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WERNER'S SYNDROME AND MALIGNANCY

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Abstract. Ten per cent of all patients with Werner's syndrome develop some form of malignant disease, half of them sarcomas. A case of Werner's syndrome is reported in which the patient had a malignant fibroxanthoma of the thigh followed by a papillary cystadenocarcinoma of the ovaries. A brother with clinical signs of Werner's syndrome died of acute leukaemia.

Key words: Werner's syndrome; Malignancy; Fibroxanthoma, malignant; Cystoadenocarcinoma

Werner's syndrome, a caricature of aging, is characterized by a high frequency of malignancy, with tumours arising from the mesenchym being predominant. The present report describes a Werner's syndrome patient who had two different malignant tumours, a sarcoma and a carcinoma.

CASE REPORT

The subject is a 41-year-old nurse.

Heredity. No consanguinity is known in the family. The subject's mother became grey-haired at the age of 30 years and one of her two brothers turned grey at an early age and had the same thin fingers and toes as the patient. He had a cataract at the age of 19 years and died of acute leukaemia when 32 years old. Her second brother also became grey-haired when young and had cataracts removed at the age of 31 years. He did not have peripheral atrophy.

The patient has been grey since her thirties; she has sparse hair, an aged appearance and small bird-like facies with hypertrichosis. Her hands and feet have been small since childhood. A gradual, slow, progressive atrophy with sclerosis of the skin has occurred distally on the extremities. Subcutaneous fat is almost completely absent on the hands and feet and pressure from the underlying bones and surrounding structures has caused tender hyperkeratoses and pressure sores. Since the age of 25 the patient has had to wear special shoes and now at 41 years she is severely handicapped because of the pain in her feet when walking. She has a feeling of tenseness and paraesthesia in her hands and feet and also pain in the joints. She has had operations for bilateral hallux valgus, which occurs in her family. Her nails are small and thin. In contrast to the atrophy of her extremities, her body fat is rather pronounced. Cataract, which was diagnosed at an early age, progressed quickly and initially had a posterior subcapsular localization. Cataract operation was performed when she was 34 years old. Her menarche was at 12; her menstruations were regular, but stopped at the age of 38. Her uterus is smaller than normal and she has small breasts. She had not succeeded in becoming pregnant. Her voice is hoarse.

The patient has increased insulin in serum, increased blood sugar, an abnormal glycose tolerance test and, periodically, sugar in urine. Although she sometimes has difficulty in swallowing, the X-ray picture of the oesophagus is normal. She has symptoms of colitis and roentgenography has disclosed lessened haustrations of the colon. A prolonged bleeding time has been attributed to a congenital thrombocytopathia, aggravated by salicylics, with a pathological release reaction and thrombocyte aggregation test with connective tissue. Other laboratory findings were normal, including EMG and muscle enzyme determinations.

Development of tumours

I. *The sarcoma.* Over a 6-month period, a slowly growing subcutaneous mass was observed on the left lateral thigh just above the knee joint. It was warm and tender but the overlying skin was normal. The mass measured 15 × 10 cm and was freely mobile in its surroundings. It was initially thought to be inflammatory in origin, but treatment with antibiotics was unavailing. The sedimentation rate, which was 87, became normal after operation. There were no palpable regional lymph nodes and the patient's chest X-ray was normal. Needle biopsy disclosed a suspicious fibromyxolipomatous malignant process. The tumour was removed, together with skin, surrounding muscles and periosteum. When cut it was firm, grey-white in colour and was composed of whorling myxomatous structures.

Histological investigations showed a partly malignant fibroxanthoma. The myxoid substance was strongly basophilic and was metachromatically stained with toluidine blue at pH 4 but not at pH 0.5 which indicated the presence of hyaluronic acid.

II. *The carcinoma.* About 10 months after the operation on her femur the patient noticed a slowly increasing painless swelling of her abdomen. Apart from slight trouble with her stools and urine there were no subjective symp-

toms. A cystic tumour arising from the pelvis and extending to the umbilicus was palpable. At operation, two large thin-walled cysts, with smooth surfaces and containing clear fluid were removed. The inner walls were covered with papillar epithelial proliferations which were microscopically seen to consist of undifferentiated, rather monomorphous cells with large pale nuclei and numerous mitoses. The tumour was classified as an anaplastic papillary ovarial cystadenocarcinoma of the ovaries. Postoperatively radiotherapy was given. Now, almost 2 years later, the patient feels well.

COMMENTS

In about 10% of patients with Werner's syndrome, malignant tumours develop and, next to vascular complications, they are the commonest cause of death. Of the 136 patients reported in the literature up to 1971 (5) 14 had malignant tumours, 6 had carcinomas, 1 a malignant melanoma and 7 sarcomas. The sarcomas have been classified as fibrosarcoma (6), fibroliposarcoma (1), osteogenic sarcoma (3), leiomyosarcoma (4), and spindle cell sarcoma, sarcoma developing from a nerve sheath (3). One patient has been described with a haemangiolipoma with mitosis (2).

In 1971 a case of another malignant disease, acute myeloid leukaemia was first described in Werner's syndrome (5). It is interesting that one of the present patient's brothers, who had clinical signs of Werner's syndrome, also died of acute leukaemia.

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