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CASE REPORT

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Coexistence of acromegaly and pancreatic adenocarcinoma — case study

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ABSTRACT

Acromegaly is a rare condition characterized by increased secretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). This disease may predispose to the development of neoplasms. This study aims to present a case of a patient with acromegaly and coexisting pancreatic adenocarcinoma and to highlight the potential positive impact of somatostatin receptor ligands used in acromegaly treatment on the potential benefits when combined with conventional pancreatic adenocarcinoma therapy.

Keywords: acromegaly, pancreatic adenocarcinoma, somatostatin receptor ligands, pasireotide

Introduction

Acromegaly is a rare disease characterized by increased secretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). Most often, an increase in GH is caused by a pituitary adenoma [1]. Acromegaly may lead to cardiovascular, respiratory, endocrine, metabolic and musculoskeletal comorbidities. This disease may be associated with malignant neoplasms such as thyroid, colorectal, gastric, prostate, pancreatic, renal, and breast cancers [2–10]. The incidence of diseases associated with acromegaly depends on the increased secretion of GH and IGF-1, which are multifunctional factors regulating cell proliferation, differentiation, and apoptosis. These factors are important in tumourigenesis [1]. The diagnosis of acromegaly is confirmed based on clinical symptoms, increased serum IGF-1, and the lack of GH inhibition after glucose administration. Pituitary magnetic resonance imaging (MRI) is recommended for patients with acromegaly to identify a pituitary adenoma [9]. Transsphenoidal surgery is typically considered the initial treatment of choice for patients with acromegaly. However, patients with macroadenomas, which are larger and more invasive tumours, may not achieve remission following the surgical procedure [9]. Medical therapies such as somatostatin receptor ligands (SRLs), cabergoline, and pegvisomant may be recommended for patients with persistent acromegaly after surgery. Radiotherapy is another possible option for management and may be utilized when surgery is not feasible or when surgery and medications have not been successful in controlling excess GH production [9, 11–13]. First-generation SRLs — octreotide acetate, octreotide long-acting release (LAR), lanreotide depot, oral octreotide, and second-generation SRLs (pasireotide LAR) activate distinct subsets of somatostatin receptors (SSTRs). By doing so, they inhibit GH secretion, promote apoptosis, and exert antiproliferative effects [9, 11, 14]. The time required to achieve disease control in patients who do not respond to first-generation SRLs can be several years due to the need for months-long evaluation periods for each modification in medical therapy. Pasireotide, a compound traditionally used in patients resistant to first-generation SRLs and those who have had unsuccessful surgery, is now being recognized as a first-line therapy for patients with specific characteristics based on available data [15].

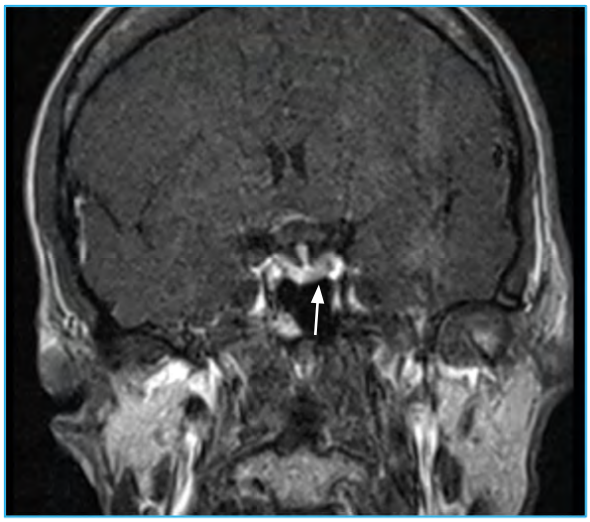

Figure 1. MRI performed in January 2010 showed a hypointense area measuring 6 × 4 mm, which may correspond to a microadenoma

Case study

We can present the history of a female patient born in 1956. The patient presented her first symptoms of acromegaly in 2009. The disease was diagnosed in September 2009 based on the following laboratory values: IGF-1 at 989 ng/mL (53–166 ng/mL) and GH at 10 ng/mL (0.126–9.880 ng/mL). Due to the manifestation of disease symptoms, treatment was started with Lanreotide 120 mg, administered subcutaneously every 28 days.

In the magnetic resonance imaging (MRI) examination in January 2010, the size of the pituitary gland was 13 × 4 × 12 mm. In the upper part, the pituitary gland is modelled by a funnel recess, in the lateral part of the pituitary gland on the left side, there was a hypointense area of 6 × 4 mm, which may correspond to a microadenoma (Fig. 1).

Surgical treatment was performed in April 2010, specifically a transsphenoidal procedure for the incomplete removal of the pituitary microadenoma. Following the surgery, the treatment with Lanreotide was continued. In December 2014, stereotactic radiotherapy, as the second-line therapy, was administered at a dose of 25 Gy.

The treatment with Lanreotide 120 mg, administered subcutaneously every 28 days, was continued until November 2015. However, due to the lack of disease control, in December 2015, Lanreotide was switched to Octreotide LAR 40 mg. Additionally, a decision was made to add a dopamine receptor antagonist, Cabergoline, with a dosage of 0.5 mg, taken orally once every 7 days.

In December 2018, due to insufficient clinical and biochemical control of disease symptoms, the decision was made to initiate the next line of treatment with a second-generation somatostatin ligand. Prior to the subsequent somatostatin analogue treatment regimen, the Patient required a neurosurgical reevaluation to confirm the infeasibility of surgical management of pituitary lesions.

The patient underwent a neurosurgical consultation but was not deemed eligible for re-operation. However, in January 2019, the patient was qualified for treatment with a second-generation somatostatin ligand, Pasireotide, with a dosage of 40 mg. At the time of starting Pasireotide treatment, the patient's IGF-1 level was measured at 271 ng/mL [53–166 ng/mL] and GH level at 4 ng/mL [0.126–9.880 ng/mL]. The patient is currently still undergoing therapy (as shown in Figure 2 and Figure 3).

The MRI conducted from July 2010 to October 2021 consistently indicated a stable radiological status of postoperative changes. Specifically, on the left side of the pituitary gland, two hypodense areas of up to 5 mm in size were observed.

The patient has developed complications associated with acromegaly, including toxic struma nodosa (following hemistrumectomy) and hypertension, which is further complicated by moderate concentric hypertrophy of the left ventricle and moderate mitral regurgitation, as described in the echocardiography report from June 2013.

An abdomen ultrasound examination conducted in March 2021 revealed dilation of the Wirsung duct and a hypoechoic structure, which was described as a lesion located in either the duodenum or the lower part of the head of the pancreas, measuring 47 × 34 × 46 mm.

Next, a computer tomography (CT) scan of the abdomen was performed, which revealed a solid-cystic lesion located at the level of the head of the pancreas, measured 37 × 40 × 55 mm in size (as shown in Figure 4). Following a cell-block biopsy of this lesion, the histopathological examination confirmed the presence of cells with characteristics consistent with pancreatic adenocarcinoma.

Induction chemotherapy with FOLFIRINOX (a scheme combined with 5-fluorouracil, calcium folinate, oxaliplatin and irinotecan) was started and consisted of 10 cycles of treatment, administered from July 19, 2021, to November 25, 2021. This was followed by radiochemotherapy with capecitabine, which was carried out from January 13, 2022, to February 22, 2022. Subsequently, pancreatic tumour surgery was performed on July 4, 2022, specifically a pancreaticoduodenectomy with gastrointestinal reconstruction using the Traverso method. During the surgery, a surgical

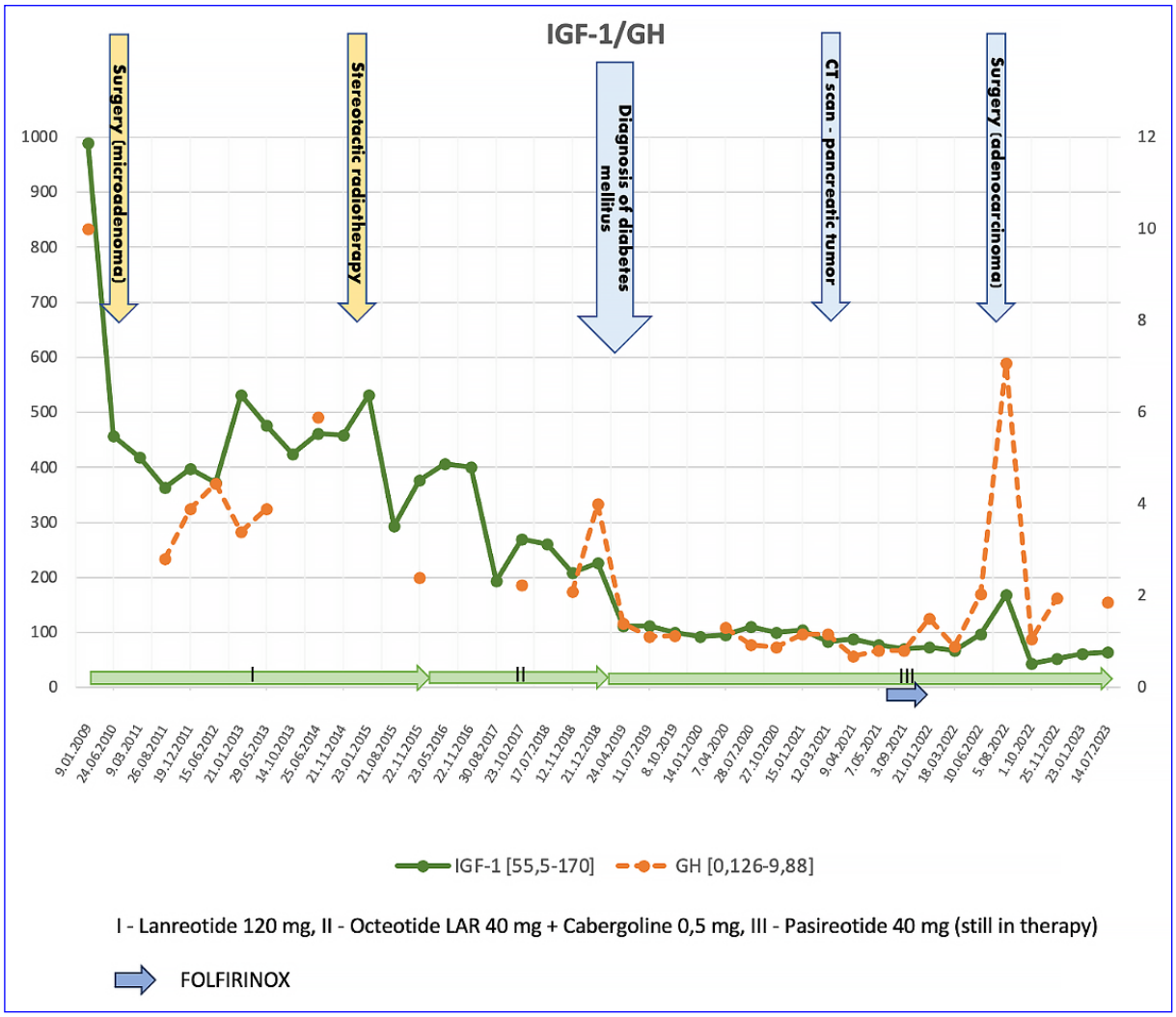

Figure 2. The change of IGF-1and GH concentration over time treatment of acromegaly

biopsy of the right lobe liver nodule was conducted, and the gallbladder was also removed. The tumour staging is reported as pT2N0M0 (stage IB), indicating the extent of the primary tumour (T2), absence of lymph node involvement (N0), and no distant metastasis (M0). The CT scan of the abdomen and chest conducted on August 16, 2022, revealed postoperative changes in the area where the surgery had been performed (Figure 5).

Despite the unfavourable prognostic outlook typically associated with pancreatic adenocarcinoma, it is worth noting that the patient is currently in good health condition.

The patient's last follow-up visit took place on July 14, 2023. The patient has continued her treatment with SRLs — pasireotide, at a dose of 40 mg, and remains in therapy until now.

Discussion

According to various studies, acromegaly is a medical condition that is linked to an increased risk of neoplastic growth. Numerous studies have provided evidence suggesting a higher prevalence of thyroid, colorectal, gastric, renal, and breast cancers among individuals diagnosed with acromegaly [3–9, 16].

Despite the progress made in surgical techniques, available radiotherapy options, and the use of long-acting somatostatin ligands, there are still some individuals with acromegaly who are unable to achieve sufficient biochemical control of the disease. Failure to attain optimal serum levels of GH and GF-1 can result in increased morbidity and mortality rates among patients with acromegaly [17]. According to Elina Ritvonen

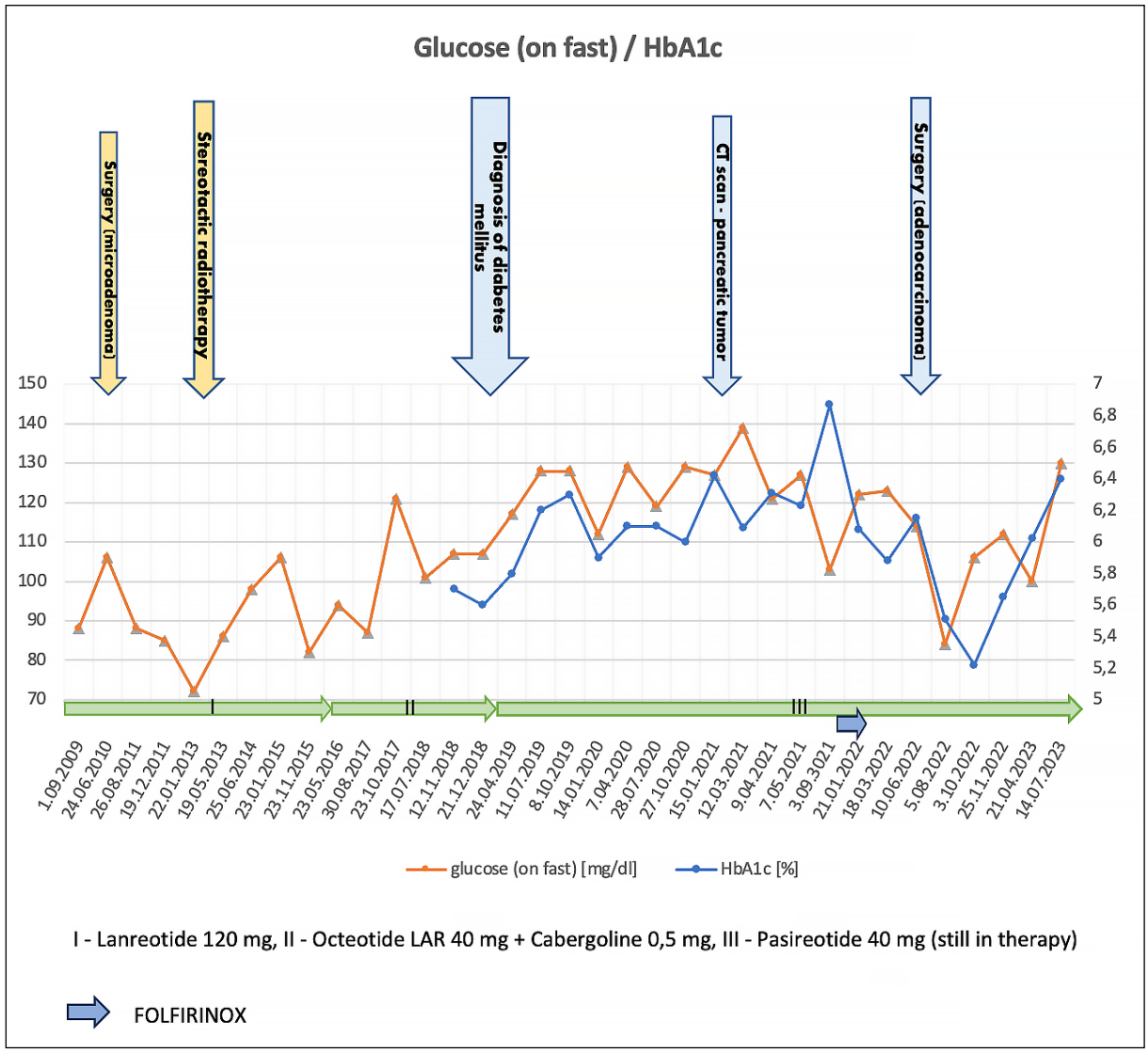

Figure 3. The change of blood glucose and HbA1c level over time treatment of acromegaly

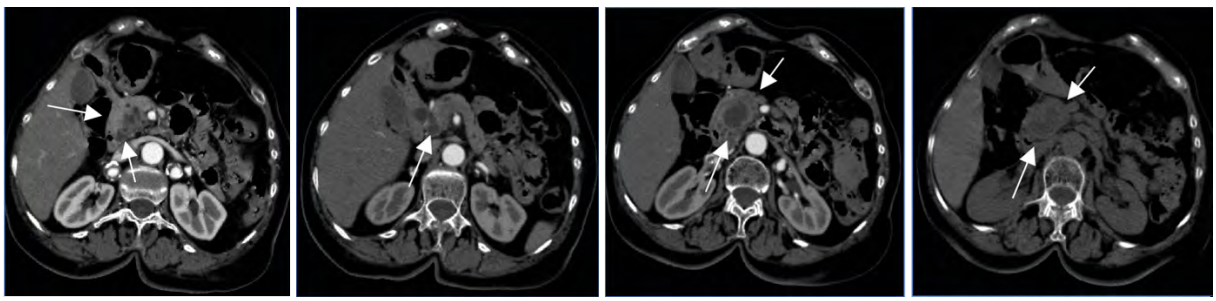

Figure 4. CT scan of the abdomen revealed a solid-cystic lesion located at the level of the head of the pancreas, measuring 37 × 40 × 55 mm in size

et al. [17], among individuals with acromegaly, cancer-related deaths were predominantly associated with pancreatic adenocarcinoma (n = 5), breast carcinoma (n = 4), lung carcinoma (n = 3), and colon carcinoma (n = 3) [17]. In contrast, some studies have put forward the argument that the incidence of cancer in the specific patient population of acromegaly does not differ significantly from that of the general population [18].

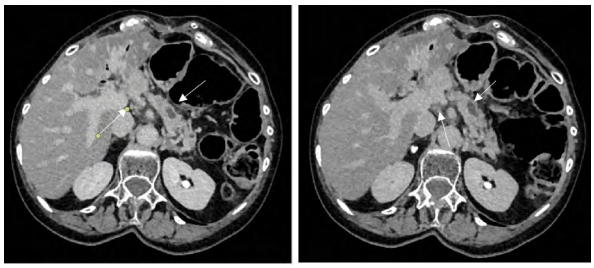

Figure 5. CT scans of the abdomen revealed postoperative changes in the area where the surgery had been performed (08.2022)

The co-existence of acromegaly and pancreatic adenocarcinoma is a very rare condition. The medical literature contains solely one documented case of the coexistence of these two diseases described by Durmaz et al. [19].

In the presented case, pasireotide was utilized as a treatment for acromegaly that was resistant to first-generation somatostatin ligands. Pasireotide was initiated in December 2019, resulting in a decrease in IGF-1 levels by April 2020. Due to the prior lack of biochemical disease control and the impact of IGF-1 on cellular proliferation, elevated levels of GH and IGF-1 before the initiation of pasireotide could have contributed to pancreatic tumour growth. Epidemiological studies have demonstrated that GH and IGF-1 may exert influence on cancer pathogenesis by modulating cellular growth and apoptosis, potentially leading to an augmented predisposition to progression to an advanced stage promoting tumour growth, metastasis, and contributing to the development of therapy resistance [1, 20].

The increase in glycaemia in Chart 2 during the first half of 2022 may be related to the adverse reaction to somatostatin analogues, characterized by an elevation in glycemia alongside a simultaneous decrease in IGF-1. Additionally, the developing pancreatic tumour, which may have also contributed to the increase in glycemia, should be considered. The patient was diagnosed with diabetes in March 2019, and metformin was initiated at an initial dose of 500 mg, with the current regimen being 3 g daily.

Alongside the treatment with pasireotide, the patient underwent 10 cycles of chemotherapy in order to reduce the size of the pancreatic tumour and become eligible for surgical treatment. Pancreatic adenocarcinoma frequently manifests in an advanced stage, leading to dismal five-year survival rates ranging from 2% to 9%, ranking firmly last amongst all cancer sites in terms of prognostic outcomes for patients [21]. According to research conducted by Yang Li et al. [22] the total median survival of patients with pancreatic adenocarcinoma classified as stage IB was 62 months, and their 1-, 3-, and 5-year survival rates were 83.8%, 58.9%, and 50.6%. At present, the patient diagnosed with pancreatic cancer two years ago is currently in a favourable state of health. One can assume the synergistic effect of chemotherapy and pharmacotherapy with the use of SRLs may result in a slowdown in the dynamics of pancreatic adenocarcinoma and prolong the patient's lifespan.

Pasireotide has demonstrated efficacy in the treatment of various types of neoplasms. It is used in the management of neuroendocrine tumours as well as non-endocrine tumours, such as breast, colon, prostate, lung, pancreatic, hepatocellular, and melanoma [10, 23–24].

Furthermore, studies have shown that pasireotide may also have therapeutic potential in treating pancreatic adenocarcinoma. Somatostatin receptors and IGF receptors are highly expressed in pancreatic cancer, thereby potentially making it a valuable target [25]. In particular, pasireotide has been found to block the protumoural features of cancer-associated fibroblasts (CAFs) in pancreatic adenocarcinoma by binding to the somatostatin receptor sst1. This effect was observed both in vitro and in immunocompromised mice [8, 25].

Conclusions

In summary, both acromegaly and pancreatic adenocarcinoma present significant challenges in treatment, and conventional therapies may not always yield optimal outcomes. Pasireotide offers a promising alternative for patients who do not respond well to conventional therapies. However, it is important to carefully monitor its use for potential adverse effects. Considering the effect of IGF-1 on tumour development and the potential for SRL inhibition of this process, further research is needed to fully understand the efficacy and safety of pasireotide both in the treatment of acromegaly and its potential use in aiding the management of neoplasms.

Article information

Ethics statement: *In accordance with the Helsinki Declaration, the case report was fully anonymised, and none of the data presented would make the identification of the patients possible. Under Polish law, such case reporting does not require the consent of a Bioethics Committee.*

Author contributions: *1) Olga Grzelak — conceptualization, data collection, and writing. Literature review and writing — review and editing. This author conducted an extensive literature search, ensuring that the report was supported by relevant and up-to-date references. 2) Violetta Rosiek — clinical expertise and critical review.*

This author, being a specialist in the field, provided expert insights, validated the clinical data, and contributed significantly to the interpretation of the case. 3) Beata Kos-Kudła — approval of the final version. This author has reviewed and approved the final version of the case report, acknowledging their contribution to the study.

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