Xeroderma Pigmentosum in Association with Spindle Cell Carcinoma- A Case Report

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Statement of Contribution

The authors collectively contributed to this project with distinct roles and expertise. Bibek Shrestha played a central role in the conceptualization, data curation, formal analysis, methodology, project administration, original writing, review, editing, and visualization. Pradeep Shrestha provided resources, supervision, validation, conceptualization, investigations, and data curation. Dhiraj Adhikari and Sudip Bastakoti both contributed to supervision, validation, and investigations. Each author's contribution was integral to the project's success, ensuring the accuracy and reliability of the findings presented in this work.

S. N	Name	Contribution
1	Bibek Shrestha	Conceptualization, data curation, formal analysis, methodology, project administration, original
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3	Dhiraj Adhikari	Supervision, validation, and investigations.
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ABSTRACT

Xeroderma Pigmentosum is a rare autosomal recessive disorder characterized by UV sensitivity, leading to skin malignancies, ophthalmologic issues, and neurological symptoms. Few cases have reported its association with lung cancer. A 22-year-old male with Xeroderma Pigmentosum presented with a 6-month history of non-productive cough, haemoptysis, fever, and shortness of breath. Examination revealed cervical lymphadenopathy, hypo- and hyperpigmented macules, and focal seizures. Blood tests indicated elevated leukocytes, ESR, and alkaline phosphatase. Imaging and biopsy confirmed spindle cell carcinoma. Neurological evaluation diagnosed focal seizures, managed with carbamazepine. Palliative care was chosen due to advanced cancer. This is the first documented case linking XP with spindle cell carcinoma and focal seizures. Palliative care was chosen due to disease progression and financial condition.

Key clinical message

Xeroderma Pigmentosum significantly increases the risk of developing skin and internal malignancies, with rare associations such as spindle cell carcinoma. Patients with XP may present with atypical symptoms

like cough, haemoptysis, and shortness of breath, which should prompt further investigation for potential malignancies. Additionally, neurological symptoms like focal seizures can occur alongside malignancies, complicating the clinical presentation and management. Early detection and treatment are crucial, but in advanced cases, palliative care may be necessary due to limited treatment options and the progressive nature of the disease.

Key words

DNA Damage; Xeroderma Pigmentosum; Ultraviolet rays.

Introduction

Xeroderma Pigmentosum is an uncommon genetic condition that is characterized by sensitivity to ultraviolet rays, ultimately leading to severe sunburn reactions and increased risk of skin cancer (1). Patients require stringent photoprotection measures, including sunscreen application and protective clothing (2). The clinical manifestations include hypo and hyperpigmented macules, premature aging, sunburns, blistering, and increased incidence of different malignancies in the skin. It also affects the eye and central nervous system (3). Patients involved in the eye can experience progressive blindness (6). A complex relationship exists between Xeroderma Pigmentosum and other malignancies, which is poorly understood (2). Priya and Janaki (2017) reported rare cases of carcinoma of the esophagus associated with xeroderma pigmentosum (4). Though susceptible to different cancers, few cases have been reported till now due to its rare nature (5). There is an association with neurological symptoms in 20 % of cases (6). Herein, we present the case of a 22-year-old male diagnosed with Xeroderma Pigmentosum who developed Spindle Cell Carcinoma and experienced focal seizures. This case report is the first documented case associating Xeroderma Pigmentosum, Spindle Cell Carcinoma, and focal seizures.

Case History/ Examination

A 22-year-old male nonalcoholic and nonsmoker with a known history of Xeroderma Pigmentosum diagnosed at six months of age presented to the hospital with chief complaints of a non-productive, intermittent cough for six months, accompanied by episodes of hemoptysis, intermittent fever, and shortness of breath of the same duration. The patient was in his usual state of health until six months ago when he developed a non-productive, intermittent cough associated with shortness of breath and left-sided chest pain. Additionally, he reported intermittent fever, with the highest recorded temperature of 102°F, accompanied by chills and rigors. He also had jerky movements on the upper limb at night for a few minutes, mainly during sleep. He had 4-5 jerky movements till now. His medical history was notable for cicatricial ectropion with corneal opacity and neovascularization, for which he underwent eye surgery ten years ago. On examination, the patient appeared ill and had cachexia but had no pallor, icterus, lymphadenopathy, cyanosis, clubbing, or signs of dehydration. His vital signs were heart rate of 80 beats per minute, respiratory rate of 18 breaths per minute, blood pressure of 110/70 mmHg, temperature of 98°F, and SpO2 of 98% on the right arm. He had level II right cervical lymphadenopathy, which was palpable (1X1 cm) and tender. His skin exhibited generalized hypo and hyperpigmented macules all over the body. Chest examination revealed crackles and decreased air entry on the left side. Cardiovascular examination showed normal heart sounds (S1 and S2), and the central nervous system examination was unremarkable.

Methods

Potential cardiac and pulmonary pathologies were considered for further diagnostic workup, including infective endocarditis, mediastinal mass, and lung or intrathoracic malignancy. These conditions were evaluated as part of the differential diagnosis. Blood investigations were sent, and Hemoglobin was found to be 11.78 g/dL (normal range: 13–18 g/dL), total leukocyte count was elevated at 22,550 cells/μL (normal range: 4,000–11,000 cells/μL), with a differential count showing neutrophils at 81% (normal range: 45–75%) and lymphocytes at 8% (normal range: 25–45%). The erythrocyte sedimentation rate (ESR) was significantly elevated at 80 mm/hr (normal range: 0–12 mm/hr), but C-reactive protein was in the normal range. The platelet count was 236,100 cells/μL (normal range: 150,000–400,000 cells/μL). Prothrombin time (PT) was prolonged at 18 seconds (normal range: 11–14 seconds). Serum sodium was slightly low at 132 mEq/L (normal range: 135–145 mEq/L), and serum potassium was notably reduced at 2.9 mEq/L (normal range: 3.5–5.2 mEq/L). Blood Sugar level was in the normal range and was 77 mg/dl (Normal range: 74-130 mg/dl); hsTroponin I was significantly high and was 2904 pg/ml (standard: less than 12 is negative). The patient's liver function test results were as follows: total protein was 6.4 g/dL (reference range: 6.4–8.2 g/dL), total bilirubin was 0.8 mg/dL (reference range: 0–1.1 mg/dL), direct bilirubin was 0.4 mg/dL (reference range: 0.0–0.4 mg/dL), alanine transaminase (ALT) was 34 U/L (reference range: 0–50 U/L), aspartate aminotransferase (AST) was 43 U/L (reference range: 0–45 U/L), alkaline phosphatase was elevated at 462 U/L (reference range: 40–140 U/L), and serum albumin was slightly low at 3.3 g/dL (reference range: 3.8–4.9 g/dL). Electrocardiography was sent and told to have sinus rhythm along with left atrial abnormality and left fascicular block. (Figure 1) Echocardiography revealed multiple hyperechoic, hypermobile large mass (17x15 mm) attached to left ventricle suggestive of embolized tumor mass. After ruling out other pathologies based on the patient's history, physical examination, and initial investigations, intrathoracic malignancy became the leading suspicion. An ultrasound of the abdomen and pelvis was performed, revealing a mass in the left lower lobe of the lung. To further confirm the diagnosis, a multi-detector computed tomography (MDCT) scan was conducted, which demonstrated a mildly heterogeneously enhancing hypodense lesion in the left lower lobe, suggestive of a malignant lung mass. Additionally, the MDCT identified metastatic lymph nodes and mild pleural effusion. Ultrasound-guided Tru-cut needle biopsy was sent from the left lung mass, and it revealed multiple cores of necrotic tissues composed of small areas of the viable tumor with a sheet of fascicles of spindle cells with a diagnosis of Spindle cell Tumor.

Conclusion and results

To manage the patient's skin condition, strict sun avoidance was recommended. Black goggles were prescribed for ocular protection to mitigate the risk of UV-ray-induced damage. Additionally, following a neurological consultation, the patient was diagnosed with focal seizures and initiated on Carbamazepine 200 mg, to be taken once daily. Palliative care was chosen by the patient. To prevent pulmonary edema in lung run due to lung cancer, Furosemide and Spironolactone twice a day for seven days were given. For chest pain and to prevent further hypertension, Metoprolol 25 mg twice a day was advised. Rivaroxaban 20 mg once a day per oral was advised to reduce thrombosis risk in the future.

Discussion

Xeroderma Pigmentosum is an unusual autosomal recessive genetic skin condition caused by nucleotide excision repair mutations or DNA Damage. Severe photosensitivity in Ultraviolet rays, skin pigmentary changes, malignant tumor formation, and, on rare occasions, progressive neurologic deterioration distinguish the illness. Patients may also exhibit oral, ophthalmologic, and neurologic signs of the condition (7). Patients with Xeroderma Pigmentosum have congenital abnormalities in the deoxyribonucleic acid (DNA) damage

repair system, which makes their skin very vulnerable to UV exposure (5). Though rare, Xeroderma Pigmentosum can be associated with Lung malignancy. Lung cancer in XP patients is caused by the carcinogen benzo(a)pyrene binding to their DNA, which is caused by defective DNA damage repair mechanisms (8). When associated with lung cancer, common symptoms include cough, wheezing, dyspnea, and hemoptysis (9). In this case, we present a case of a 22-year-old male with a known history of Xeroderma Pigmentosum who came with a nonproductive cough associated with hemoptysis, intermittent fever, and shortness of breath. Blood parameters have emerged as significant prognostic factors in lung cancer patients. There can be deranged lymphocyte count, platelet count, albumin level, and other inflammatory markers (10). Metastasis can further derange other blood markers, including thyroid and liver function tests, depending upon the organ it invades. In this, total leukocyte count, neutrophils, erythrocyte sedimentation rate (ESR), prothrombin time, and alkaline phosphatase were found to be increased. Non-small cell lung cancer has various histological subtypes and treatment approaches (12). One of the non-small cell lung cancers is Spindle Cell Carcinoma. This is the first case report associated with Spindle cell carcinoma and xeroderma pigmentosum. Spindle cell carcinoma is an aggressive and unusual form of lung cancer, representing only 0.2-0.3% of primary pulmonary cancers (11). In a study of lung tumors, spindle cell carcinoma was among the rarer, with squamous cell carcinoma being the most common. It can metastasize to the brain, causing neurological symptoms such as vertical one-and-a-half syndrome. Endobronchial biopsy findings reveal that squamous cell carcinoma is the most common centrally arising lung tumor, followed by small cell carcinoma and adenocarcinoma, with spindle cell carcinoma being relatively uncommon (11). Endoscopic ultrasound-guided biopsy has emerged as a valuable alternative to conventional biopsy methods for various tissues. Endoscopic and ultrasound-guided biopsies are effective techniques for diagnosing lung cancer and mediastinal lymphadenopathy (13). In this case, the patient underwent an endoscopic ultrasound-guided trust biopsy of left lung mass, and it revealed multiple cores of necrotic tissues composed of small areas of the viable tumor with a sheet of fascicles of spindle cells with a diagnosis of Spindle cell Tumor. Multi-detector computed tomography (MDCT) has shown promise in lung cancer screening and diagnosis. MDCT and its post-processing techniques can accurately detect primary trachea and central bronchus tumors, providing crucial information for surgical treatment (15). Recent studies have highlighted the significance of electrocardiogram (ECG) changes in non-small-cell lung cancer (NSCLC) patients. Specific ECG abnormalities, such as increased ventricular rate, QRS voltage decrease, ST-segment depression, and new atrial fibrillation, were associated with higher mortality within three months in NSCLC patients compared to controls (14). In this, the patient had sinus rhythm, left atrial abnormality, and left fascicular block with average QRS voltage and ST segment. The main treatments for lung cancer include surgery, chemotherapy, radiotherapy, and immunotherapy, often used in combination as multimodality therapy (16). While survival is a primary goal, patients and caregivers also prioritize quality of life and functionality when defining treatment success (17). Treatment decisions should consider factors such as expected performance status, toxicity, and hospitalization rates (18). For Spindle cell Lung Cancer, first-line treatment typically involves platinum-based chemotherapy, with the addition of immunotherapy agents like atezolizumab or durvalumab in some cases (18). However, due to expensive chemotherapy and immunotherapy, the patient was under palliative care with different medications. The limitation of the research is that this study could not track the effectiveness of cancer therapy, which includes platinum-based chemotherapy and immunotherapy, due to the patient chosen palliative care; however, this case report has highlighted the critical association between xeroderma pigmentosum and spindle cell carcinoma and tracked the diagnostic and treatment approach.

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Images

Figure 1: Electrocardiography showing sinus rhythm, posterior left atrial abnormality and left anterior fascicular block

Declerations

1. Ethics approval and consent to participate: The Institutional Review Board of the Institute of Medicine, Nepal, does not mandate ethical approval for the writing or publication of case reports, and patient consent was obtained. Informed written consent was obtained from the patient before writing this case report.
2. Consent for publication: Informed written consent was obtained from the patient for the publication of this case report in a scientific journal.
3. Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.
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