Journal Homepage: - www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI: 10.21474/IJAR01/xxx
DOI URL: http://dx.doi.org/10.21474/IJAR01/xxx
ISSN NO. 2320-5407

RESEARCH ARTICLE

INSULINOMA AND METABOLIC URGENCY CASE REPORT

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Manuscript Info

Manuscript History
Received: xxxxxxxxxxxxxxx
Final Accepted: xxxxxxxxxxx
Published: xxxxxxxxxxxxxxx

Key words:-
Insulinoma, Neuroendocrine Tumor, Hypoglycemia

Abstract

Insulinoma is a rare neuroendocrine tumor, occurring almost exclusively in the pancreas. Most often unique and benign in 90% of cases. Usually sporadic, 10% of lesions become part of type 1 multiple endocrine neoplasia. The main manifestation of insulinoma is hypoglycemia, which is a life-threatening metabolic emergency. The hypoglycemia occurring in this context are particularly serious and frequent with sometimes harmful cerebral consequences. Topographic diagnosis remains difficult due to the small size of the lesions justifying the importance of the preoperative imaging required for the location of the tumor. Enucleation is the surgical indication of choice in the presence of a sporadic insulinoma that is presumably benign. Pathological and immunohistochemical examination confirms the diagnosis of neuroendocrine tumor. Our observation is particular by the circumstances of discovery of the insulinoma, the severe nature of the symptoms.

Introduction:-

Insulinoma is the most common neuroendocrine tumor of the pancreas. This rare tumor is benign in 90% of cases and can lead to severe hypoglycemia impacting a patient's quality of life with this neurological sequelae. Usually sporadic, about 10% of lesions are seen in type 1 multiple endocrine neoplasia (MEN) [1]. The diagnosis is clinical and biological, the localization assessment necessary to guide the therapeutic action is difficult due to the small size of the lesions [2]. We report a case revealed by severe hypoglycemia which constitutes a metabolic emergency and a limiting factor of his quality of life.

Case report

This is a 44-year-old patient, a trader by profession, without personal pathological history.
He came complaining of hypoglycemic discomfort for 3 years preceded by neurovegetative and neuroglucopenic signs in particular asthenia, dizziness, headache, visual blurring with the notion of loss of consciousness that can go as far as hypoglycemic coma, confirmed by a fasting venous blood sugar level at 0.46 g /l. That was requiring admission to the emergency room. In addition, a head trauma causing the patient to cease all professional activity. The family history was not contributory and there was not similarly case.

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These discomforts occurring on an empty stomach and away from meals, unrelated to exertion, becoming more severe and frequent, at a rate of 3 to 4 episodes / week, giving way to re-sugaring. Physical examination was without particularities.

Before the Whipple triad, an insulinoma was evoked, confirmed by the biological profile of an inappropriate secretion of insulin and C peptide.

As part of the localization assessment, a pancreatic MRI revealed a nodular lesion of the pancreatic tail measuring 1.5cm.

A scintigraphic supplement carried out in particular with the OctreoScan revealed a unique hyperfixation corresponding to a tissue mass of the tail of the pancreas, compatible with a neuro-endocrine origin(figure 1) found on CT-coupled tomoscintigraphic sections (SPECT / CT) (figure 2, figure 3).

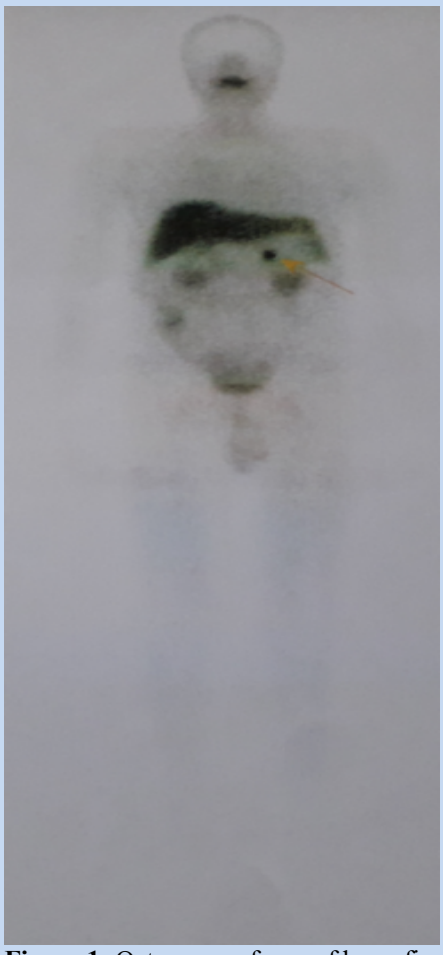

Figure 1: Octreoscan: focus of hyperfixation corresponding to a tissue mass of the tail of the pancreas, compatible with a neuro-endocrine origin.

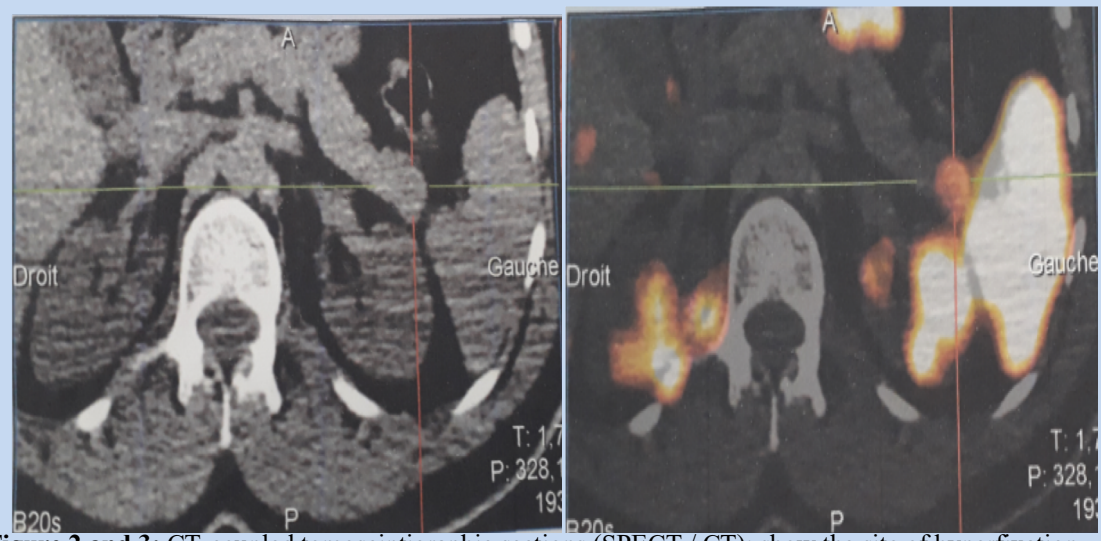

Figure 2 and 3: CT-coupled tomoscintigraphic sections (SPECT / CT): show the site of hyperfixation, corresponding to a tissue mass from the tail of the pancreas.

In addition, the results of NEM1 came back negative, no clinical or paraclinical evidence pointing to primary hyperparathyroidism or pituitary adenoma. The genetic assessment of NEM1 was not made.

A caudal pancreatectomy by laparotomy was performed with simple operative consequences, complete disappearance of hypoglycemia. The operative part was an ovoid one weighing 8g and measuring 3x2.2x1.3 cm (figure 4).

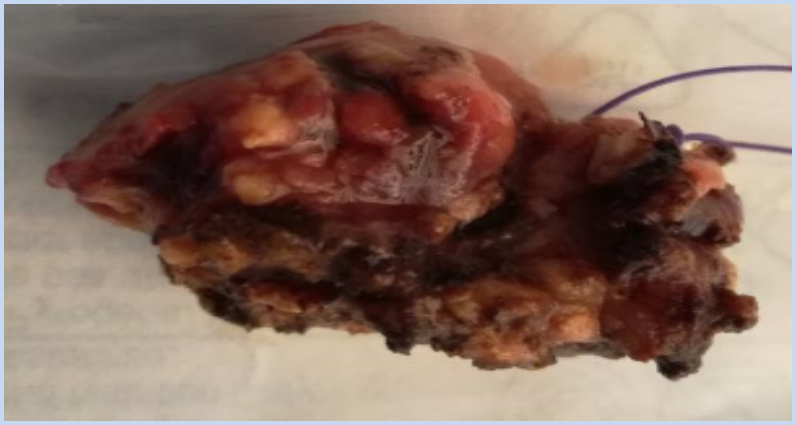

Figure 4: Operative part: ovoid pancreatic parenchyma weighing 8g and measuring 3x2.2x1.3 cm.

The anatomopathological study of the operative specimen showed a tumor proliferation infiltrating the pancreatic parenchyma, arranged in nests and clumps, tumor cells are monomorphic, the nucleus is discreetly irregular with a thin nucleolus, the cytoplasm is abundant and eosinophilic (figure 5). There were some medium sized monomorphic cells with stroma fibro-inflammatory reaction (Figure 6).It was also confirmed the neuroendocrine nature of the tumor with acytoplasmic and granular expression of chromogranin A and synaptophysin by tumor cells (figure 7). It

concluded in a tumor well differentiated, classified grade 2 according to the 2010 WHO classification with a Ki67 index of 2%. Healthy resection limits, with absence of necrosis and vascular embolism and classified as PT1NxMx (PTNM 2009).

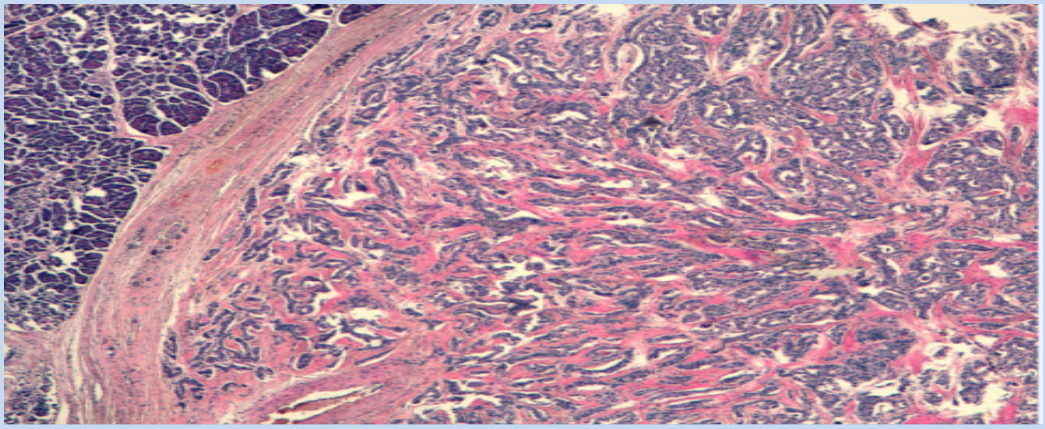

Figure 5: Tumor proliferation infiltrating the pancreatic parenchyma, arranged in nests and clumps; tumor cells are monomorphic, the nucleus is discreetly irregular with a thin nucleolus, the cytoplasm is abundant and eosinophilic.

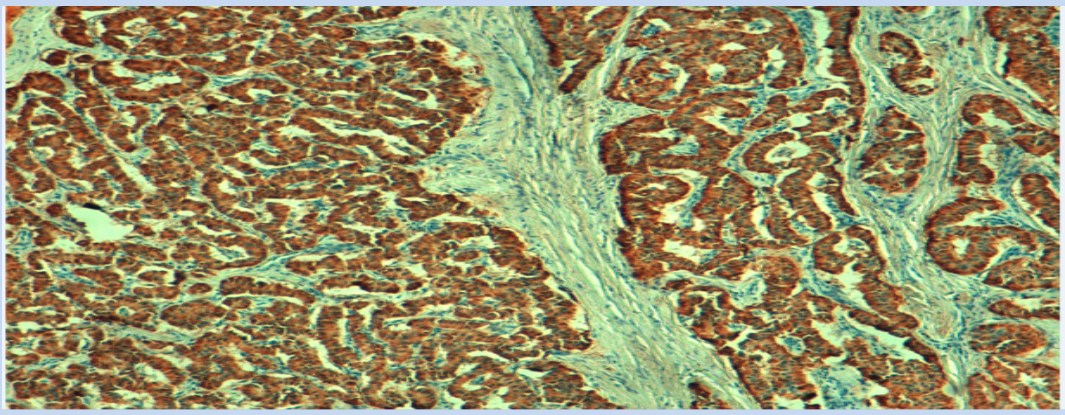

Figure 6: Medium sized monomorphic cells with stroma fibro-inflammatory reaction.

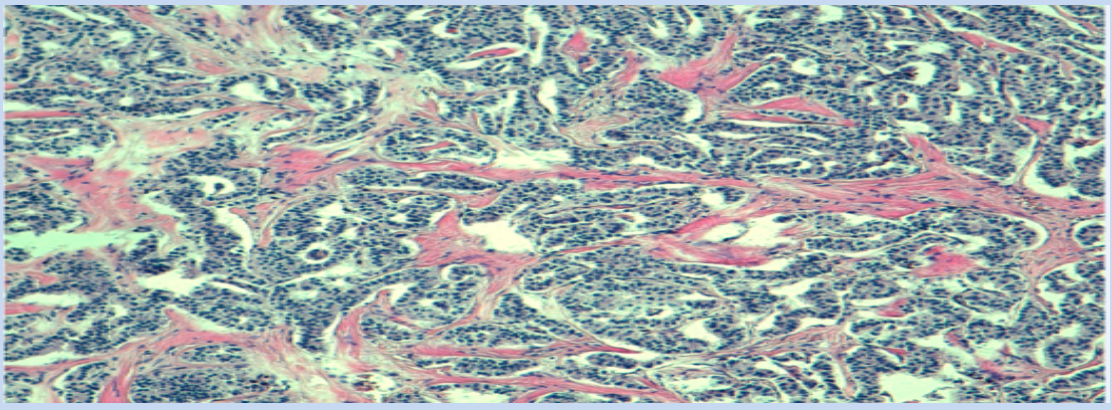

Figure 7: Cytoplasmic and granular expression of chromogranin A and synaptophysin by tumor cells .

The follow-up time was done by clinical and blood glucose monitoring

Discussion:-

Insulinoma remains a rare tumor, most series report an incidence of 0.5 to 1 case per 1 million patients per year [2,3]. It is the most common functional endocrine tumor of the pancreas. Often single and benign lesion in 90% of cases, malignant forms are rare and represent approximately 5-11% of cases [4].

The multiplicity of lesions must first suggest NEM1, found in 10% of cases [5], associating endocrine tumors of the parathyroid, the anterior pituitary sometimes the adrenal cortex, the thymus or the lung. No evidence for other endocrine damage was found in our patient.

The majority of patients with insulinoma are between 30 - 60 years old, an average age of 52 years with a female predominance as 59% [2,6]. Exceptionally reported in the elderly and children.

The diagnostic time is relatively long due to the lack of specific clinical signs, ranging from 12 to 18 months on average sometimes up to 30 months [6]. In the case of our patient, it was 3 years old. Symptoms reflecting hypoglycemia occur in particular on an empty stomach and away from meals. In our patient's case, the clinical picture was typical of a triad of Whipple, neuroglycopenic disorders with unconsciousness, hypoglycemic coma, multiple falls from height causing head trauma.

The laboratory diagnosis of insulinoma is based on the association of hypoglycemia with a high level of insulinemia and C peptide. In case of doubt, a youth test for up to 72 hours can be performed [7].

Topographic diagnosis is difficult due to the small size of the lesion. Insulinomas are always pancreatic with an average size less than 2 cm long axis in 90% of cases, well limited and hypervascular [6, 8].
The preoperative detection of these small lesions is essential for locating the tumor and asserting its uniqueness, in order to be able to determine the modalities of intervention. Non-invasive imaging techniques are preferred, but their sensitivity varies between studies. Thus, CT is the imaging method of first choice, in case of suspicion of pNT(pancreatic neuroendocrine tumor), with a sensitivity of over 80%, that of MRI even reaches 92% [1,8]. Preoperative endoscopy is performed by most teams, is the reference method for the detection of small pancreatic tumors (2-5 mm) and its sensitivity nevertheless remains very high, between 79% and 94%. Functional imaging with somatostatin analogues (OctreoScan) is currently the gold standard examination for the extension assessment of patients with neuroendocrine tumors, approximately 80-90% of pNTs express several somatostatin receptors (SSR) [9]. In the case of our patient, the diagnosis of insulinoma was confirmed by cross-sectional and functional imaging data (pancreatic MRI and OctreoScan) showing a nodular lesion measuring 1.5 cm with a single fixation opposite. of the tail of the pancreas.

In general, the search for a (NEM1) is essential, before any treatment of a neuroendocrine tumor of the pancreas. In this context of NEM1, the surgical strategy is different with the need for a total pancreatectomy with some exceptions [10].

The therapeutic objective is twofold, notably tumor excision and the control of hormonal secretions. Therefore, the use of surgery and / or tumor reduction are systematically proposed. Secretory control can be obtained with diazoxide (oral, 150–600 mg / day), usually sufficient preoperatively. In advanced forms or in cases of diazoxide intolerance (edema resistant to thiazide diuretics, hirsutism, nausea), Everolimus (5–10 mg / day) or somatostatin analogues are used as a second-line secretory symptomatic treatment due to their good tolerance and rapid action [11,12].

In the presence of a sporadic, presumably benign insulinoma, enucleation is generally the intervention of choice. This is indicated for tumors smaller than 2 cm.This helps to spare the pancreatic parenchyma and prevent postoperative diabetes. The operative method varies according to the topography of the lesion. A tail resection may be discussed if the lesion is in the tail of the pancreas or a midline pancreatectomy for lesions of the body of the pancreas. Duodenopancreatectomy, exceptionally indicated, in case of impossibility of enucleation for tumors located at the head of the pancreas. In the case of our patient, the surgical procedure consisted of a caudal pancreatectomy by laparotomy. Currently, the laparoscopic approach is often preferred, as it is better suited for the enucleation of an insulinoma located in the anterior part of the head, body and tail of the pancreas. After insulinoma removal, monitoring of normalization of insulinemia (half-life of 5 min) by rapid intraoperative dosages is not routinely used. The

maintenance of normal blood sugar levels when intravenous intakes have been stopped after the tumor has been removed, most often testifies to the completeness of the excision [13, 14,15].

Anatomopathological and immunohistochemical exploration confirms the diagnosis of neuroendocrine tumor (NET), the degree of differentiation, the histological grade according to the WHO classification (2010) and the pTNM according to the ENETS (2007) and WHO (2010) classifications. Insulinomas present as well-differentiated NETs in the majority of cases, and do not have cytoarchitectural features to differentiate them from other neuroendocrine tumors. Insulinoma considered to have an uncertain prognosis if the presence of one of the pathological criteria, in particular height greater than 2 centimeters or grade 2 according to the WHO classification (2010) or vascular and / or peri-nervous invasion or presence of necrosis. In addition, it is said to be benign if the abovementioned criteria are absent. The malignancy of the insulinoma is confirmed for tumors classified as grade 3 according to the WHO (2010) or by the demonstration of a relapse, of an extra-pancreatic or lymph node locoregional tumor extension or at a distance [5,15].

Conclusion:-

A common emergency symptom as hypoglycemia can reveal a serious metabolic disease. Insulinoma is a rare tumor that is usually small and benignbut impacts the quality of life. Its diagnosis is clinico-biological. The challenge of the management is to locate the tumor.

In general, enucleation remains the surgical indication of choice. Pancreatic resections are reserved for malignant or entering insulinomas in the setting of NEM 1.

Informed patient consent:
The patient's oral informed consent was taken.

Conflict of interest:
The authors declare no conflicts of interest.

Author contribution:
All authors contributed to the development of this work.

Figures:
Figure 1: Octreoscan: focus of hyperfixation corresponding to a tissue mass of the tail of the pancreas, compatible with a neuro-endocrine origin.
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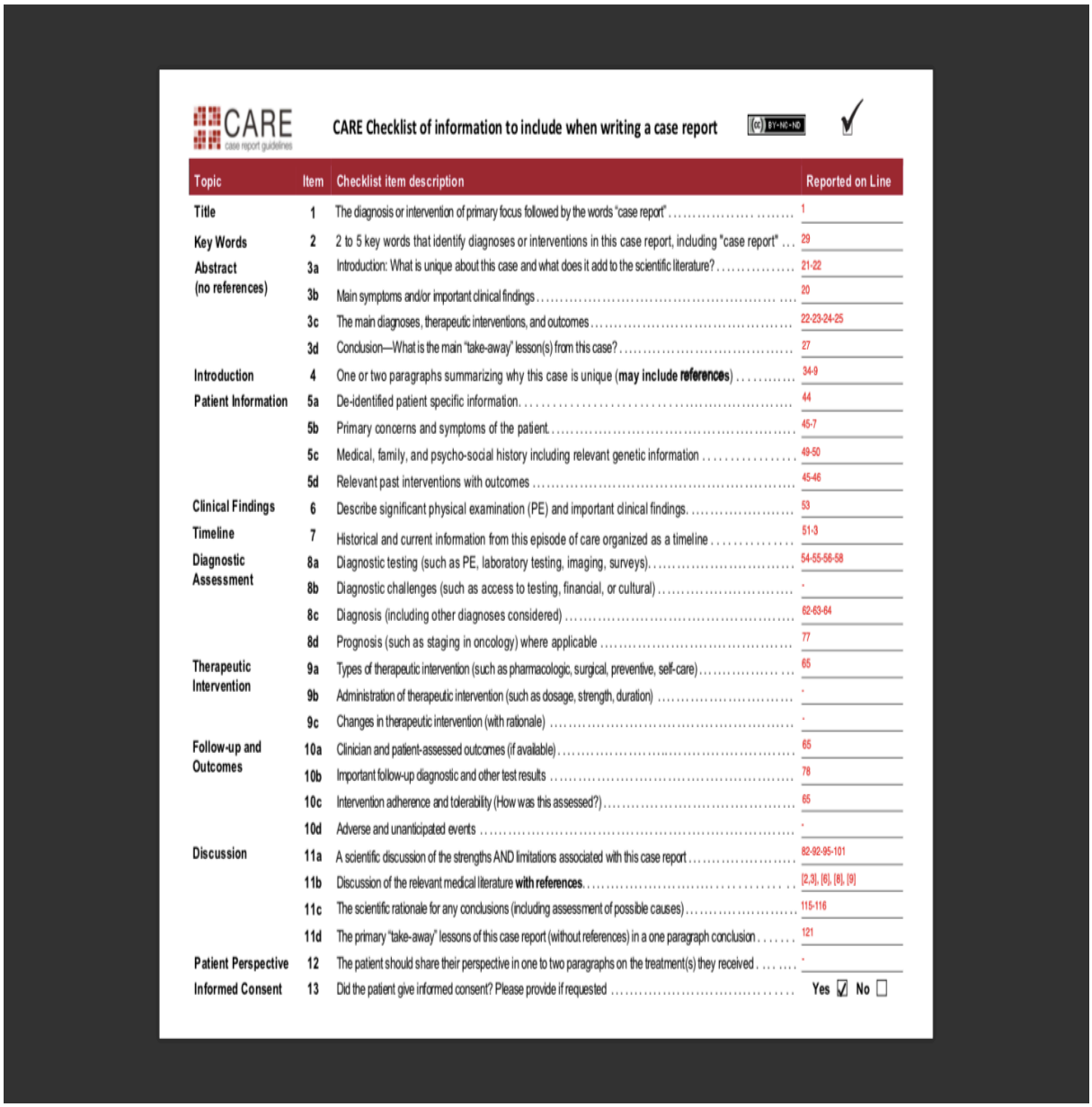

CARE case report guidelines

CARE Checklist of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Line
Title	1	The diagnosis or intervention of primary focus followed by the words "case report"	1
Key Words	2	2 to 5 key words that identify diagnoses or interventions in this case report, including "case report"	29
Abstract (no references)	3a	Introduction: What is unique about this case and what does it add to the scientific literature?	21-22
	3b	Main symptoms and/or important clinical findings	20
	3c	The main diagnoses, therapeutic interventions, and outcomes	22-23-24-25
	3d	Conclusion—What is the main "take-away" lesson(s) from this case?	27
Introduction	4	One or two paragraphs summarizing why this case is unique (**may include references**)	34-9
Patient Information	5a	De-identified patient specific information.	44
	5b	Primary concerns and symptoms of the patient.	45-7
	5c	Medical, family, and psycho-social history including relevant genetic information	49-50
	5d	Relevant past interventions with outcomes	45-46
Clinical Findings	6	Describe significant physical examination (PE) and important clinical findings.	53
Timeline	7	Historical and current information from this episode of care organized as a timeline	51-3
Diagnostic Assessment	8a	Diagnostic testing (such as PE, laboratory testing, imaging, surveys).	54-55-56-58
	8b	Diagnostic challenges (such as access to testing, financial, or cultural)	"
	8c	Diagnosis (including other diagnoses considered)	62-63-64
	8d	Prognosis (such as staging in oncology) where applicable	77
Therapeutic Intervention	9a	Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care)	65
	9b	Administration of therapeutic intervention (such as dosage, strength, duration)	"
	9c	Changes in therapeutic intervention (with rationale)	"
Follow-up and Outcomes	10a	Clinician and patient-assessed outcomes (if available)	65
	10b	Important follow-up diagnostic and other test results	78
	10c	Intervention adherence and tolerability (How was this assessed?)	65
	10d	Adverse and unanticipated events	"
Discussion	11a	A scientific discussion of the strengths AND limitations associated with this case report	82-92-95-101
	11b	Discussion of the relevant medical literature **with references**.	[2,3], [6], [8], [9]
	11c	The scientific rationale for any conclusions (including assessment of possible causes)	115-116
	11d	The primary "take-away" lessons of this case report (without references) in a one paragraph conclusion	121
Patient Perspective	12	The patient should share their perspective in one to two paragraphs on the treatment(s) they received	"
Informed Consent	13	Did the patient give informed consent? Please provide if requested	Yes ☑ No ☐

References:

1. SebbagSfezaD et al.Insulinome pédiculé au bord antérieur de la tête dupancréas : une localisation exceptionnelle à connaître. Journal de Radiologie Diagnostique et Interventionnelle. 2013; 94 :335-338. **Google Scholar**
2. Ketari-Jamoussi S, Debbiche-Chedly A, Ben Dhaou B, Boussema F, Cherif O, Cherif AR, Ben Ayed M, Bouzaine A, Rokbani L. Un insulinome géant : à propos d'un cas. Ann Endocrinol (Paris). 2009 Mar; 70(1):71-5.**PubMed** | **Google Scholar**
3. Bouslama K et al.L'insulinome pancréatique. J. Afr. Hépatol. Gastroentérol. 2014 ; 8:11-15. **Google Scholar**
4. MitryE. Tumeurs neuroendocrines digestives. EMC - Gastro-entérologie. 2013;8(4):1-13. **Google Scholar**
5. Al-Salameh A,Aparicio T, Cohen R. Tumeurs neuroendocrines digestives : mise au point. EMC -Endocrinologie -Nutrition. 2014 ;11(1) :1-11. **Google Scholar**
6. Cazabat L, Chanson P. Hypoglycémie et insulinome [Hypoglycemia and insulinoma]. Ann Endocrinol (Paris). 2009 Sep;70 Suppl 1:S2-11.**PubMed** | **Google Scholar**

7. van Bon AC, Benhadi N, Endert E, Fliers E, Wiersinga WM. Evaluation of endocrine tests. D: the prolonged fasting test for insulinoma. Neth J Med. 2009 Jul-Aug;67(7):274-8.**PubMed** | **Google Scholar**
8. Dromain C, Déandréis D, Scoazec JY, Goere D, Ducreux M, Baudin E, Tselikas L. Imaging of neuroendocrine tumors of the pancreas. DiagnInterv Imaging. 2016 Dec;97(12):1241-1257.**PubMed** | **Google Scholar**
9. Amador Cano A, García F, Espinoza A, Bezies N, Herrera E, De LeijaPortilla J. Nonfunctional neuroendocrine tumor of the pancreas: Case report and review of the literature. Int J Surg Case Rep. 2013;4(2):225-8.**PubMed** | **Google Scholar**
10. Falconi M, Bartsch DK, Eriksson B, Klöppel G, Lopes JM, O'Connor JM, Salazar R, Taal BG, Vullierme MP, O'Toole D; Barcelona Consensus Conference participants. ENETS Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms of the digestive system: well-differentiated pancreatic non-functioning tumors. Neuroendocrinology. 2012;95(2):120-34. **PubMed** | **Google Scholar**
11. Baudin E, Goere D, Caramella C, De Baere T, Deschamps F, Duvillard P, et al. Tumeurs neuroendocrines du pancréas : diagnostic caractérisation clinique pronostic et traitement EMC- hépatologie. 2013 ;8 (1) : 1-16. **Google Scholar**
12. Baudin E, Caron P, Lombard-Bohas C, Tabarin A, Mitry E, Reznick Y, Taieb D, Pattou F, Goudet P, Vezzosi D, Scoazec JY, Cadiot G, Borson-Chazot F, Do Cao C; pour la Société française d'endocrinologie et le Groupe d'étude des tumeurs endocrines. Recommandations pour la prise en charge de l'insulinome malin. Presse Med. 2014 Jun;43(6 Pt 1):645-59. **PubMed** | **Google Scholar**
13. Peix JL, Lifante JC. Stratégies et techniques dans le traitement chirurgical des tumeurs endocrines duodénopancréatiques. EMC-Techniques chirurgicales-Appareil digestif. 2014 ; 9 :1-9. **Google Scholar**
14. Jensen RT, Cadiot G, Brandi ML, de Herder WW, Kaltsas G, Komminoth P, Scoazec JY, Salazar R, Sauvanet A, Kianmanesh R; Barcelona Consensus Conference participants. ENETS Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms: functional pancreatic endocrine tumor syndromes. Neuroendocrinology. 2012;95(2):98-119.**PubMed** | **Google Scholar**
15. Anoun N, Hasnaoui H, Hassani FA, Idrissi MB, Ousadden A, Ouahabi HE, Taleb KA. Insulinome de haut grade découvert après 5 ans d'hypoglycémies graves. Pan Afr Med J. 2017 Aug 4;27:250.**PubMed** | **Google Scholar**.