Introduction

Endometrial cancer is the most common gynecologic malignancy of the female, and its incidence is increasing in the world [1]. Immune-mediated necrotizing myopathy (IMNM) is characterized by clinical features, myositis-specific antibody (MSA), and reported its association with malignant disease. Among MSAs, the anti-3-hydroxy-3-methylglutaryl coenzyme A reductase antibody (HMGCR antibody) was initially found as an MSA strongly associated with statin exposure [2, 3]. HMGCR antibody-associated myopathy is also reported its association with malignant disease [4-6]. In previous reported HMGCR antibody-associated myopathy cases, the original site of appearance of the tumor was stomach, esophagus, colon, pancreas, lung, breast, kidney, lymph node, ovary, fallopian tube, and uterine cervix, while there is no case of HMGCR antibody-associated myopathy of uterine endometrium in the English language medical literature. Here, the authors present a rare case of HMGCR antibody-associated myopathy in patient with endometrial cancer.

Case Report

A 60-year-old woman without a past medical history of interest including statin exposure was referred to this hospital with atypical genital bleeding. Two months before this admission, she noted deteriorating muscle weakness and finally difficulty in walking. On neurologic examination, the authors observed muscle weakness and atrophy in the patient’s proximal upper and lower limbs without abnormal sensation, coordination, or reflexes. No other symptoms were observed. Examination of the pelvis, which demonstrated a necrotic tissue and bleeding in uterine cavity, suggesting an endometrial cancer. Ultrasonography revealed an echogenic endometrial mass. Magnetic resonance imaging (MRI) examination of the pelvis, which demonstrated 10x10cm sized endometrial mass, multiple lymph node swelling in pelvis suspecting metastasis, suggesting an advanced endometrial cancer. Computed tomography (CT) examination of the abdomen and chest demonstrated no metastases. Laboratory investigations showed no remarkable findings. Laboratory investigations

Summary

Background: Anti-3-hydroxy-3-methylglutaryl coenzyme A reductase antibody (HMGCR antibody) antibody-associated myopathy is a rare disease. HMGCR antibody-associated myopathy in patient with endometrial cancer is extremely rare. Case Report: A 60-year-old woman without statin exposure presented with endometrial cancer Stage IIIC1 (T2N1M0) and HMGCR antibody-associated myopathy. After diagnosis, the patient received chemotherapy combining paclitaxel and carboplatin for endometrial cancer, and steroid and immunoglobulin for HMGCR antibody-associated myopathy. Two months after two cycles of chemotherapy, she died. Autopsy revealed that she died of HMGCR antibody-associated myopathy. Conclusion: In case of myopathy in patients with endometrial cancer, HMGCR antibody-associated myopathy should be considered.

Key words: Endometrial cancer; HMGCR antibody-associated myopathy.
showed highly elevated serum creatine kinase (CK) levels (5,473 IU/L; normal, 30-1,401 IU/L). Laboratory results showed no other remarkable findings without slightly elevated liver enzymes. Serum tumor markers were as follows: SCC: 0.6 ng/mL, CEA: 1.8 ng/mL, CA19-9: 54 U/mL, and CA125: 181 U/mL. Histological examination of endometrial tumor showed poorly differentiated carcinoma. Needle EMG showed active myogenic changes in the muscles of the rectus femoris and the biceps, suspecting myositis. Laboratory investigations showed that ARS antibody, Mi-2 antibody, TIF-γ antibody, and MDA-5 antibody was negative. MRI examination of the muscle showed high intensity part of the rectus femoris muscle suspecting myositis (Figure 1). CT examination of the muscle showed no remarkable findings. Muscle biopsy of the rectus femoris muscle revealed no cell infiltrates, mild necrosis, and an increase in perimysial connective tissue. Expression of major histocompatibility complex (MHC) class I was negative by immunohistochimistry. Muscle fibers expressed CD8-positive T-lymphocytes. Elevated serum anti-HMGCR antibodies was detected using antigen-capture ELISA. Based on these findings, the authors diagnosed the patient with HMGCR antibody-associated myopathy. Therefore, primary endometrial cancer and HMGCR antibody-associated myopathy related with endometrial cancer was initially considered the most likely diagnosis.

The authors performed hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node biopsy. Macroscopically, there was a tumor in uterine cavity. The bilateral ovary and fallopian tube appeared to be normal. There was multiple lymph node swelling in pelvis suspecting metastasis. There was no intra-abdominal tumor dissemination or ascites. The pathological examination showed that the tumor was densely cellular, and the tumor cells had scanty cytoplasm and small to medium-sized hyperchromatic nuclei that were oval to spindle shaped. Therefore, the pathological examination showed an endometrioid carcinoma of grade 3 type. The tumor cells were arranged in uterine body, and there was myometrial invasion > 1/2 and cervical invasion by the tumor cells. There was no abnormal findings in ovary, fallopian tube, and ascites. There was metastasis in pelvic lymph node. Finally, the authors confirmed the diagnosis of primary endometrial cancer Stage IIC1 (T2N1M0) according to the International Federation of Gynecology and Obstetrics (FIGO) staging system.

After diagnosis, the patient received chemotherapy combining paclitaxel and carboplatin (TC therapy) for endometrial cancer. Although steroid and immunoglobulin were used for HMGCR antibody-associated myopathy, the decrease of serum CK levels and improvement of clinical symptoms was not recognized. Two months after two cycles of chemotherapy, she died. Autopsy revealed a remarkable muscle atrophy (Figure 2). There was no metastatic tumor macroscopically. Therefore, the authors confirmed that she died of HMGCR antibody-associated myopathy related with endometrial cancer.

**Discussion**

IMNM is characterized by clinical features, myositis-specific antibody (MSA) [2, 3]. IMNMM is a novel clinical type of inflammatory myopathy that is characterized by the presence of anti-body, such as a signal recognition particle antibody (SRP antibody), and reported its association with malignant disease [2-6]. Among MSAs, the HMGCR antibody is induced by statins, which are HMGCR inhibitors. However, approximately 30% of anti-HMGCR antibody-positive IMNN patients have not been exposed to statins, and reported its association with malignant diseases and collagen diseases [2-6]. To date, the relationship between anti-HMGCR antibody–associated myopathy and malignant disease remains unclear. In previous reported HMGCR antibody-associated myopathy cases, the original site of appearance of the tumor were stomach, esophagus, colon, pancreas, lung, breast, kidney, lymph node, ovary, fallopian tube, and uterine cervix, while there is no case of HMGCR antibody-associated myopathy relating uterine endometrium in the English language medical literature [4-6]. Therefore, the present case is first report of HMGCR
antibody-associated myopathy in patient with endometrial cancer.

Kadoya et al. reported that ten (83%) patients had advanced cancers, and nine (75%) patients died of cancers between 0.2 and 2.7 years after myopathy diagnosis (median: 1.2 years, within one year in six patients) among 12 HMGCR antibody-associated myopathy patients with cancer association [6]. In the present case, the diagnosis was endometrial cancer Stage IIIC1, and the patient died two months after operation following chemotherapy. This case was an aggressive one. A study also reported that three patients without relapses achieved normalization of serum CK levels and improvement of myopathy, six patients who died of cancers within one year showed worsening of myopathy, and three patients who died of cancers more than two years had periods showing decrease in serum CK levels and improvement of myopathy, however, myopathy reoccurred along with cancer progression [6]. In the present case, there was no decrease in serum CK levels and her clinical symptoms of myopathy worsened after complete resection of cancer. In a previous reported case of HMGCR antibody-associated myopathy patient with cervical cancer, the woman died of cancer progression in spite of recognizing the decrease of serum CK levels and improvement of clinical symptoms by oral prednisolone therapy [4]. Tsujikawa et al. observed decreased serum anti-HMGCR antibody levels after resection of esophageal carcinoma, which then increased with recurrence [5]. The relationships between condition of myopathy and cancer status remains controversial in HMGCR antibody-associated myopathy patients with cancer association.

Although steroid and immunoglobulin were used for HMGCR antibody-associated myopathy, there was no decrease in serum CK levels and her clinical symptoms of myopathy worsened in the present case. There is a few reports showing that serum CK levels was reduced and clinical symptoms gradually improved during steroid and immunoglobulin treatment [4, 5]. There is no reported case of HMGCR antibody-associated myopathy patient with cancer achieving complete remission of myopathy. There is no established treatment of HMGCR antibody-associated myopathy patient with cancer.

In conclusion, in case of myopathy in patients with endometrial cancer, HMGCR antibody-associated myopathy should be considered.

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