PET-CT), and magnetic resonance imaging (MRI) of the brain (ESMO, 2021). Therapeutic interventions are inherently stage-

dependent. While individuals presenting with limited-stage disease may undergo potentially curative regimens involving concurrent chemoradiotherapy, those with extensive-stage SCLC typically require systemic chemotherapy, targeted radiation, and appropriate palliative care measures (NCCN, 2024).

This case report details the clinical trajectory of a patient admitted to Wangaya General Hospital with small cell lung carcinoma, further complicated by superior vena cava syndrome and concurrent coronary artery disease. We comprehensively review the diagnostic workup, symptomatology, and the clinical rationale guiding the patient's management. Notably, the subject is a never-smoker presenting with substantial cardiovascular risk a unique demographic that remains insufficiently documented in contemporary oncological literature. By detailing this specific presentation, this report seeks to shed light on potential oncogenic pathways in non-smokers and offer practical clinical perspectives to guide future therapeutic protocols and research initiatives.

RESEARCH METHODS

This study employed a descriptive observational design using a case report approach to present the clinical findings, diagnostic process, and management of a patient diagnosed with small cell lung carcinoma (SCLC) at Wangaya Regional General Hospital, Denpasar, Bali, Indonesia.

The subject of this study was a single patient who met the clinical and pathological criteria for SCLC, complicated by superior vena cava syndrome and concomitant coronary artery disease. Data were collected retrospectively from the patient's medical records, including demographic characteristics, clinical presentation, physical examination findings, laboratory results, imaging studies, histopathological reports, and therapeutic interventions.

Diagnostic evaluation was conducted through a comprehensive clinical workup, including thoracic imaging (contrast-enhanced computed tomography scan), laboratory examinations, electrocardiography, echocardiography, and histopathological confirmation via CT-guided lung biopsy. Disease staging was determined according to the American Joint Committee on Cancer (AJCC) staging system.

Data analysis was performed qualitatively by systematically describing the patient's clinical course and comparing findings with existing literature on SCLC, particularly in non-smoking populations. This approach aimed to identify unique clinical features, potential non-smoking-related risk factors, and challenges in management.

Ethical considerations were maintained by ensuring patient confidentiality and anonymity. All identifying information was removed, and the case was reported solely for academic and scientific purposes in accordance with institutional and ethical guidelines.

RESULTS AND DISCUSSIONS

The subject of this report is a 75-year-old female who sought clinical evaluation for dyspnea that had progressively worsened over the preceding month, accompanied by a productive cough yielding tenacious, yellowish sputum. Additional intermittent complaints included palpitations, epigastric discomfort, ancomorbidpain, alongside a noticeable decline in oral intake and appetite. Her past medical history was notable for a prior total thyroidectomy,

gastroesophageal reflux disease (GERD), and underlying coronary disease awaiting elective cardiac catheterization. Crucially, her social history was entirely negative for both active tobacco use and passive smoke exposure.

Classic presentations of small cell lung carcinoma (SCLC) predominantly involve males in their eighth decade of life, characterized by rapid clinical deterioration emerging within an 8- to 12-week window. While this patient's age aligns with established epidemiological profiles, her gender and strict non-smoking status represent a notable clinical divergence. Tobacco consumption is the primary oncogenic driver in roughly 85% of SCLC diagnoses, though environmental exposures to asbestos, radon, and secondhand smoke are also well-documented risks (Basumallik & Agarwal, 2023). Nevertheless, contemporary epidemiological analyses underscore a shifting paradigm, revealing a rising incidence of SCLC among elderly, never-smoking females (Zhang et al., 2021). To better comprehend this evolving demographic, experts increasingly advocate for multi-omics evaluations to isolate actionable molecular alterations and refine precision therapeutics (Gazdar, 2018).

Patients lacking a smoking history typically present with more advanced SCLC pathology; extensive-stage disease is observed in 68% of never-smokers at initial diagnosis, compared to 52% in their smoking counterparts (Ito et al., 2020). The aggressive nature of her disease is evidenced by extensive regional lymphadenopathy and a substantial 11.8 cm primary lesion. Such late-stage presentations are frequently attributed to diagnostic delays, as SCLC is rarely the primary clinical suspicion in tobacco-naïve individuals (Powell et al., 2019). Furthermore, the physical findings of wheezing, fine crackles, and a concomitant pleural effusion align with literature indicating that non-smoking SCLC variants frequently generate obstructive pulmonary symptoms secondary to massive tumor burden (Zhou et al., 2022).

Despite the absence of tobacco exposure, the patient's comorbid GERD presents a compelling pathophysiological mechanism. Chronic microaspiration, prevalent in GERD, can trigger pro-carcinogenic pulmonary inflammation driven by IL-8 and TNF-α mediated pathways (Lagergren et al., 2022). Consequently, meta-analyses suggest GERD elevates lung cancer risk by a factor of 1.89, with a particularly robust association for neuroendocrine subtypes like SCLC (Nieto et al., 2021). A history of recurrent pneumonia (≥2 episodes) further amplifies SCLC susceptibility by 1.5-fold (Koshiol et al., 2021). Additionally, persistent oxidative damage inherent to conditions like chronic obstructive pulmonary disease (COPD) multiplies the risk in non-smokers by 3.2 (Durham et al., 2023).

Her previous total thyroidectomy also introduces significant endocrine variables. Population data indicate that hypothyroid individuals have a 1.4-fold increased vulnerability to lung cancer, with the risk for SCLC climbing to a hazard ratio of 1.72 (Kitahara et al., 2022). At the mechanistic level, an absence of thyroid hormone downregulates thyroid hormone receptor beta, thereby disrupting the regulatory proliferation of pulmonary neuroendocrine cells (Kim et al., 2023). Furthermore, metabolic syndromes, notably type 2 diabetes, have been linked to a 1.3-fold increase in SCLC incidence among non-smokers (Tsilidis et al., 2021). The patient's presentation with electrolyte disturbances (hypokalemia and hyponatremia) is highly indicative of

the paraneoplastic syndrome of inappropriate antidiuretic hormone secretion (SIADH), which manifests in 38% of non-smoking SCLC cohorts compared to just 24% of smokers (Fan et al., 2022).

Genetic predisposition plays a critical role in non-smoking SCLC pathogenesis. Genome-wide association studies have identified polymorphisms in specific DNA repair pathways, notably the XPC and ERCC2 genes, which augment susceptibility by 2.3 to 4.1 times in tobacco-naïve individuals (Chen et al., 2020). Modern next-generation sequencing reveals that non-smokers exhibit unique genomic signatures, including an elevated frequency of NOTCH pathway mutations (27% vs. 8% in smokers) and a comparative reduction in TP53 mutations (62% vs. 89%) (George et al., 2022). This patient's tumor pathology mirrors data showing that non-smokers experience higher rates of RB1 loss (94% vs. 71%) and prominently display neuroendocrine differentiation markers (Rudin et al., 2021). Additionally, altered HIF-1α signaling resulting from thyroid hormone deficiency may facilitate accelerated tumor progression, offering a potential explanation for the aggressive clinical course observed in this thyroidectomized individual (Martinez-Iglesias et al., 2023).

The presence of coronary artery disease (CAD) in this clinical scenario requires meticulous management. Cardio-oncology research warns that pre-existing CAD heightens the risk of chemotherapy-induced cardiac toxicity by 2.1-fold (Lyon et al., 2021). Fortunately, her robust ejection fraction (73.5%) confers a degree of cardioprotection; an EF exceeding 70% has been shown to curtail adverse cardiac events by 31% during platinum-based chemotherapy (Gulati et al., 2022). Regarding her hematological profile, the moderate anemia (Hb 9.8–9.9 g/dL) is presumably a consequence of cancer-related chronic inflammation, supported by findings that interleukin-6 concentrations inversely correlate with hemoglobin metrics in non-smoking SCLC patients (Zhang et al., 2023).

The phenotypic expression of SCLC heavily relies on the primary tumor's spatial distribution. While most patients report acute respiratory symptoms (dyspnea, hemoptysis, wheezing, cough) emerging 8 to 12 weeks prior to discovery, symptoms resulting from invasive local spread, such as Superior Vena Cava Syndrome (SVCS), are also documented (Basumallik & Agarwal, 2023). This patient presented without hemoptysis but exhibited definitive clinical signs of SVCS.

Occurring in 10–15% of SCLC cases, SVCS is a true oncological emergency indicative of an aggressive predilection for mediastinal infiltration (Wilson et al., 2020). Up to 90% of affected individuals display the classic clinical triad: collateral vein distension, facial swelling, and dyspnea (Matos et al., 2019). SCLC accounts for 50–60% of all malignancy-induced SVCS, primarily through direct extrinsic vascular compression by the rapidly proliferating mass, though cancer-induced hypercoagulability and subsequent intraluminal thrombosis can also play a role (Ito et al., 2020; Zhang et al., 2021). Diagnosis is typically confirmed in approximately 95% of cases via CT venography, which maps collateral pathways and pinpoints the venous obstruction. Extraordinarily, imaging in this patient revealed concurrent compression of both the superior and inferior vena cava by the right lung mass—a dual involvement rarely described in the medical literature

(Powell et al., 2019; Basumallik & Agarwal, 2023).

Therapeutic prioritization in SVCS demands immediate palliation of symptoms. Endovascular stents can alleviate venous obstruction in up to 92% of cases within 48 hours; implementing this before initiating chemotherapy diminishes symptomatic recurrence by roughly 40% compared to chemo-first strategies (Matos et al., 2019; Wilson et al., 2020). For SCLC-mediated SVCS, definitive therapy involves platinum-based chemotherapy paired with etoposide, yielding 70–80% response rates and median clinical improvement within 7 to 10 days (Zhang et al., 2021). Furthermore, integrating chemo-immunotherapy combinations (e.g., atezolizumab plus platinum-etoposide) has extended the one-year survival metric to roughly 53%, a marked improvement from the 30% observed with chemotherapy alone (Ito et al., 2020).

Nevertheless, overall outcomes remain poor. Advanced-stage SCLC complicated by SVCS, particularly in the presence of T4N3M1 disease or adverse prognostic features, typically yields a median survival of merely 6 to 12 months (Powell et al., 2019). Significant clinical knowledge gaps persist, including a lack of randomized trials optimizing the sequence of stenting versus systemic therapy, a deficit in predictive biomarkers for immunotherapy efficacy specifically in SVCS patients, and a historical underrepresentation of non-smokers in research despite their growing incidence (Gazdar, 2018; Zhou et al., 2022; Basumallik & Agarwal, 2023).

This case specifically highlights how non-smoking SCLC—especially in elderly patients with concurrent cardiovascular morbidities—may follow a distinctly different biological trajectory. Such phenotypes implicate alternative drivers, including potential genetic susceptibility, hormonal dysregulation, and chronic inflammatory states (Wiguna et al., 2025). The tendency for late presentation, severe progression, limited therapeutic windows due to CAD, and the highly unusual simultaneous compression of both vena cavae emphasize the urgent need for personalized management protocols tailored to the unique biological characteristics of tobacco-naïve SCLC populations (Basumallik & Agarwal, 2023; Wiguna et al., 2025).

Definitive diagnosis in this case was achieved through a multimodal synthesis of laboratory, pathological, and radiological data. CT imaging demonstrating venous obstruction and extensive mediastinal lymphadenopathy perfectly aligns with typical imaging phenotypes for SCLC-associated SVCS. This corroborates radiogenomic analyses indicating that non-smoker SCLC exhibits more frequent pulmonary venous invasion (42% vs. 28%) and intense metabolic activity (SUVmax >10) on PET-CT (Park et al., 2021). The presence of a right pleural effusion is also compatible with malignant spread; proteomic profiling of effusions in non-smoker SCLC has demonstrated elevated VEGF and IL-8, suggesting a strongly pro-angiogenic and inflammatory microenvironment (Wang et al., 2020).

The patient's mild leukocytosis ($11.8 \times 10^3/\mu L$) likely reflects tumor-associated inflammation rather than isolated infection. In non-smoking SCLC cohorts, an elevated neutrophil-to-lymphocyte ratio (>3.5) is associated with more aggressive tumor biology and poorer survival (Sonehara et al., 2022). Histopathological confirmation via percutaneous needle biopsy of the right lung mass revealed the classic

cytomorphologic hallmarks of SCLC: clusters of small to medium-sized cells possessing hyperchromatic nuclei, scant cytoplasm, and an absence of squamous or glandular differentiation. Combined with radiographic evidence, these features fulfill current SCLC diagnostic criteria.

Applying the AJCC TNM staging system, the malignancy was classified as T4N3M1 (extensive disease) based on the substantial 11.8 × 8.5 × 12.8 cm primary mass in the right middle lobe, which caused partial obstruction of the right pulmonary vein and compressed both the superior and inferior vena cava, alongside widespread nodal and distant extension. The clinical picture was compounded by a right pleural effusion, pneumonia, moderate anemia, electrolyte disturbances (hyponatremia, hypokalemia, hypochloremia), left-convex thoracolumbar scoliosis, CAD with ischemia and preserved ejection fraction, and established SVCS characterized by upper limb edema and collateralized chest wall veins.

These diagnostic elements align with recent clinical evidence suggesting non-smoker SCLC represents a distinct biological subtype. This subgroup demonstrates heightened susceptibility to immune checkpoint inhibitors (hazard ratio 0.62 vs. 0.81 in smokers), possibly due to alternative carcinogen-driven mutational signatures (Horn et al., 2023). Conversely, her advanced age (>75 years) introduces a 38% increased risk of severe immunotherapy-related toxicity (Schneider et al., 2021), and the presence of hyponatremia significantly raises the concern for heightened cisplatin nephrotoxicity risk during systemic therapy (Perazella et al., 2022). Balancing these considerations is crucial for therapeutic planning in complex, comorbid non-smoker SCLC populations such as the one described here.

Figure 1. American Joint Committee on Cancer (AJCC) criteria

Despite advances in SCLC research, critical knowledge deficits remain particularly regarding non-smoker phenotypes. The precise mechanisms behind their increased tendency for venous invasion remain unclear, as does the influence of comorbid endocrine conditions (e.g., hormone replacement or thyroid dysfunction) on tumor progression and behavior (Pillai et al., 2023). Likewise, the exact contribution of chronic inflammation such as IL-17A signaling associated with GERD to SCLC initiation in tobacco-naïve patients remains insufficiently defined (Song et al., 2021). These uncertainties highlight the need for prospective multi-omics studies designed to characterize the molecular drivers in non-smoker SCLC and identify novel targets for personalized therapy (Gazdar et al., 2022). By documenting this case of non-smoking SCLC complicated by profound vascular invasion and cardiovascular comorbidity, this report reinforces the imperative to recognize alternative risk pathways beyond tobacco exposure and supports the urgency of further mechanistic investigation within this underrepresented subgroup.

CONCLUSION AND SUGGESTION

The clinical trajectory of this tobacco-naïve patient complicated by concurrent coronary artery disease and superior vena cava syndrome demonstrates that fulminant small cell lung carcinoma can develop entirely independent of smoking, presumably fueled by alternate oncogenic drivers. Furthermore, the profound degree of venous infiltration combined with the patient's intricate comorbidities reinforces an emerging consensus: SCLC in non-smokers likely constitutes a wholly distinct molecular and clinical entity. Ultimately, by detailing this atypical presentation, this report underscores the critical necessity for heightened clinical vigilance regarding non-tobacco-related risk factors. It concurrently emphasizes the urgency of deploying sophisticated molecular and multi-omics profiling to optimize the classification, prognostication, and therapeutic management of this historically marginalized patient demographic.

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