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# Epidermoid skin cancer a in patient with scleroderma

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Scleroderma (systemic sclerosis; Ssc) is a chronic, idiopathic autoimmune/inflammatory disease that is characterised with fibrosis of skin, blood vessels and visceral organs of the body, particularly gastrointestinal system, heart and kidneys. Because it is rare and clinically heterogen, the pathogenesis of the disease is still not completely clarified. Characteristics of Ssc's pathogenesis include triade of vasculopathy, immune activation and fibrosis. There is an increased risk of malignancy of internal organs and tissues which are affected from fibrosis. Patients have increased frequency of skin, lung, esophagus, breast cancer and lymphoma. Recent studies that particularly focus on vascular pathology and lung involvement provided benefits on morbidity and mortality and increased interest to the disease. The aim of this case report is to point at the vital consequences of scleroderma coexisting with malignity.

**Keywords:** Malignity – scleroderma - autoimmune diseases

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## СКЛЕРОДЕРМИЯСЫ БАР НАУҚАСТАРДАҒЫ ЖАЛПАҚЖАСУШАЛЫ ТЕРІ ОНЫ

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Склеродермия (жүйелі склероз, ЖС), бұл терінің, қантамырлардың зақымдалуымен, әсіресе висцеральды мүшелердің, оның ішінде асқазан-ішек жолдарының, сонымен қатар жүрек пен бүйректің фиброзды зақымдалуымен сипатталатын этиологиясы белгісіз, созылмалы аутоиммунды/қабыну ауруы. Аурудың клиникалық көріністерінің гетерогенды болуы және өте сирек кездесуіне байланысты патогенезі әлі де белгісіз болып отыр. Алайда, қазіргі таңда ЖС патогенезі васкулопатиялар, иммундық жүйенің белсенділігі мен фиброздан тұратын үштігі ретінде қабылдануда. Фиброзға ұшыраған мүшелер мен тіндерде қатерлі ісіктердің даму қаупі артуда. Әсіресе тері, өкпе, өңеш зақымданулары, сүт безі обыры және лимфомалардың кездесу жиілігі артып келеді. Соңғы жылдары өкпе зақымдалуы мен васкулопатиялардың патологиясын анықтау мақсатында жүргізілген ғылыми-зерттеу жұмыстарының нәтижелері аурудың кездесу жиілігі мен өлім-жітім көрсеткіштеріне оң әсерін тигізді және осы ауруға деген қызығушылықтың артуына себепкер болды.

Берілген клиникалық жағдайды сипаттаудың негізгі мақсаты: склеродермиямен бірге кездесетін қатерлі ісіктің болжамын талдау.

**Маңызды сөздер:** қатерлі ісік - склеродермия - аутоиммунды аурулар

## ПЛОСКОКЛЕТОЧНЫЙ РАК КОЖИ У ПАЦИЕНТОВ СО СКЛЕРОДЕРМИЕЙ

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Склеродермия (системный склероз, СС), это хроническое аутоиммунное/воспалительное заболевание неизвестной этиологии. СС характеризуется поражением кожи и кровеносных сосудов. При СС особенно часто поражаются висцеральные органы, в частности желудочно-кишечный тракт. Также встречается фиброзное поражение сердца и почек. Из-за редкой встречаемости и гетерогенности со стороны клиники, патогенез заболевания до сих пор неизвестен. Однако в наше время патогенез СС воспринимается как триада поражения, состоящая из васкулопатии, активации иммунной системы и фиброза.

При СС увеличивается риск развития малигнизации органов и тканей, подвергшихся фиброзированию. Особенно высок риск поражения кожи, легких, пищевода, рака молочной железы и лимфомы. В последние годы проведено много исследований по изучению поражения легочной ткани и васкулопатии, которые положительно отразились на заболеваемости и смертности. Они и стали причиной увеличения интереса к данной патологии.

Целью данного клинического случая, является обсуждение прогноза совместимости склеродермы и малигнизации.

**Ключевые слова:** рак – склеродермия – аутоиммунные заболевания

## Introduction

Systemic sclerosis (Ssc), is a heterogeneous and chronic disease which affects many organs such as lung, skin, and cardiovascular system. Systemic sclerosis, clinically shows a standard course and each patient shows different signs and symptoms according to affected organ system. The disease's pathogenesis also shows the same heterogeneity; by the presence of autoimmune antibodies, by increased fibroblastic activity and finally, endothelial dysfunction ranging from vasospasm, up to vaso occlusive disease. The risk of disease occurrence in the child of a Ssc patient is increased 13-15 fold. However, the precise relationship of the disease with any specific gene has not been proven. Fibrosis is especially seen in the vascular structures and the interstitium. Microscopic vascular changes due to endothelial activation can be detected long before clinical symptoms develop. Deposition of fibrotic proteins such as type I collagen, elastin, fibrillin and proteoglycans eventually lead to the destruction of normal structures and cause functional disturbances.

Scleroderma has rich clinical systemic properties. Initial major clinical symptoms are skin involvement, Raynaud's phenomenon, edema of hands, fatigue, muscle and joint pains. Jaw and mouth problems, motility disorders and gastroesophageal reflux, gastric emptying problems, lung pathology (interstitial lung disease and pulmonary arterial hypertension), cardiac involvement, renal crisis, common myalgia, arthralgia and myopathies may also be seen.

In addition, there is increased risk of malignancy in Ssc patients. Especially malignancies of skin, esophagus, breast, lung and lymphoid organs which are affected by fibrosis most are seen in high rates. Our aim is to remind the importance of early diagnosis and treatment, thereby reducing the mortality and morbidity expected from the possible malignancies.

## Case

68-year-old male patient fatigue, presented with swelling in the legs and eyelids. The patient was diagnosed as squamous skin cancer of the UK in 2011. Bilateral cervicax lymph node dissection along with parotis tail resection was performed and he had received six cycle of chemotherapy (cisplatin). He had also received radiation therapy to head and neck region.

The patient was admitted to our hospital with sudden onset of high blood pressure, and elevated levels of serum urea, creatinine, swelling of the legs and scrotum and fatigue. Dry cough and mild dysphagia were available. There was no history of smoking and alcohol use.

Physical examination: BP 180/90 mm Hg, pulse - 78 / min, rhythmic, pale skin, oral mucosa and skin was dry slightly. Decreased breath sounds in the bilateral basal lung areas was observed. He had 3+ pretibial and scrotal edema. Mouth opening was measured as of 2.5 cm and thick shiny appearance of body skin, with facial mask like features. Hand and finger stiffness and edema, sclerodactyly, flexion deformities of fingers were detected (Image 1).



**Image 1** - Swelling of the fingers of the patient

Laboratory findings: Hb -8.2 g / dL, hematocrite-24%, WBC - 6900 / mm<sup>3</sup>, platelets - 139,000 / mm<sup>3</sup>, urea-215 mg / dL, creatinine-5.5 mg / dL, Na - 131 mmol / L, K - 4.07 mmol / L, albumin -2.4 g / dL, total proteins 5.4 g / dL, 24-hour urine protein-0.03 mg, TSH-12 mIU / mL, anti-DS- DNA – normally, ANA (+++), ENA profile was normal expect weak anti centromere antibody positivity and anti SS-Ab positivity at 52nd minute. In PA lung radiography pleural effusion and increased reticular densities at bilateral basal zones were noted. ECG was normal. With the present clinical and laboratory findings, the patient was diagnosed as Scleroderma, Scleroderma renal crisis and secondary Sjogren syndrome. ACE inhibitors were started for control of blood pressure. With the consequent decrease of urine volume, decrease of creatinine clearance under 10 ml/ min and developing metabolic acidosis and hypervolemia, the patient was signed up for haemodialysis treatment.

## Discussion

Scleroderma (systemic sclerosis, Ssc) is an inflammatory autoimmune chronic disease characterized with widespread fibrosis of skin and internal organs [1-3]. Although the etiology of the disease is still not fully enlightened, genetic predisposition, environmental factors, infections and microchimerism are stated as possible triggering factors. The role of genetic factors in the etiology Ssc has been investigated intensively. The risk of developing Ssc in the first-degree relatives of individuals with Ssc is increased prominently. In normal population this risk is 0.026% whereas in genetically risky group these rates are 2.6% [2]. The incidence and prevalence of Ssc can show prominent variations in relation to ethnic and regional factors. The disease is most oftenly seen between 30-50 years of age and male / female ratio of 8/1 [4]. Silica powder, vinyl chloride, L-tryptophan, silicon breast implants are environmental factors that are associated with Ssc. Many other risk factors which are being investigated may be absent in Ssc patients and they can not be held responsible by themselves at the aetiopathogenesis of the disease [5]. Several bacterial and / or viral infectious agents such as (*Helicobacter pylori*, cytomegalovirus (CMV), parvovirus B19, Epstein-Barr virus (EBV), and retroviruses) are reported to be playing role for the aetiology of Ssc. By molecular mimicry or by evoking immunologic reactions against host's autoantigens or endothelial cell these infectious agents may take role in the aetiopathogenesis of the disease [6]. The proofs of immune activation can be shown prior to formation of skin fibrosis [7-8]. There are proofs of humoral immune activation as well as innate and acquired cellular immune response. Changes in B lymphocyte homeostasis, polyclonal hyperactivation, increase of sensitized B lymphocytes and decrease of memory B lymphocytes have been shown in Ssc [9-10].

There are many reports about the relationship between rheumatic disease and tumor growth.

Many various factors (genetic, viruses, smoking) including the autoimmune disease itself play a common etiologic role in the pathogenesis of tumor growth. The relationship between rheumatic disease and cancer can be seen in various forms: the musculoskeletal symptoms and syndromes can be seen as paraneoplastic syndrome during the development of malignancy [11]. Tumor incidence may increase in various systemic inflammatory and autoimmune diseases. Certain immunosuppressive agents including DMARD's can increase cancer risk. In Ssc patients the risk of developing malignancy in fibrotic organs is increased as well as B-cell malignancies [12]. Pathogenic factors such as: common genes, viruses, constant

B cell activation are proven in autoimmune disease related carcinogenesis. Patients with Ssc have been shown to have 1.5-10.7 times increased risk for developing lung, skin, esophagus, breast carcinomas and non-Hodgkin lymphomas according to various cohort studies. Scleroderma like disease is also related to lung, skin, breast and over carcinoma. Anti- topoisomerase type 1 antibodies are found positive in numerous paraneoplastic cases. The patient and his age also are considered as risk factors for developing cancer in Ssc [13].

However, it is not easy to discriminate potential oncogenic

characteristics of immunosuppressive drugs from disease related mechanisms. If the autoimmune disease and malignancy appears in a short time, it may be difficult to make a distinction between a malignancy secondary to autoimmune disease or autoimmune paraneoplastic state due to carcinoma. With present findings, it is not easy to say which one of epidermoid carcinoma or Scleroderma started first in our patient. We would like to emphasize that early diagnosis and treatment of rheumatic disease may prevent future malignancies that may be developing and increase survival rates of patients.

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