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Case report

Sudden death of a middle aged woman with a series of undiagnosed gynaecologic diseases

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ABSTRACT

Gynaecologic diseases unrelated to pregnancy are not generally associated with sudden death, which limits the number of case reports published in the field of forensic medicine. Presented in this paper is a fatal case in a middle aged woman with an early stage endometrial cancer and a series of gynaecologic diseases, in whom such typical features of sudden death were not applicable. Forensic autopsy revealed the hypoplasia of left circumflex coronary artery, Stage 1B endometrial cancer, endometriosis, polycystic ovary syndrome (PCOS) and micro pituitary adenoma, whereas histochemical analyses confirmed hyperprolactinemia and hyperestradiolemia. It was considered that the hypoplasia of coronary artery, chronic anaemia and electrolyte imbalance due to endometrial cancer all collaborated to induce acute cardiac failure. The association between prolactinoma, PCOS and endometrial cancer was also suggested, though they are rarely observed synchronously.

It was speculated that the deceased had been anaemic for a substantial period of time and lacked clear subjective symptoms, which made the antemortem diagnosis of her underlying diseases difficult. Forensic pathologists must always consider the possibility of gynaecologic diseases taking significant part in a fatal cause of reproductive-aged women.

1. Introduction

Sudden cardiac death is frequently observed in forensic practice, including a significant number of cases of young people [1]. Gynaecologic diseases unrelated to pregnancy are not generally associated with sudden death, which limits a number of case reports available in the field of forensic medicine [2]. Presented in this paper is a sudden death case of a middle aged woman with a series of chronic gynaecologic diseases, including synchronous endometrial cancer, which are believed to have significantly contributed to the fatal process, disclosed postmortem via forensic autopsy.

2. Case history

The deceased was a fulltime working woman in her forties. Although she had no clear subjective symptoms, a detailed examination had been planned for anaemia (haemoglobin level: 7.9 g/dl), which was pointed out 5 weeks prior to death by regular medical check-up. Her family heard her collapse while having a shower in the morning and vaginal bleeding was observed at the scene. She was found in a state of cardiac pulmonary arrest and death was confirmed on arrival at hospital.

3. Autopsy findings

Forensic autopsy was carried out about 24 h after death. The decedent was 160 cm in height and weighed 76 kg (body mass index = 29.7). No remarkable findings at external of body were present. No hirsutism or progression of facial and pubic hair were clinically significant. All organs were anaemic. The heart weighed 414 g and the left circumflex coronary artery was hypoplastic from its origin, whereas slight arteriosclerosis was observed in the right coronary artery (Fig. 1). Small amount of clots were found in the heart blood. The uterus was enlarged to 17 cm × 15 cm × 6.5 cm and a yellowish, cylindrical tumour was found in the endometrial cavity, 11 cm × 8 cm × 5 cm in size, half of which had undergone necrosis (Fig. 2). The tumour was solidly filled by atypical cells rich in cytoplasm, presenting a histopathological image of differentiated adenocarcinoma, intermixed with hyperplasia of endometrium. Thrombus formation, tumour cell invasion and coagulation necrosis were all observed in tumour vessels (Figs. 3 and 4). An invasion was seen in half of the myometrium without metastasis to the distant organs. A few myomas, 5 cm in maximum diameter, were observed

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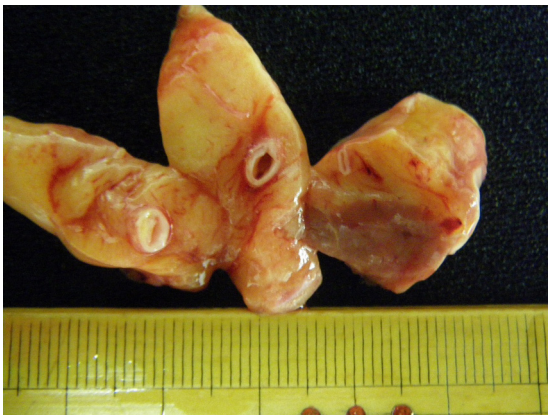

Fig. 1. Cross section of the coronary arteries (from left to right: right coronary artery, left descending artery and left circumflex artery).

in the non-tumour lesion of the endometrium. Left and right ovaries were 4 cm × 2.5 cm × 2.5 cm and 4 cm × 3 cm × 2 cm in size, respectively. Primordial follicles were present in both ovaries and at least 14 Graafian follicles of 0.1–0.5 cm in diameter, some of which containing corpora lutea and albicantia, were found in long strands in each ovary (Fig. 5). Pituitary gland weighed 0.75 g and multiple adenomas, several millimetres in diameter, were found in the anterior lobe. These adenomas were eosinophilic and positive in immunohistochemical staining for prolactin (Fig. 6). Biological sample from heart blood was reserved but no urine could be obtained for toxicological investigation. Alcohol and drugs were not detected by toxicological analysis. Glycated haemoglobin (HbA1c) level was 5.2%. Serum concentrations of hormones are shown in Table 1. These findings confirmed the diagnosis of Stage 1B endometrial cancer based on the classification by the FIGO, the Fédération Internationale de Gynécologie et d'Obstétrique, endometriosis, polycystic ovary syndrome (PCOS) and prolactinoma.

4. Discussion

The endometrial cancer in the present case is unlikely to have been the sole cause of death as it was in an early stage. Apart from the cancer, the anaemic organs and the hypoplastic left circumflex artery were observed at autopsy and are likely to have contributed significantly to cardiac death. In addition, an electrolyte imbalance, caused by paraneoplastic syndrome may have existed due to the prominent coagulative necrosis in the cancer. It is conceivable that all these factors collaborated to induce acute cardiac failure.

Endometrial cancer is a malignant epithelial tumour that occurs in the endometrium and a dualistic model of carcinogenesis has been proposed. Approximately 80% of endometrial cancer is related to excessive estrogen exposure of the endometrium unopposed by

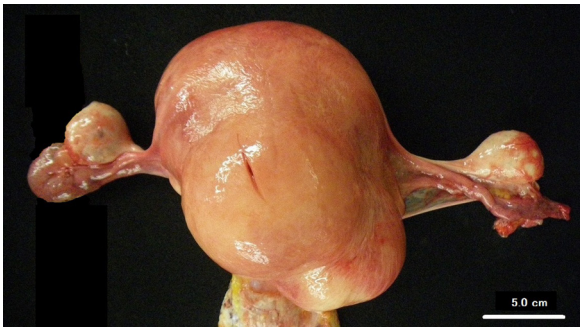

Fig. 2. Macroscopic view of the uterus and bilateral ovaries.

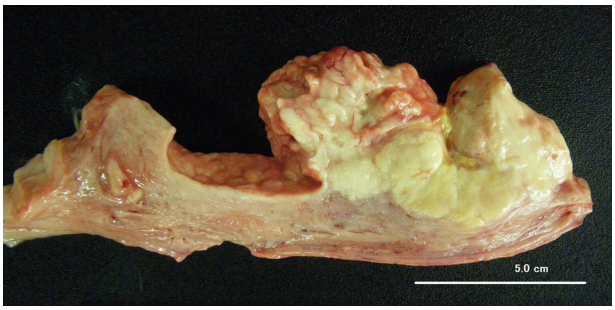

Fig. 3. Macroscopic view of the endometrium.

progestines, whereas the remaining 20% is unrelated to estrogen stimulations. Common major symptoms include metrorrhagia, hypermenorrhea and sterility [3]. The present case is considered to be the former, based on the histopathological diagnosis of endometriosis and the histochemical feature of a high serum level of estradiol. Several possible risk factors for this type of endometrial cancer have been documented to date, which include obesity, family history, infertility, nulliparity, hormone replacement therapy, oral contraceptives, tamoxifen and diabetes mellitus [4]. The obesity and nulliparity could have been predisposing factors in the present case. It is hypothesized that the risk factors for estrogen-dependent endometrial cancer operate via a single etiologic pathway [5]. Exposure to estrogen unopposed by progesterone leads to increased mitotic activity of endometrial cells, increased number of DNA replication errors and somatic mutations, resulting in the pathogenesis of the endometrial cancer [6].

However, in addition to estrogens, other hormones such as progesterone, androgens, gonadotropins, prolactin, insulin, and insulin-like growth factors may also play a role in the process of the carcinogenesis of endometrium. There is a paper stating that prolactin may inhibit the mitogenicity of endometrial cancer by inhibiting membrane associated phosphatidylinositol kinase of the human endometrial fibroblast [7]. In addition, the high circulating level of prolactine is regarded to block gonadotropin-releasing hormone, inhibiting FSH and LH, leading to chronic anovulation with unopposed estrogen secretion, which can also increase the risk of endometrial cancer. The hormonal evaluation in the present case revealed a marked elevation of estradiol, a slight elevation of prolactin, normal LH and a depression of FSH in serum concentrations. This is in accordance with the presumption that prolactin has played a role in the development of endometrial cancer [8].

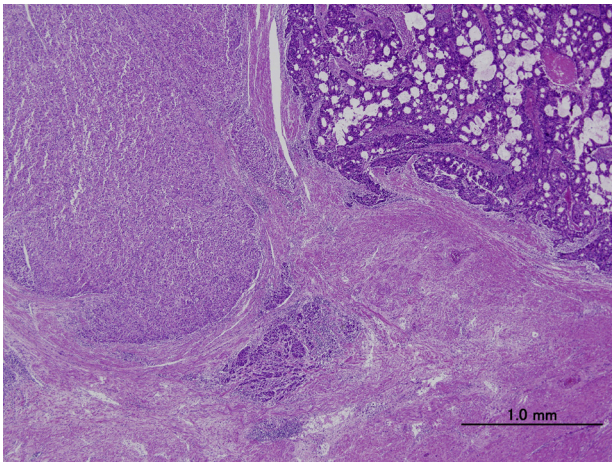

Fig. 4. Pathohistological section of the endometrium (haematoxylin-and-eosin stain).