

## Systemic Sclerosis Associated with Rectal Cancer. Case Report and a Brief Review of the Literature

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**Abstract.** Autoimmune diseases may appear as paraneoplastic syndromes during the course of a neoplastic disease, the most common being dermatomyositis/polymyositis. The association of systemic sclerosis and cancer is not clear. The case of a 56-year-old male with rectal cancer and systemic sclerosis where the coexistence of the two diseases was closely related, so that scleroderma was considered a paraneoplastic syndrome rather than a concomitant morbid condition, is presented.

Paraneoplastic syndromes occur during the course of several neoplastic diseases and are most commonly seen with small cell lung cancer (1). Autoimmune disorders constitute a subgroup of paraneoplastic syndromes (2) and symptoms related to the autoimmune disease may precede the first symptoms or appear during the course of the neoplastic disease. The case of a man with rectal cancer and systemic sclerosis is presented.

### Case Report

A 56-year-old male, who experienced rectal bleeding in 1999, was diagnosed with locally advanced adenocarcinoma of the rectum, underwent a left hemicolectomy with a permanent stoma and refused any further medical intervention.

Three months after surgery, he noticed small skin lesions on his cheeks. These lesions were very small but kept increasing in size (Figures 1A and B), making the skin thinner, hairless, and pink in colour with visible blood vessels (telangiectasias). The patient did not seek medical advice as these lesions were not causing any pain.

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Within a few months he developed sclerosis in the fingers. The course of the development of these changes was very slow.

Five years after surgery, the patient experienced dyspnea which rapidly aggravated and he was examined at a district hospital. Chest X-rays and CT revealed four metastatic nodular lesions in each lung. There was an indication of diffuse interstitial infiltration on both lower lobes thus giving the picture of 'honeycomb lung'.

The patient was then referred to St. Savvas Hospital (Athens, Greece). On clinical examination, it was evident that there were atrophic lesions on the cheeks, the lesion on the right side being 3x4 cm and the lesion on the left side 2x3 cm. The skin around the mouth appeared to have shrunk and his nose was thin (Figure 2). There were also telangiectasias. The patient also presented clubbing of the fingers (Figure 3), thickening of the skin proximal to the metacarpophalangeal joints and purple lesions over the interphalangeal regions of the fingers (Figure 4). The lung examination revealed reduced expansion of the lung parenchyma. There was also tenderness on palpation of the sacral bone.

Laboratory tests were conducted with the following results (\* indicates normal values): White blood cells:  $5.9 \times 10^3/\mu\text{l}$  ( $4-11 \times 10^3/\mu\text{l}$ )\* (neutrophils 54%, lymphophils 35%, monophils 7%, eosinophils 4%); Haemoglobin: 13.3 g/dl (13.2-16.2 g/dl)\*; Haematocrit: 40.1% (38-52%)\*; Platelets:  $338 \times 10^3/\mu\text{l}$  ( $150-400 \times 10^3/\mu\text{l}$ )\*; Alkaline phosphatase: 117 U/l (20-70 U/l)\*; Lactate dehydrogenase 258 U/l (85-250 U/l)\*. There were no other abnormal findings on biochemistry. Urinalysis [Hb (++)], Nitrates (+)] was conducted and carcinoembryonic antigen (CEA):19.7 (<3)\* and CA 19-9:35.4 (<40)\* were also assessed. Antinuclear antibodies (ANA) were >1:640 and anti-scl-70 was positive.

X-Ray of the sacral bone and bone scan showed a lytic lesion of the sacrum. The patient was then referred to the radiotherapist and had a single fraction of 8 Gy at the above site.

Barium swallow did not reveal involvement of the oesophagus. On ultrasound the liver was normal and the right

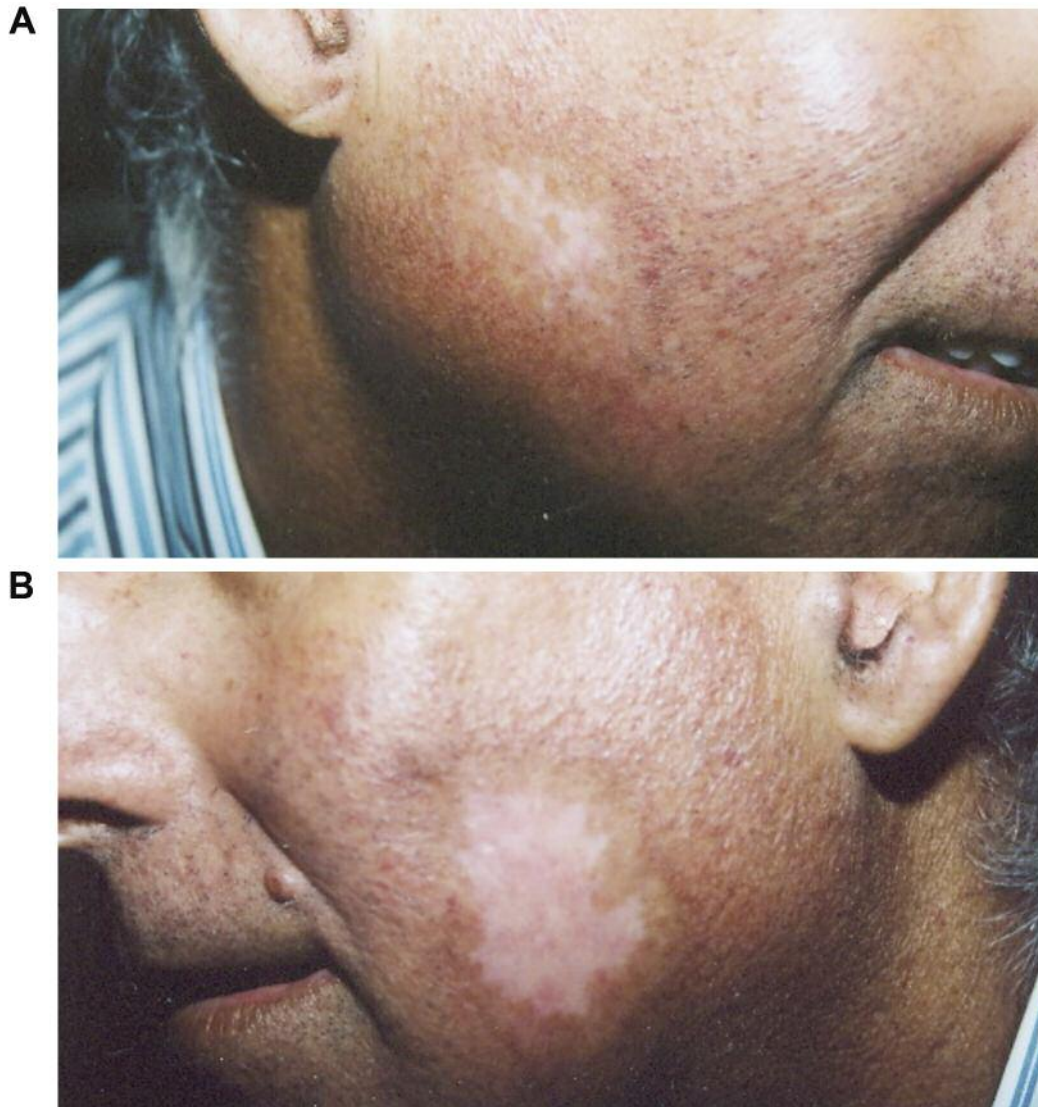


Figure 1A and B. *Skin lesions on both cheeks.*



Figure 2. *Typical sclerodermic appearance of the mouth and nose.*



Figure 3. *Clubbing of the fingers.*



Figure 4. *Purple lesions and thickening of the skin of the fingers.*

kidney had severe hydronephrosis (history of renal stones). The results from spirometry were suggestive of a constrictive syndrome.

On skin biopsy, the epidermis did not reveal any pathological abnormalities. In the papillar dermis, there

appeared to be homogenization of the collagen fibers and perivascular infiltration of lymphocytes. In the reticular dermis, thickening of collagen fibers was observed and immersion of sweat glands. In the subcutaneous tissue, there was thickening of fibrous septulum.

The findings were considered to be compatible with those of scleroderma in the area examined. There was no evidence of malignancy.

After the diagnosis of systemic sclerosis was established, the patient was referred to a rheumatology unit for evaluation. Treatment with high-dose corticosteroids was suggested and methylprednisolone, 48 mg daily, was then administered with rapid symptomatic improvement, however, all attempts to decrease the steroids resulted in reappearance of the symptoms.

The patient died five months after the diagnosis of systemic sclerosis from respiratory failure.

## Discussion

Autoimmune diseases may present in the course of a neoplastic disease, in which case they are included in the paraneoplastic syndromes. A possible imbalance in the immune system could cause the autoimmune disease (3), but it may also be associated with cancer. The most common paraneoplastic syndrome associated with many types of cancer is dermatomyositis/polymyositis. Progressive systemic sclerosis is rarely seen and is mainly associated with lung (4), breast (5-7) and oesophageal cancer (8, 9), while the relationship with colorectal cancer is ambiguous. In the literature, there are only scattered case reports in which the two diseases are either correlated or considered coincidental. Valcani *et al.* (10) reported a case in 1963 of a young woman who developed rectal cancer four years after the diagnosis of systemic sclerosis; the two diseases were rather coincidental.

Joliot *et al.* (11), on the other hand, described the case of a patient whose symptoms of systemic sclerosis developed seven months after the appearance of the first clinical symptoms of rectal cancer, while the surgical removal of the tumour resulted in regression of the sclerodermal lesions. The case reported by Lefevre *et al.* (12) was quite similar to the present case and concerned a 75-year-old patient who developed sclerodactyly and progressive pulmonary fibrosis after diagnosis and surgical removal of a Dukes C adenocarcinoma of the colon with high titers of serum antinuclear antibodies. Both cases followed the same pattern in terms of skin and lung involvement with sclerodactyly and pulmonary fibrosis, the presence of sclerodermal changes after surgery and positivity of serum autoantibodies. Less convincing is the report by Marino *et al.* (13) in which a patient who underwent surgery for a locally advanced cancer of the caecum, developed tightening of the skin of the face, trunk, arms, legs, hands and fingers following the second infusion of 5-fluorouracil (5-FU). No visceral involvement was demonstrated although the patient experienced dysphagia for solids. A temporary discontinuation of 5-FU

would have clarified whether those skin changes were related to the patient's cancer or should have been attributed to the 5-FU.

The hypothesis that sclerodermal changes may be induced by chemotherapeutic agents was supported by a report of Kono *et al.* (14), who noticed a sclerodermal-like reaction in a patient treated with UFT, a combination of uracil and tegafur. Other drugs that can cause scleroderma-like reactions are bleomycin, the taxanes (15) docetaxel (16) and paclitaxel (17), and interleukin-2 (18). All the cases discussed above involved adenocarcinomas, which was also noted by Basten and Bonnin (19), who reported that the majority of patients with any malignancy related to scleroderma had either adenocarcinoma or carcinoid. Interestingly, they described skin involvement in all the patients, but visceral involvement in only about half of them. Probably the cutaneous manifestations are the first to appear in the course of the autoimmune disease and when the cancer progresses visceral involvement may follow. Curative treatment of the cancer would lead to regression of the skin changes and would not allow progression to involve the internal organs.

## Conclusion

In summary, systemic sclerosis is occasionally seen in the course of neoplastic diseases, mainly with lung, oesophageal and breast cancer, while sclerodermal skin changes may also be seen with bleomycin, the taxanes, interleukin-2 and probably 5-FU treatment. The small number of cases reported with rectal or colon cancer and systemic sclerosis are only suggestive of a possible correlation between the two diseases. However, when the first symptoms of systemic sclerosis appear close to the diagnosis of cancer, regress after a curative operation, or expand to internal organs (particularly the lung) with cancer progression, a paraneoplastic disorder could possibly be the cause.

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