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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

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INSULINOMA OF THE TAIL OF THE PANCREAS – A CASE REPORT

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Abstract.

Insulinoma is a rare neuroendocrine functional tumor of the pancreas of unknown etiology which manifests itself through hypoglycemic symptoms which resolve by administering glycose. Common autonomic symptoms of insulinoma include diaphroresis, tremor, and palpitations, whereas neuroglycopenenic symptoms include confusion, behavioural changes, personality changes, visual disturbances, seizure, and coma. In most cases, these are benign solitary tumors of the pancreas, and in 5% of the cases they are associated with MEN1 syndrome. A characteristic of the diagnosis is the presence of hypoglycemia, and increased levels of C-peptide and insulin. Further radiological verification (non-invasive imaging procedures: computed tomography and magnetic resonance imaging; and invasive modalities, such as endoscopic ultrasonography and arterial stimulation venous sampling) of the tumor are required as well as its surgical extraction. We present a case of a middle-aged male with history of recurrent hypoglycemic episodes with vertigo, sweating, tremors, anxiety, fatigue, and loss of consciousness, all of which resolved after eating food. The diagnoses were confirmed after we performed non-invasive imaging procedure, such as Computed Tomography and Magnetic Resonance Imaging. The patient underwent successful resection of the tumor, and his symptoms showed complete resolution. Despite the low incidence of these tumors, they should be suspected, in cases where the patient presents with repetitive hypoglycemic episodes, with symptoms, which resolve after eating a meal. Timely diagnosis and adequate treatment in most cases equals to complete withdrawal of symptoms.

Key words. Insulinoma, pancreas, hypoglycemia, computed tomography, magnetic resonance imaging.

Introduction.

Insulinoma is a rare neuroendocrine functional tumor of unknown etiology, which is benign in its features but due to endogenous hyperinsulinemia is manifested by hypoglycemic episodes [1]. As many as 90% of insulinomas have been reported to be benign (usually small, well-encapsulated, solitary tumours), 90% are solitary, > 90% occur in intrapancreatic sites, and 90% are < 2 cm in diameter [2-4]. They are rarely associated with MEN1 syndrome (4-5%), and less than 10% are malignant. Insulinomas may occur at any age, mainly during the 5th decade of life, and show a slight female predominance [5]. The incidence is 1-32/1,000,000 cases annually [6]. Extra pancreatic insulinomas causing hypoglycemia are extremely rare (< 2%) and are most found in the duodenal wall [7]. The clinical presentation is with glycemic values <3.3 mmol/L and acute hypoglycemic symptoms that resolve after glucose administration [7].

Following biological and biochemical confirmation of an insulinoma, preoperative localization is sought using computed tomography (CT) [8], magnetic resonance imaging (MRI) [9], and endoscopic ultrasonography (EUS) [10,11]. Surgical resection is the primary treatment modality for insulinomas, and so accurate localization of the tumor before or during surgery is important. Intraoperative manual palpation of the pancreas by an experienced surgeon and intraoperative ultrasonography are both sensitive methods with which to localize insulinomas [12,13]. The presented case is a middle-aged male patient with history of recurrent hypoglycemic episodes accompanied by loss of consciousness, which had resolved after a successful resection of the tumorous changes.

Case Report.

A 62-year-old Caucasian male, presented at Outpatient Clinic, sought medical assistance due to vertigo, sweating, tremors, anxiety, fatigue, and loss of consciousness, with insidious onset over 4 weeks ago. The patient had already noted that his symptoms were ameliorated with eating. The patient did not have any history of chronic illness and surgeries and he was not receiving any drug therapy. The physical examination revealed afebrile patient, with blood pressure levels of 130/85mmHg, heart rate of 62 pulses/minute and SpO2 of 98%. The clinical examination did not reveal any abnormal findings and cardiorespiratory examinations were normal. Neurological examination did not reveal any focal deficit. His routine laboratory parameters were within the reference values. The patient underwent hormonal evaluation to assess the function of the pituitary, thyroid, and parathyroid glands. All findings were in reference values. Chest X-rays showed no abnormal findings. We performed these analyses for the differential diagnosis (among other things to rule out the diagnosis of MEN-1). The patient was advised to measure his glycemic levels during these episodes, and the measured values ranged between 1.6-2.5mmol/L during the given intervals. He was referred to an MRI of the abdomen, which presented a solitary oval change with clear margins at the tail of the pancreas with dimensions 21x16mm (Figures 1A, 1B, 1C). The same change was verified with ultrasound as oval hypoechoic change at the tail of the pancreas in direction of the pancreatic hilum, and even a more descriptive image was obtained with a multiphase CT series which showed enhanced contrast - hyperdensity at the arterial phase (Figure 1D). The radiological evaluation of the change indicates insulinoma at the pancreatic tail. Afterwards the patient was subjected to a fasting test, during which we measured insulinemia, glycaemia and c-peptide from peripheral venous blood at intervals of half an hour due to initial glycemic value <3.3mmol/L. We interrupted the test at the fourth hour because of deterioration of the patient's consciousness, presented with somnolence, decreased reflexes, and impaired cognition. The patient received an IV solution

of 5% dextrose and was given a meal. During the period from 09:20 h to 13:50 h, his insulinemia was ranging from 10.41 to 17.72 µIU/ml, glycemia ranging from 2.1 to 2.4 mmol/L and C-peptide levels ranging 2.47 – 3.75 ng/ml (Table 1).

Table 1. *Values of insulinemia, glycemia and c-peptide during the fasting test.*

Hour	Insulinemia	Glycaemia	C-peptide
09:20 h	17,72 µIU/ml	2.4 mmol/L	2.91 ng/ml
09:50 h	13.38 µIU/ml	2.1 mmol/L	2.86 ng/ml
10:20 h	13.73 µIU/ml	2.4 mmol/L	3.01 ng/ml
10:50 h	15.74 µIU/ml	2.4 mmol/L	3.17 ng/ml
11:20 h	14.83 µIU/ml	2.4 mmol/L	2.84 ng/ml
11:50 h	12.41 µIU/ml	2.4 mmol/L	2.78 ng/ml
12:20 h	10.41 µIU/ml	2.4 mmol/L	2.47 ng/ml
13:20 h	16.61 µIU/ml	2.4 mmol/L	3.23 ng/ml
13:50 h	16.61 µIU/ml	2.3 mmol/L	3.75 ng/ml

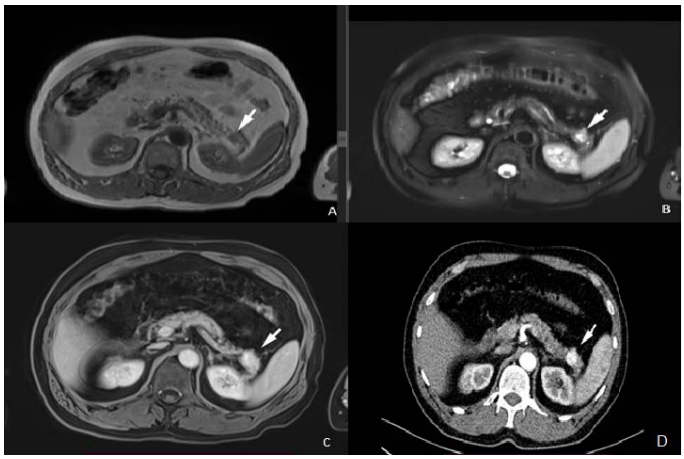

Figure 1. *Different imaging modalities that point the lesion. (A) MRI-T1 reveals oval lesion in pancreatic tail, shows predominantly low signal intensity (white arrow). (B) High signal on fat-suppressed T2-weighted image (white arrow). (C) MRI T1with contrast: Same lesion with typical enhancement on post-contrast T1 (white arrow). (D) CT contrast enhanced: Well defined pancreatic tail focal lesion, presents homogenous arterial enhancement (white arrow).*

The patient was advised to have an endoscopic ultrasound, but the patient refused to do it. We consulted digestive surgeon for possible resection of the tumor and the patient was advised to undergo urgent surgical treatment due to the increased frequency of the hypoglycemic episodes. After being discharged from our institution, the patient was referred to a digestive surgery clinic, where he underwent laparoscopic distal pancreatectomy with splenectomy, due to difficulties in perceiving spleen veins. The surgery was concluded without complications.

The retrieved operative material was forwarded for pathohistological examination, with reported macro- and microscopic findings, presented in figure 2. The operative material was provided in a vial containing a spleen segment and a pancreatic tail weighing 118.5 grams. Seven distinct spleen fragments were submitted in the same vial, the smallest measuring 2.5x2.1 cm, and the largest measuring 4x2.5x1.5 cm. The spleen was 8x6x2.5 cm large, and cross sections showed congestive changes. The tail of the pancreas was 5x2.5x2 cm in size. Serial sections of the pancreas revealed a 1.2x1 cm solid whitish nodule. Representative samples were taken and embedded in 11 paraffin blocks for pathohistological analysis. Microscopic analysis of the samples taken from the pancreatic nodule demonstrated benign neoplasm arranged in trabecular, tubulo-acinar, and solid growth pattern. The cells displayed a monotonous appearance, with eosinophilic granular cytoplasm, round to slightly oval nuclei, and salt and pepper-like chromatin. Additionally, neoplastic cells were separated by bands of collagenous, focally hyalinized tissue. The spleen was histologically unremarkable.

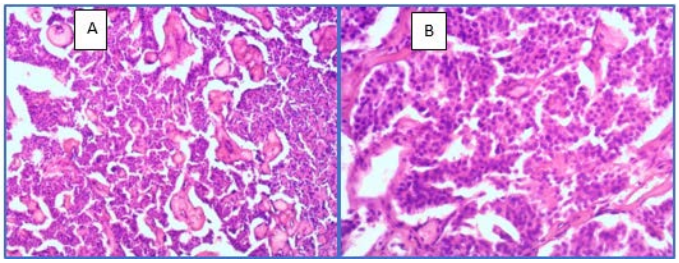

Figure 2*. Histopathological appearance of Insulinoma. A) Photomicrograph of the tumor demonstrating trabecular, tubulo-acinar, and solid growth pattern. (Haematoxylin-eosin, original magnification x 40) B) Photomicrograph of the cellular features of insulinoma. Neoplastic cells have eosinophilic granular cytoplasm, monotonous round to slightly oval nuclei and salt and pepper-like chromatin. (Haematoxylin-eosin, original magnification x 100).*

Clinically, the patient follow-up exam three months after surgery showed complete resolution of the symptoms and fasting glycaemia values range between 5,5 – 6,8 mmol/L. Postoperative insulin and C-peptide levels were not measured because of symptomatic improvement.

Discussion.

The presented case depicts the diagnostic process and the intervention behind this rare tumor. Initially, more common causes of persistent hypoglycemia were excluded. The patient findings revealed the widely known Whipple's triad: symptoms of hypoglycemia (in 85% of the cases), recorded low values of glycaemia during the symptoms and resolution of the symptoms after administering glycose. In our case, the symptoms of hypoglycemia were diplopia, tremor of the hands, palpitations. With lower values or persistence of hypoglycemia, confusion, amnesia, and loss of consciousness may ensue [14]. The persistence of hypoglycemia after initial treatment and the presence of the Whipple's triad lead to suspicion of insulin-secreting tumor. Insulinomas are diagnosed within less than 1.5 years from initial occurrence of symptoms [15]. Differential diagnosis covers psychiatric disorders, hepatic illnesses, autoimmune hypoglycemia, nesidioblastosis, or another insulin producing extra pancreatic tumors [15,16].

The golden standard for diagnosis of insulinoma is the 72-hour fasting test, with sensitivity of 90-95%, which is conducted in hospital conditions under strict medical supervision. Depending on the patient's symptoms, the levels of glycaemia, c-peptide and proinsulin are measured at different time intervals. The test is interpreted as positive if the values of glycaemia are

<2.2mmol/L, insulinemia > 10μIU/ml, c-peptide >2.5ng/ml and proinsulin ≥22 pmol/L [16].

Insulinomas are mostly benign solitary tumors of the pancreas. 5% of the cases are associated with MEN1 syndrome, which includes hyperplasia of the parathyroid gland, adenoma of the hypophysis and neuroendocrine tumor of the pancreas or duodenum. MEN1 syndrome is an autosomal dominant disease caused by mutation of the MEN1 gene of the 11th chromosome. Insulinomas associated with MEN1 are multicentric and develop earlier compared to sporadic insulinomas. If we suspect insulinoma associated with MEN1, additional investigations and genetic analyses should be made [7,17].

Further diagnostics of insulinoma would involve investigations to confirm the lesion by imaging techniques. Computer tomography and magnetic resonance imaging are the methods of choice with sensitivity exceeding 90%. If the insulinoma is not visualized, the following are further visualization techniques which may be indicated: Endoscopic ultrasound, trans-abdominal ultrasound, PET/CT scan with gallium-68-DoTa octreotate (Ga-DOTATATE) and somatostatin-receptor scintigraphy (Osteoscan SPECT). If these examinations are also negative, a selective arterial stimulation with calcium could be performed [18,19]. Imaging type may be limited to what is available at each institution.

Treatment of choice is surgical excision of the tumor, in most cases laparoscopically. In cases of difficult enucleation or malignant form of insulinoma, the approach is resection of the distal pancreas or the Whipple's approach (pancreatoduodenectomy) [17,19]. In cases of malignant insulinomas, an aggressive medical approach is used for enhancing the quality of life by preventing hypoglycemic episodes and improving survival [18,19].

In patients in whom a pancreatic lesion has not been confirmed with certainty and/or who due to comorbidities cannot undergo surgical treatment, pharmacological therapy may be administered for a period of time, including Diazoxide, Hydrochlorothiazide, Everolimus in patients with metastatic insulogram as well as chemotherapy in malignant forms. In half of the cases, depending on the presence of somatostatin receptors subtype 2 of tumor cells, a somatostatin analogue is included in the treatment (octreotide, pasireotide, lanreotide) [20]. After the surgical removal of the tumor, in most of the patients the symptoms completely resolve [17,18].

In the geriatric population, particularly in those above the age of 75, the treatment plan can be medical or surgical. Due to the higher risks of surgical and postsurgical complications in this population, patients and physicians should engage in shared medical decision-making [17-19]. Operative mortality is described in 3.7% and major postoperative morbidity in 33% of cases. The most common postoperative complications are pancreatitis, pancreatic pseudocysts, pancreatic leaks, and fistula [21-27].

Conclusion.

Insulinomas are a rare pancreatic endocrine tumor and disease but can threaten with severe neurologic damage and complications resulting from repeated hypoglycemia in patients. Insulinomas are a difficult diagnosis to make and require a high index of clinical suspicion focusing on the significant recurrent hypoglycemic episodes.

Despite the low incidence of these tumors, we should suspect them in cases where the patient presents with repetitive hypoglycemic episodes with symptoms, which resolve after eating a meal. Timely diagnosis and adequate treatment in most cases equals complete withdrawal of symptoms.

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