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Assessment of the relationship between selected parameters of inflammation in patients with neuroendocrine neoplasms

Chaired by DR. ALFREDO BERZAL-HERRANZ;
Co-Chaired by PROF. DR. MARIA EMÍLIA SOUSA

pharmaceuticals MDPI

Marlena Budek[1,*], Jarosław Nuszkiewicz [1], Jolanta Czuczejko[2,3] and Karolina Szewczyk-Golec [1]

[1]Department of Medical Biology and Biochemistry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, 24 Karłowicza St, 85-092 Bydgoszcz, Poland;

[2]Department of Psychiatry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, 9 M. Curie Skłodowskiej St, 85-094 Bydgoszcz, Poland;

[3]Department of Nuclear Medicine, Oncology Centre prof. Franciszek Łukaszczyk Memorial Hospital, Bydgoszcz, 2 dr I. Romanowskiej St, 85-796 Bydgoszcz, Poland.

***** Corresponding author: mmarkiewicz@doktorant.umk.pl

UNIWERSYTET MIKOŁAJA KOPERNIKA W TORUNIU
Wydział Lekarski
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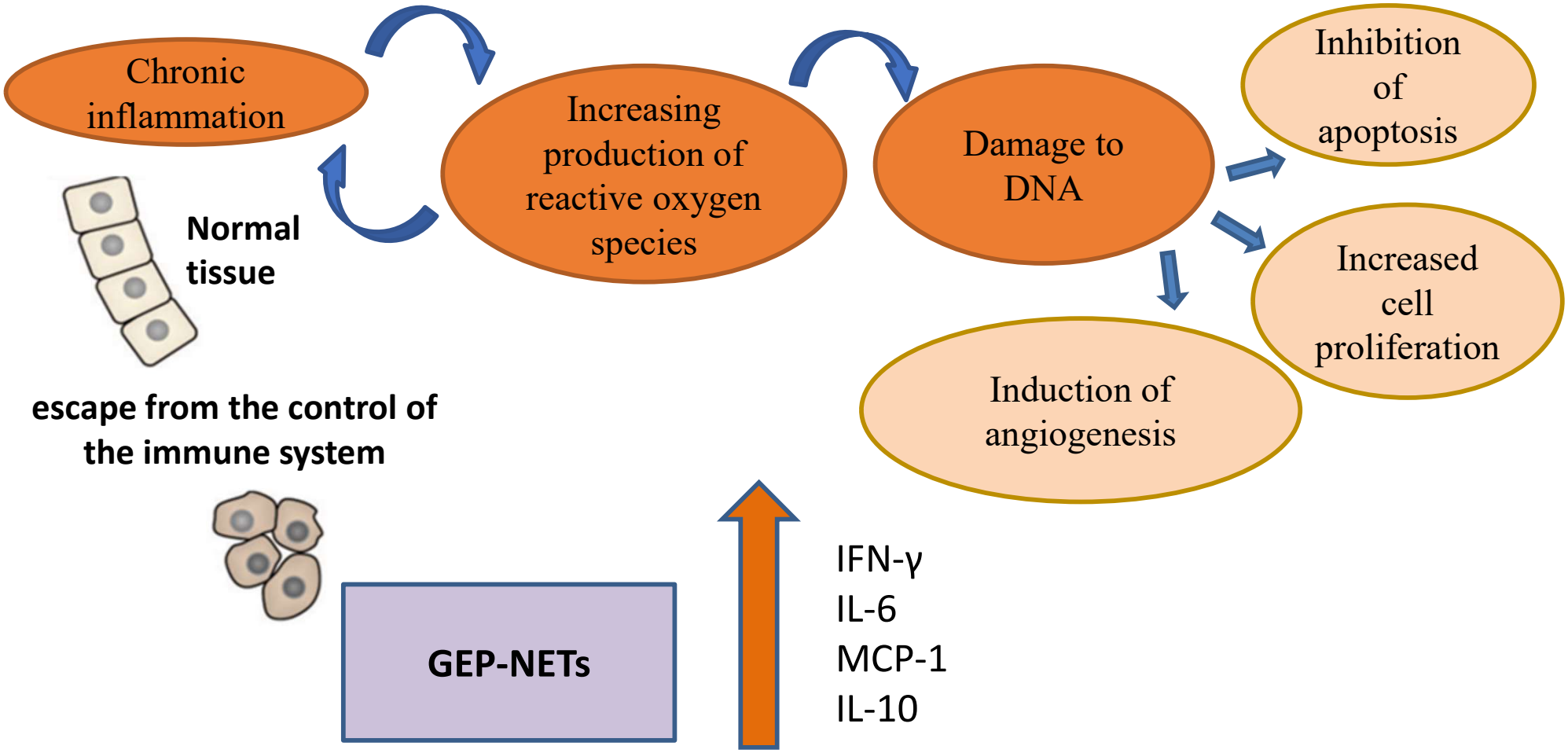
Graphical Abstract



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Abstract:

Neuroendocrine tumors (NENs) originate from neuroendocrine cells located in a wide variety of organ systems. Gastrointestinal-pancreatic tumors (GEP-NETs) constitute the largest group (approx. 70%). NENs are heterogeneous in terms of location, malignancy potential, prognosis, treat-ment methods and functionality, which often makes their diagnosis difficult. Accumulating evidence points to the role of inflammatory factors in the GEP-NETs microenvironment.

The aim of the study was to determine the concentrations of interferon gamma (IFN-γ), interleukin 6 (IL-6), monocyte chemoattractant protein-1 (MCP-1) and interleukin 10 (IL-10) in patients with GEP-NETs.

The study included 63 patients of the Prof. F. Łukaszczyk Oncology Center in Bydgoszcz with a diagnosis of neuroendocrine neoplasms of the gastrointestinal tract (GT, n = 42) and pancreas (PA, n = 21). The concentration of cytokines was measured by the enzyme immunoassay method using ready-made ELISA kits. A statistical analysis was performed and $P<0,05$ was considered as statistically significant. The results were presented as the mean value and the standard error.

The levels of IFN- γ, IL-6 and MCP-1 were statistically higher in the PA group than in the patients with GT-NENs. The concentration of IL-10, which is a factor inhibiting cytokine synthesis, did not show a significant difference between the GT and PA groups. Increased levels of inflammation in pancreatic NENs compared to gastrointestinal NENs have been observed. It has been noted that the disturbed balance between pro-inflammatory and anti-inflammatory factors may play a role in the development of neuroendocrine tumors.

Keywords: cytokine, gastroenteropancreatic neuroendocrine tumors, inflammation, neuroendocrine

Introduction

- NENs - a heterogeneous group of neoplasms originating in cells of a dispersed neuroendocrine system.
- Epidemiological data show that primary tumors are most often located in the digestive system and pancreas (62-67%) and in the bronchopulmonary system (22-27%).
- Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are heterogeneous in terms of location, malignancy potential, prognosis, treatment methods and functionality, which makes their diagnosis difficult.
- Primary tumors are usually small and do not show symptoms until metastasis occurs, which delays diagnosis and effective therapy for up to 5-7 years.
- Multidisciplinary management strategies have improved the survival of patients with NENs.
- The median age is 60 years or more and is similar among males and females.
- General markers used to screen patients without characteristic symptoms from hormone overproduction include chromogranin A (CgA), neuron specific enolase (NSE), pancreatic polypeptide and glycoprotein hormone subunits.
- GEP-NETs are more common in chronic inflammation, which probably stimulates neuroendocrine cells in the gastrointestinal mucosa to hyperplasia and neoplastic transformation.

Material and methods

- The aim of the study was to determine the concentrations and correlations between selected markers of inflammation in patients with GEP-NET.

- The study group consisted of 63 patients of the Prof. F. Łukaszczyk Oncology Center in Bydgoszcz with a diagnosis of GEP-NETs: 42 subjects with the neuroendocrine tumor located in gastrointestinal tract (GT-NET) and 21 subjects with the neuroendocrine tumor located in the pancreas (PA-NETs).
- Blood serum samples were obtained after collecting venous blood.
- The concentration of the inflammatory markers was measured with ready-made Multi-Plex Immunoassay System.
- The results were presented as means and the standard error of the mean (SEM).
- $p < 0.05$ was considered as statistically significant.

Results and discussion

	PA-NETs	GT-NETs	p
n	21	42	
Age [years]	60.9±1.87	57.05±1.96	p=0.23
Body mass [kg]	83.0±2.96	73.45±2.20	p=0.01
Height [cm]	169.2±1.93	169.79±1.24	p=0.79
BMI [kg/m^2]	28.9±0.77	25.36±0.59	p=0.0001

The results are presented as the mean value ± SEM.

BMI: body mass index; PA-NETs: pancreatic neuroendocrine tumors; GT-NETs – gastrointestinal tract neuroendocrine tumors.

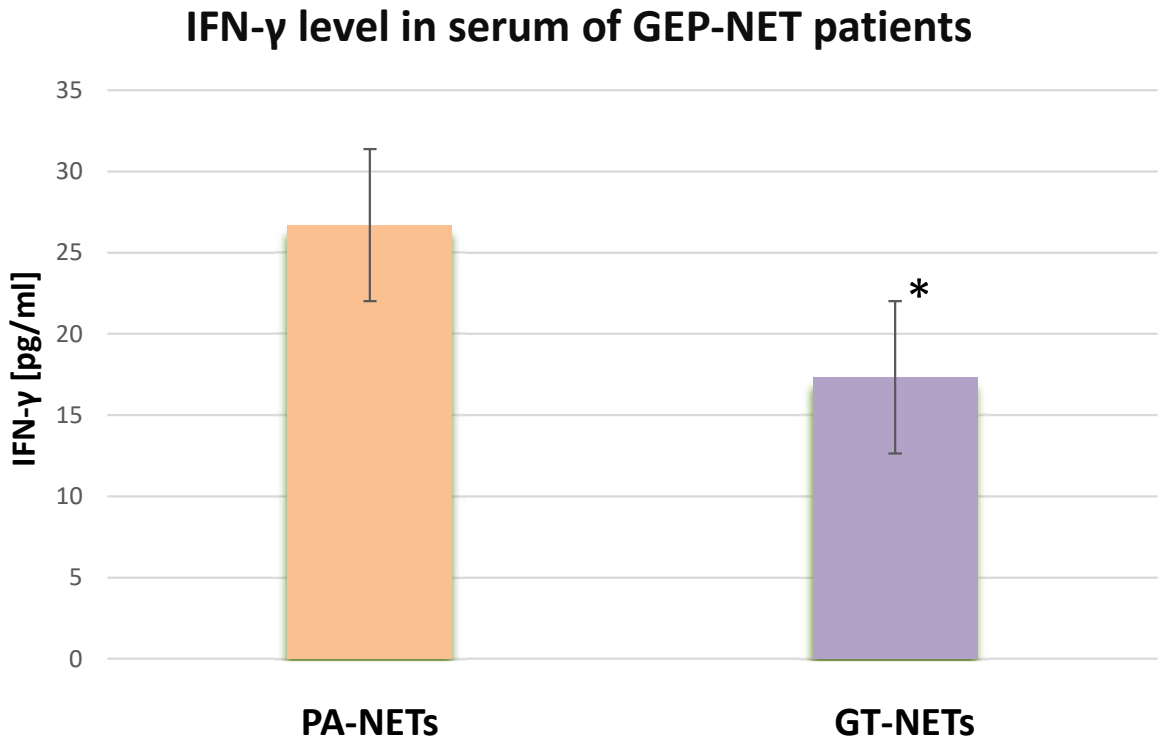
Results and discussion

Parameter [pg/ml]	Research group		Significance level
	PA-NETs n=21	GT-NETs n=42	P< 0.05
IFN-γ	26.7 ± 5.88	17.33 ± 1.49	0.04
IL-6	36.6 ± 12.48	18.40 ± 1.40	0.03
MCP-1	164.2 ± 16.42	127.36 ± 6.99	0.01
IL-10	6.5 ± 0.78	5.94 ± 0.51	0.48

The results are presented as the mean value ± SEM.

GT-NETs – gastrointestinal tract neuroendocrine tumors; IFN-γ: interferon gamma; IL-6: interleukin 6; IL-10: interleukin 10; MCP-1: monocyte chemoattractant protein-1; PA-NETs: pancreatic neuroendocrine tumors.

Results and discussion

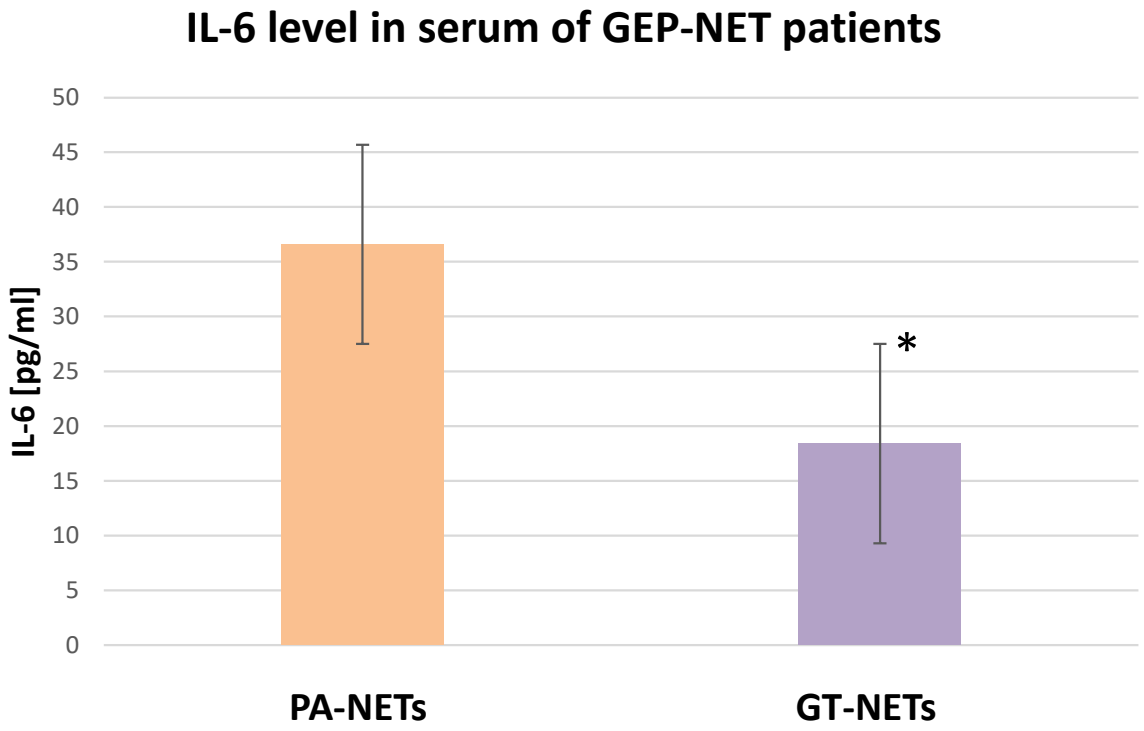


The results are presented as the mean value ± SEM

- **Statisticaly significant difference p<0.05**

GT-NETs – gastrointestinal tract neuroendocrine tumors; IFN-γ: interferon gamma; PA-NETs: pancreatic neuroendocrine tumors.

Results and discussion



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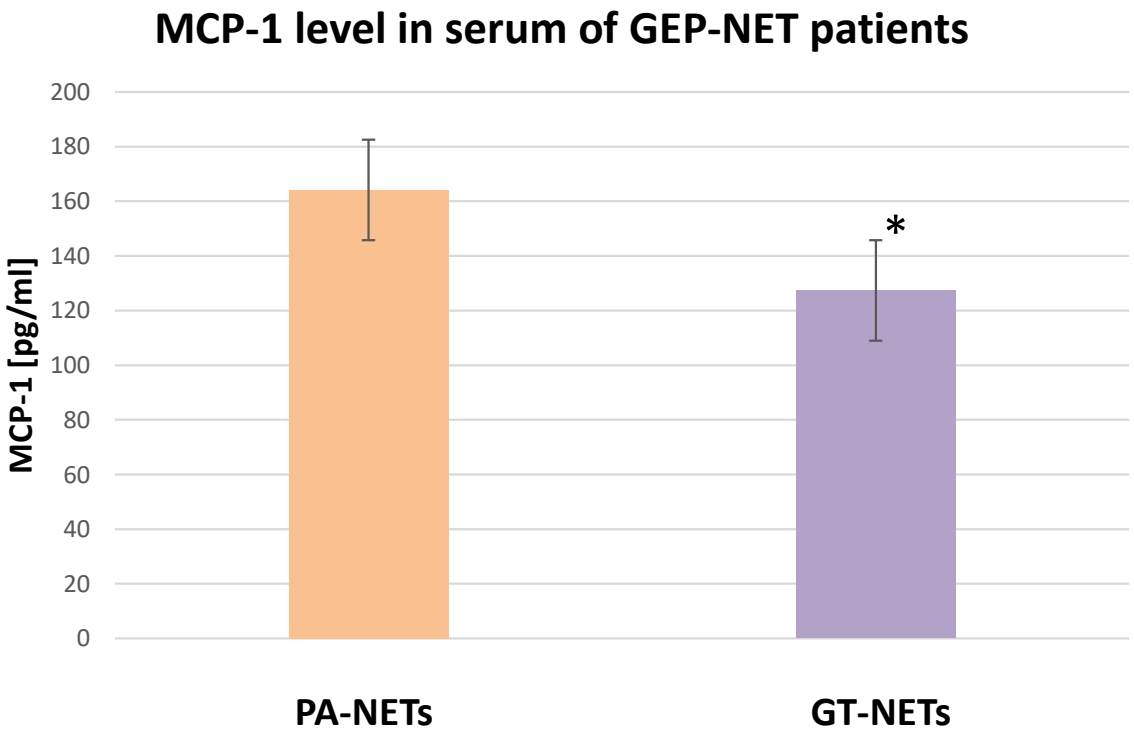
GT-NETs – gastrointestinal tract neuroendocrine tumors; IL-6: interleukin 6;
PA-NETs: pancreatic neuroendocrine tumors.

Results and discussion



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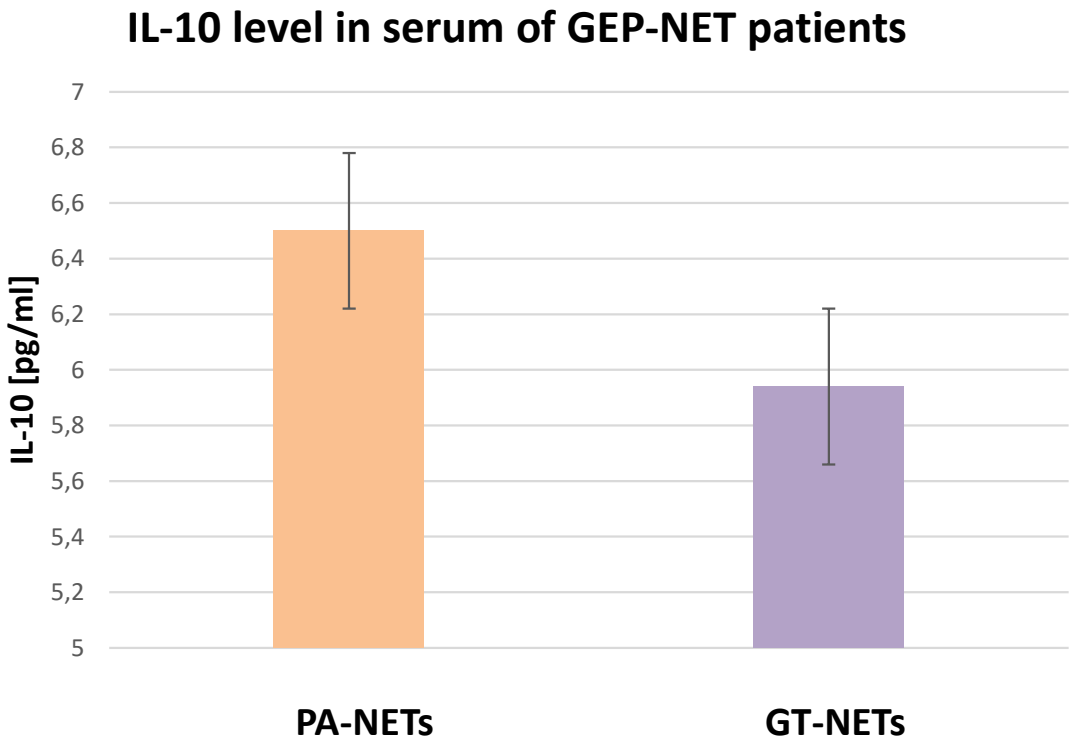
GT-NETs – gastrointestinal tract neuroendocrine tumors; MCP-1: monocyte chemoattractant protein-1; PA-NETs: pancreatic neuroendocrine tumors.

Results and discussion



The results are presented as the mean value ± SEM

- **Not statisticaly significant difference**

GT-NETs – gastrointestinal tract neuroendocrine tumors; IL-10: interleukin 10;
PA-NETs: pancreatic neuroendocrine tumors.

Conclusions

- An increased effect of pro-inflammatory factors on pancreatic neuroendocrine neoplasms compared to gastrointestinal neuroendocrine neoplasms has been observed.
- Levels of IL-6 and MCP-1, known as inducers of NET cell proliferation, were statistically higher in the PA group than in the GT group, but the concentration of IL-10, which is a factor inhibiting cytokine synthesis, did not show a significant difference between the GT and PA groups
- Inflammation has been found to play a role in the development of neuroendocrine tumors.

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