EJGO European Journal of Gynaecological Oncology

Cancer-associated retinopathy in a patient with synchronous fallopian tubal and uterine corpus cancers

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Summary

Background: Cancer-associated retinopathy (CAR) is a paraneoplastic syndrome that significantly diminishes the quality of life of patients. *Case Report:* A 53-year-old woman with a history of glaucoma, cataract, and cerebral infarction was diagnosed with synchronous FIGO Stage IVB fallopian tubal cancer and Stage IA uterine corpus cancer. She complained of acute low vision and ring scotoma during the examination. Although her visual acuity was 25/20 in both eyes, and neither fundoscopy nor brain CT showed any abnormalities, electroretinography recorded no responses. Anti-recoverin antibodies were detected in her serum, and both fallopian tubal, and endometrial malignant cells expressed recoverin. These malignant tumours caused CAR. Although surgical debulking and chemotherapy reduced the size of the tumours, her low vision progressively worsened and anti-recoverin antibodies were still detected in her serum. *Conclusion:* The authors treated a rare case of CAR with synchronous fallopian tubal and endometrial cancer. This rare paraneoplastic syndrome should be considered during the differential diagnosis of ophthalmological symptoms in patients with malignant disease, as well as in the gynaecological field.

Key words: Cancer-associated retinopathy; Fallopian tubal cancer; Uterine corpus cancer; Recoverin; Paraneoplastic syndrome.

Introduction

Many types paraneoplastic syndromes have been reported to occur secondary to various malignant diseases. Among them, hypercalcemia, Trousseau's syndrome, anti-N-methyl-D-aspartate receptor encephalitis, cerebral degeneration, and subacute sensory neuropathy have commonly been described in the gynaecological field [1]. The present authors experienced a case of synchronous fallopian tubal and endometrial cancer with cancer-associated retinopathy (CAR). Although CAR in gynaecological malignant diseases is relatively rare, all types of cancer can cause this disease.

Case Report

A 53-year-old woman (non-gravida) with histories of glaucoma for five years, cataract for three years, and cerebral infarction three years previously, presented to her local hospital with a complaint of acute abdominal tension. CT detected a tumour in the uterine cavity, with suspicion of metastasis to the bilateral ovaries, omentum, and liver, accompanied with severe ascites. Histological examination of the uterine tumour revealed endometrioid carcinoma. Biochemical examination revealed elevated cancer antigen 125 levels (2363 U/mL). One week after the first examination, she experienced acute low vision and ring scotoma especially of the left eye, without any other neurological symptoms. Brain CT did not detect any abnormal changes. Subsequently, she was admitted to this hospital, and her bilateral low vision progressively worsened. Although her visual acuity was 25/20 in both eyes and fundoscopy did not demonstrate any other abnormalities, Humphrey visual fields showed ring scotoma in both eyes. In addition, electroretinography did not record any responses (Figure 1). Later, she underwent laparotomy with total abdominal hysterectomy and bilateral salpingo-oophorectomy to control her abnormal genital bleeding. In the peritoneal cavity, ascites were evident and numerous disseminated tumours of the omentum, on the peritoneum, and on the surface of intestine were present. Pathological examination revealed endometrioid carcinoma of the uterine corpus, which slightly invaded the myometrium, and incidental high-grade serous carcinoma of the bilateral fallopian tubes, which invaded the peritoneum and bilateral ovaries (Figures 2A and 2B). In addition, the cells in ascites had originated from the serous carcinoma. Western blot analysis detected anti-recoverin antibodies, which are specific autoantibodies for paraneoplastic syndrome, in her serum before surgery. Moreover, immunohistochemical analysis using a standard protocol [2] showed diffusely positive staining for anti-recoverin antibodies (Millipore, ab5585) on the cells of both the fallopian tubal and uterine corpus cancers (Figures 2C and 2D). In contrast, other autoantibodies such as anti-amphiphysin, anti-CV2, anti-PNMA2, anti-Ri, anti-Yo, anti-Hu, anti-SOX1, anti-titin, anti-zic4, anti-GAD65, and anti-Tr antibodies were not detected in the serum by Western blot analysis. These findings indicated that our patient had synchronous FIGO Stage IVB fallopian tubal cancer and stage IA uterine corpus cancer accompanied with CAR.

Two weeks after surgery, she was treated with combined chemotherapy (paclitaxel [180 mg/m^2] and carboplatin with an area under the curve of 6, every three weeks). Although CT revealed a decrease in the size of the metastatic tumours and no ev-

Revised manuscript accepted for publication June 19, 2018

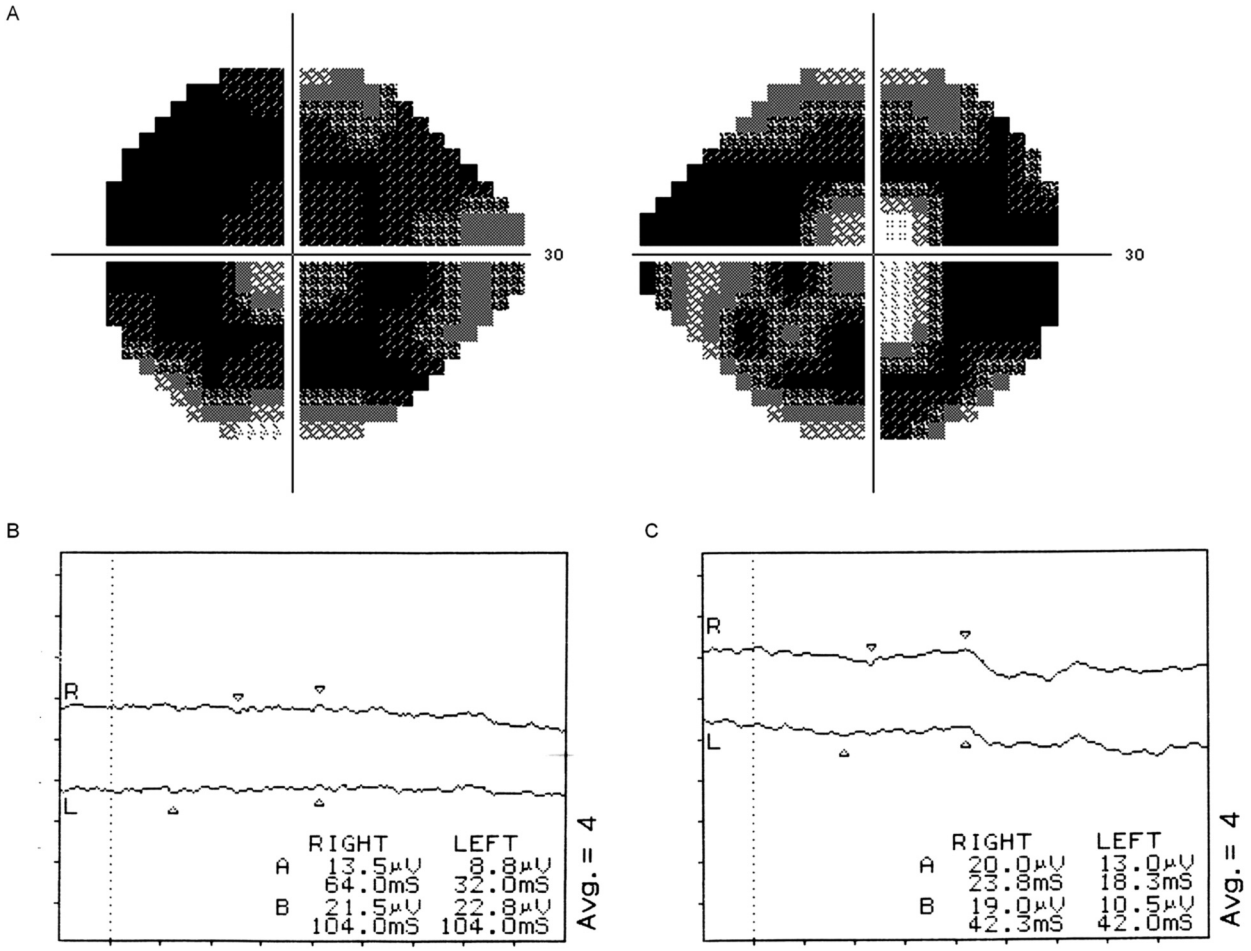

Figure 1. — Humphrey visual fields showing a ring scotoma in both eyes (A). Electroretinography did not detect any responses in both rods (B) and cones (C).

idence of re-occurring ascites after three cycles of combined chemotherapy, the chemotherapy did not prevent the progression of her low vision, and anti-recoverin antibodies were still detected in her serum after chemotherapy.

The authors obtained signed consent to publish the information from the patient.

Discussion

CAR is one of the paraneoplastic syndromes, and occurs secondary to many types of cancers including three cases of fallopian tubal cancer [3, 4] and up to ten cases of endometrial cancer, mostly consisting of the small cell carcinoma type [4-6]. These paraneoplastic syndromes are occasionally detected early when the symptoms first appear and before the diagnosis of primary malignant disease. In one study, visual loss appeared around the time the gynaecological cancer was diagnosed; the visual symptoms appeared at the same time the ovarian and endometrial cancer was diagnosed, and preceded the diagnosis of fallopian tubal cancer [4].

Cancer cells can express specific antigens, such as recoverin. The present immunohistochemical analysis revealed that both the fallopian tubal carcinoma and endometrial carcinoma cells expressed recoverin. It was shown that specific autoantibodies for this antigen are produced, and these attack the retinal cells in the presence of tumour-produced circulating factors [7]; anti-recoverin antibody was detected in the patient's sera. However, long-term immunosuppression and corticosteroid therapy might be slightly effective because CAR is an autoimmune-mediated disease, specific treatments for CAR have not been reported, and recovery of vision is difficult [8]. Moreover, although surgical cytoreduction of melanoma might decrease the amount of antiretinal antibody production [8], removal of the main tumour could not change the visual failure in the present case. Nevertheless, rapid treatment should be considered to stop the progression of CAR, as CAR can largely diminish the quality of life of patients. Especially for patients with a medical history of ophthalmological or neurological dis-

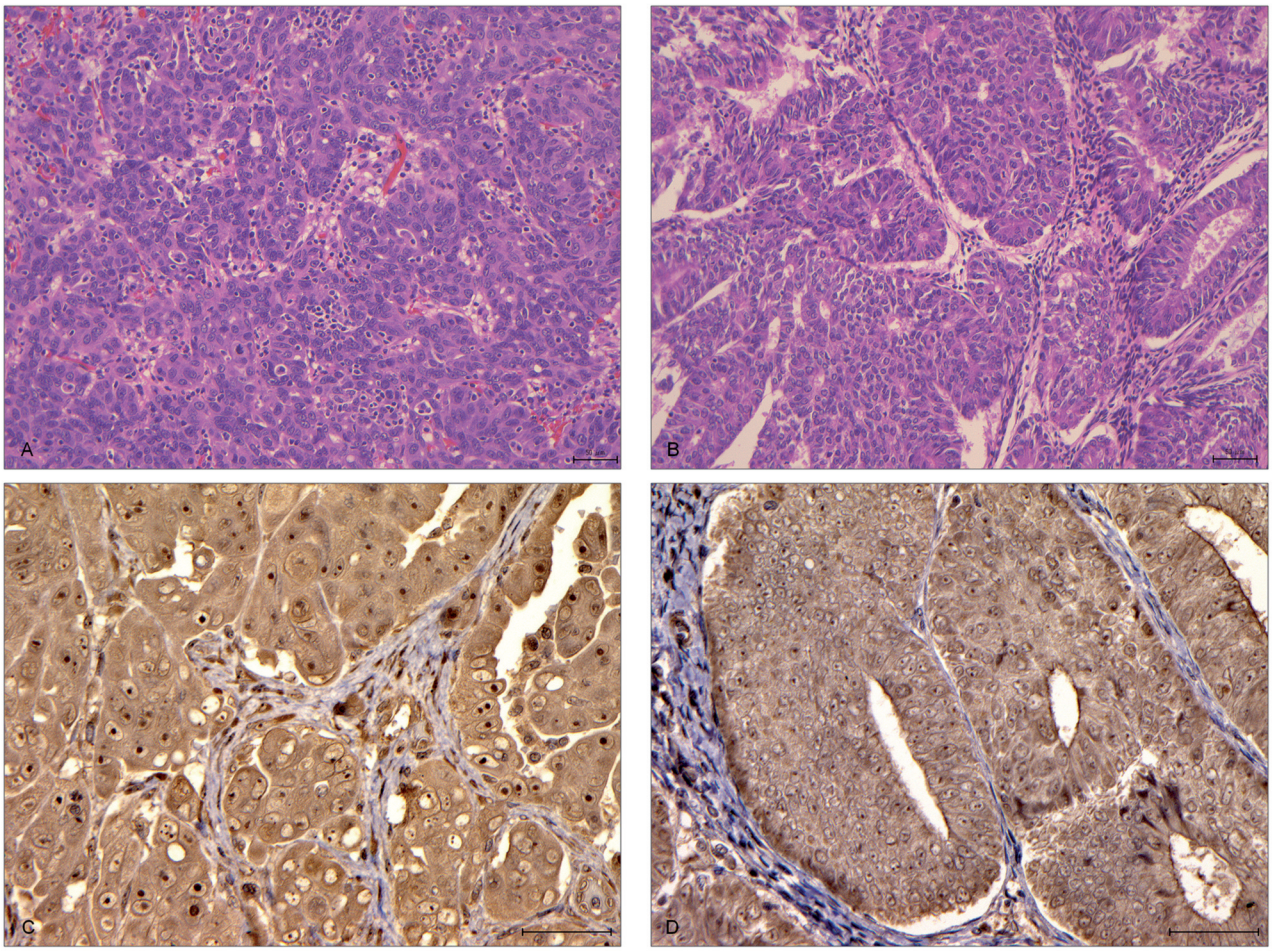

Figure 2. — Pathological findings of the fallopian tubal and uterine corpus cancers. Hematoxylin and Eosin staining of the fallopian tubal (A) and uterine corpus cancers (B). The cytoplasm of both the fallopian tubal cancer cells (C) and uterine corpus cancer cells (D) are stained with anti-recoverin antibody. Scale bar = 50 µm.

ease, we should consider the possibility of CAR without prematurely categorising this as a simple ophthalmological or neurological disease.

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