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Ovarian metastasis in a patient with neuroendocrine tumour of the small intestine

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Neuroendocrine tumours (NETs) are rare pathologies, the incidence of which in the population is estimated at 25 people per million [1]. Primary NETs of the female reproductive system comprise less than 2% of all neoplasms. Focusing on the ovary itself, the statistics are similar: ovarian NETs affect 1–2% of patients with ovarian tumours [2]. Primary NETs account for only 0.1% and are observed more often than metastatic tumours [3].

A 64-year-old patient reported to a gynaecological clinic (previous visit 4 years earlier) with recurrent post-menopausal vaginal bleeding, yellow vaginal discharge, abdominal pain, and weight loss (5 kg during one year). In addition, less specific complaints, including hot flushes and facial skin redness, were observed. The gynaecological examination presented moderate bleeding. Additionally, ultrasound (US) examination revealed a large, multilocular, cystic, smooth tumour with moderate vascularity, with the largest dimension of 17 cm, in the projection/region of the left adnexa (Fig. 1). Following routine recommendations, the patient was referred for dilatation and curettage procedure (D&C). The first histopathological diagnosis was simple endometrial hyperplasia. To extend and differentiate the diagnosis, a computed tomography (CT) scan of the abdomen and lesser pelvis was performed. It confirmed the first US scan result. Following this, a total abdominal hysterectomy with bilateral salpingo-oophorectomy and peritoneal metastatic implant removal was performed. The final postoperative histopathological diagnosis was a tumour with immunohistochemical features of neuroendocrine differentiation. Histopathological re-consultation confirmed the metastatic, neuroendocrine origin of the tumour cells. The biochemical diagnostics detected elevated levels of neuroendocrine tumour markers (chromogranin A, serotonin, 5-hydroxyindoleacetic acid).

[^{68}Ga]Ga-DOTA-TATE PET/CT, which was done afterward, revealed a disseminated process with overexpression of somatostatin receptor (SSTR) at the anterior chest wall, in the liver, in para-aortic lymph nodes, and peritoneum with the probable origin from the ileum. Extending the diagnostics resulted in a change of the previous primary tumour diagnosis. Thus, the small intestine was considered to be the primary lesion, while the ovary would be the location of the metastasis. To reduce symptoms of carcinoid syndrome (abdominal pain, hot flushes, and diarrhoea) and also to prepare for surgery, the patient was qualified for treatment with somatostatin analogue (SSA) (Lanreotide Autogel). The next step was resection of part of the small

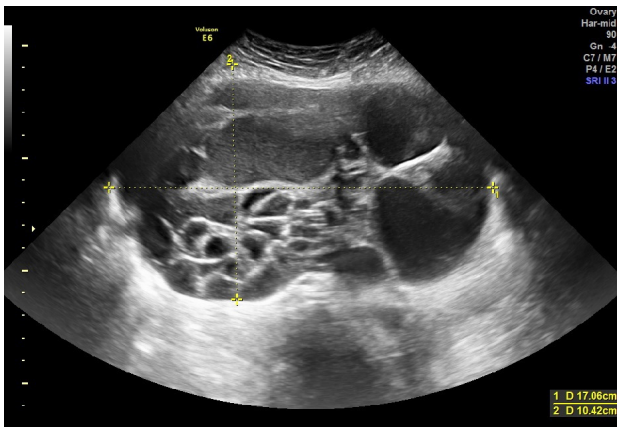

Figure 1. *Ultrasound image demonstrates a multilocular, cystic, smooth tumour with thin-walled partitions with the largest dimension of 17 cm in the projection of the left adnexa*

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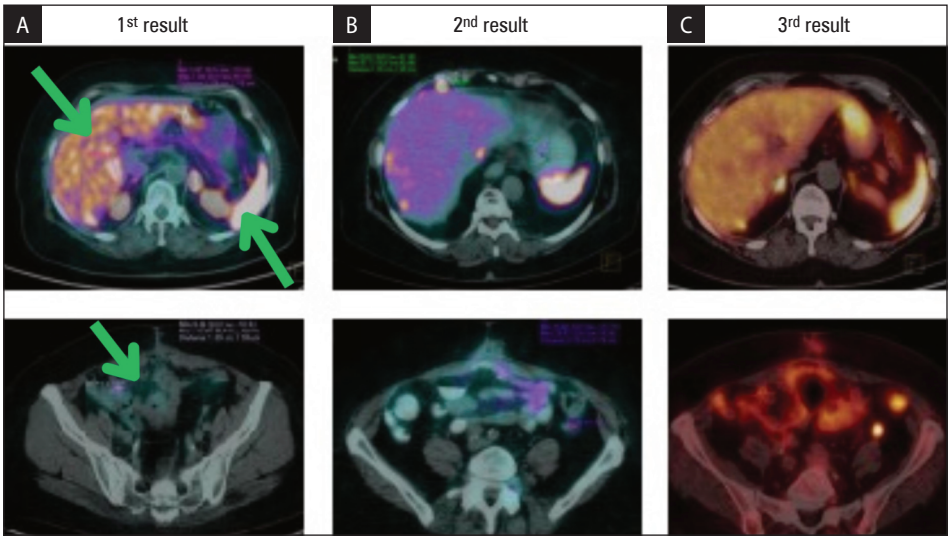

Figure 2. *[^{68}Ga]Ga-DOTA-TATE PET/CT of the abdominal cavity and lesser pelvis.* **A.** *Visibly increased somatostatin receptor (SSTR) expression in the liver, lymph nodes, peritoneum, and focus in the lesser pelvis (arrows).* **B.** *New metastatic foci and implants in the lesser pelvis.* **C.** *Stabilization in relation to earlier examinations*

intestine and right hemicolectomy. The postoperative tissues were examined, and the diagnosis was NET G1, Ki-67 1%, T4N1M1. The surgery was followed by SSA pharmacotherapy with periodic monitoring of biochemical parameters and radiological images (Fig. 2A). Surgical and pharmacological treatment resulted in a reduction of clinical symptoms of the carcinoid syndrome and improvement of the patient's well-being.

After a 2-year period of relative clinical stabilization, during the [^{68}Ga]Ga-DOTA-TATE PET/CT examination, a radiological progression was observed (Fig. 2B), followed by biochemical progression. The patient was therefore qualified for peptide receptor radionuclide therapy (PRRT) (3 cycles of ^{90}Y+^{177}Lu-DOTA-TATE), achieving clinical, biochemical, and radiological stabilization again (Fig. 2C).

Carcinoid syndrome is a clinical manifestation accompanying neoplasms, most often in cases of midgut NET (mNET). Disturbing symptoms such as facial flushing and persistent diarrhoea in post-menopausal patients can be difficult to differentiate from carcinoid syndrome during ovarian NETs. In presented case, primary symptoms suggested cancer of the reproductive system, but it turned out to be a secondary ovarian tumour, which developed from NET of the small intestine. Neuroendocrine ovarian metastases are mainly derived from mNET and spread in about 25% of women with advanced stages of this neoplasm [4].

An important diagnostic step was the histopathological verification of the specimens from the gynaecological surgery (the structures of the lesser pelvis). Differential diagnosis was based on achieving an SSTR image (confirming overexpression of neoplastic lesions) and markers of NETs. The entire procedure paved the way to implement appropriate surgical, pharmacological, and radioisotope treatment [5], finally achieving clinical stabilization of the patient. This problematic case confirms that a successful prognosis in advanced NETs requires a multidisciplinary approach to implement optimal patient treatment.

Author's statement
B.T. is the first author.

Conflict of interest
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Ethics statement
None.

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