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RESEARCH ARTICLE

CONTRIBUTION OF SOMATOSTATIN RECEPTOR SCINTIGRAPHY IN THE DIAGNOSIS OF DIGESTIVE NEUROENDOCRINE TUMORS: ANALYSIS OF 72 CASES

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Abstract

Digestive neuroendocrine tumors (DNETs), rare and accounting for 1–2% of digestive cancers, are diagnosed through a combination of biological tests,biopsy,and imaging. Somatostatin receptor scintigraphy (SRS) plays a key role in their detection. In this retrospective study conducted at Mohammed VI University Hospital in Marrakech between 2016 and 2021, 72 patients (mean age 54 ± 14.3 years, female predominance) were included. The main symptoms were abdominal pain and hypoglycemia. In 69 patients, 99mTc-octreotide SRS demonstrated a specificity of 91.6% and a sensitivity of 84.2%, with 71.4% for staging, outperforming CT for primary tumor localization (80.9% vs. 51.5%). Detection of insulinomas remained limited (50%). Primary tumors were mainly pancreatic and gastric, with metastases primarily hepatic and nodal. SRS remains a major tool for localizing primary tumors and small lesions,and the integration of complementary techniques, such as hybrid imaging, dual-tracer scintigraphy,and combined biological and histopathological evaluation, could improve sensitivity and allow earlier detection, which is essential for patient prognosis.

Introduction:-

Digestive neuroendocrine tumors (DNETs) are rare pathologies, representing approximately 1 to 2% of all digestive cancers. According to World Health Organization (WHO) data, it is estimated that there are around 40,000 new cases of DNETs per year worldwide. However, despite their low incidence, DNETs are aggressive pathologies that can cause significant morbidity and mortality. Indeed, the five-year survival rate of patients with DNETs is approximately 50 to 60%. The diagnosis of DNETs can be challenging, as the symptoms may be vague and nonspecific. The diagnosis is complex and relies on a combination of blood tests to detect tumor markers, imaging tests (CT, MRI, endoscopic ultrasound, etc.) to locate the tumor, and biopsy to confirm the diagnosis. Early and accurate diagnosis is therefore essential to improve patient survival, highlighting the importance of using an appropriate diagnostic imaging technique [1].Somatostatin receptor scintigraphy (SRS) is a molecular imaging technique that uses radiopharmaceuticals labeled with somatostatin analogues to detect the expression of

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somatostatin receptors on digestive neuroendocrine tumors. DNETs expressing these receptors, particularly type 2 (SSTR2), can be accurately detected by this technique, making it a useful method for the diagnosis and staging of DNETs.99mTc-octreotide scintigraphy is a diagnostic method that can be used to detect digestive neuroendocrine tumors. This method is based on the use of a radioactive tracer, Technetium-99m (99mTc) labeled with octreotide, administered intravenously and taken up by tumor cells. This technique allows visualization and localization of tumor lesions. Several studies have been conducted to evaluate the contribution of 99mTc-octreotide scintigraphy in the diagnosis of digestive NETs, with variable results [2]. The sensitivity of 99mTc-Tektrotyd scintigraphy for detecting primary tumors was 80%, specificity 92%, positive predictive value 98%, and negative predictive value 47%. A study by Zhang X. et al. (2015) reported a sensitivity of 88% and specificity of 93% for this method [3].
The objective of our study is to evaluate the effectiveness of somatostatin receptor scintigraphy (SRS) in the diagnosis of digestive neuroendocrine tumors (DNETs), by analyzing epidemiological data including frequency, age and sex distribution, and clinical signs. We will also assess the performance of SRS according to its indication using statistical tests, compare it with other diagnostic methods, and examine the concordance of our results with published data.

Patients and Methods:-

This is a retrospective study conducted at the Nuclear Medicine Department of Mohammed VI University Hospital in Marrakech over a six-year period, from January 2016 to December 2021. It included all patients who underwent somatostatin receptor scintigraphy as part of the assessment of digestive-origin neuroendocrine tumors (NETs).
Data collection was carried out with strict respect for patient anonymity and confidentiality of medical information. Within this framework, we collected epidemiological, clinical, biological, histopathological data, as well as information derived from somatostatin receptor scintigraphy, from medical records and departmental archives.

Inclusion criteria for this study were:

- Patients who underwent 99mTc-Tektrotyd somatostatin receptor scintigraphy.
- Adolescents and adults aged 15 years or older.
- Patients with histologically confirmed digestive NETs, or suspected based on clinical or biological evidence.
- Complete and usable records, including all necessary clinical, biological, and scintigraphic information.

Exclusion criteria included:

- Somatostatin receptor scintigraphy performed for non-digestive NETs.
- Incomplete or unusable records.
- Records lacking a scintigraphy report.

The collected data were subsequently analyzed to evaluate the diagnostic performance of somatostatin receptor scintigraphy in digestive neuroendocrine tumors, including its sensitivity, specificity, and overall clinical utility.

Results:-

Our series included 72 patients, comprising 42 women and 30 men, with a sex ratio of 0.71. Patient ages ranged from 15 to 89 years, with a mean of 54 years. The majority of patients (44.4%) were in the 46–60-year age group. Analysis by sex showed that women tended to develop the disease at a slightly older age, with 30.95% over 60 years and 40.47% between 46 and 60 years, whereas among men, 33.3% were over 60 years and 50% between 40 and 60 years. Socioeconomically, 88.9% of patients were of low level and 11.1% of medium level.Regarding medical history, most patients had a history of digestive neoplasia, observed in 46 patients, explained by the fact that many patients were undergoing restaging for a previously known digestive NET. The most frequent comorbidities were diabetes and arterial hypertension, each present in eight patients. Surgical history included thyroid surgery in two patients, cholecystectomy in one patient, and nephrectomy in one patient, while two patients were chronic smokers. Some family history was noted, including a father deceased from lung cancer and two cases of maternal diabetes.The circumstances of diagnosis were variable. The most frequent symptom was abdominal pain, observed in 20 patients, followed by recurrent hypoglycemia in 13 patients. Five patients presented with abdominal masses, four with chronic diarrhea, and three with general condition deterioration. A tumor syndrome was observed in two patients, while carcinoid syndrome, flushing, and intestinal obstruction were each found in one patient. In 22 cases, the discovery was incidental. Functionally, 20 patients had functional neuroendocrine tumors, including insulinomas, gastrinomas, and carcinoid tumors, whereas 52 patients had non-functional tumors.Laboratory evaluation, performed in most patients, revealed various abnormalities. Seven patients were anemic, four had hypoglycemia, four an inflammatory syndrome, three hypoproteinemia, and one patient hyperbilirubinemia. Tumor

markers were available for 51 patients; plasma chromogranin A was measured in 28 patients: normal in 14, moderately elevated (1.5 - 3 times normal) in nine, and highly elevated (> 3 times normal) in seven patients. Urinary 5-HIAA was measured in seven patients, positive in five. Among other markers, CA19-9 was abnormal in one patient out of eight, and CEA in two out of eight. Gastrin and insulin levels were measured in five and six patients, respectively, with abnormal results in four and five patients, respectively.

Functional medical imaging was essential for diagnosis and follow-up of digestive NETs. Somatostatin receptor scintigraphy labeled with technetium-99m (Tektrotyd®) was performed for all indications: screening in 18 patients, staging in seven patients, and restaging in 47 patients. After excluding three patients due to lack of Gold Standard, analysis included 69 patients. For screening, 15 patients were tested: eight positive and seven negative. For staging, among seven patients, five were positive and two negative. For restaging, among 47 patients, 36 were positive and 11 negative. The primary tumors detected were mainly pancreatic (11 cases), followed by duodenum (2), stomach (4), small intestine (3), colon (3), rectum (2), liver (1), mesentery (1), and ileocecal region (2). In the screening group, eight primary lesions were identified, including two in the duodenum and six in the pancreas.Overall, scintigraphy results compared to the Gold Standard showed 48 true positives (69.6%), one false positive (1.4%), 11 true negatives (15.9%), and nine false negatives (13%). This corresponded to a sensitivity of 84.2%, specificity of 91.6%, and positive predictive value of 97.9%. The ROC curve had an area under the curve of 0.879, and the Youden index was 0.758, reflecting good diagnostic performance.

Comparison with CT in 43 patients showed that scintigraphy had a sensitivity of 80.9%, superior to that of CT (51.5%), a statistically significant difference ($p = 0.012$, McNemar test). Scintigraphy was therefore more effective in detecting primary tumors.Analysis according to tumor grade (Ki67), available for 39 patients, showed better detection of low-grade tumors (Ki67 ≤ 20%). Among patients with Ki67 <3%, five had a positive scintigraphy and three negative. For Ki67 3–20%, 24 were positive and five negative; for Ki67 >20%, one patient was positive and one negative.Regarding insulinomas, among nine patients included, five had positive scintigraphy and four were false negatives, giving a sensitivity of 55.5%.Localization of primary tumors showed a pancreatic predominance (19 patients, 45.2%), followed by stomach and duodenum (four patients each). Three patients had undetected primaries but present metastases, and one patient had a hepatic primary tumor. Metastases were mainly hepatic (28 patients, 54.9%), nodal (9 patients, 17.6%), pulmonary (6 patients, 11.8%), and spinal (4 patients, 7.8%), with other isolated locations. Most patients with hepatic metastases had multiple lesions.

Other imaging studies showed that thoraco-abdominopelvic CT, performed in 43 patients, identified the primary tumor in 26, hepatic metastases in nine, and pulmonary metastases in five patients. Abdominal ultrasound, performed in 19 patients, was normal in seven and abnormal in 12, showing hypoechoic pancreatic or hepatic lesions. Hepatic MRI, performed in nine patients, revealed at least one hepatic lesion in eight patients. MR enterography identified the primary in seven out of nine patients examined. PET-FDG, performed in three patients, was positive in two and normal in one. Endoscopic examinations, performed in 13 patients, identified duodenal NETs, adenomatous polyps, and pancreatic nodules.Histological analysis, performed on 54 specimens (75%), showed mainly well-differentiated NETs in 20 patients, poorly differentiated or undifferentiated in four each, and unspecified in 26 patients. Histological grade, available for 39 patients, was G1 in eight, G2 in 29, and G3 in two. Immunohistochemistry Ki67 proliferation index, available in 39 patients, showed Ki67 <3% in eight, 3–20% in 29, and >20% in two.

Twenty-eight patients underwent surgery, with procedures varying according to tumor site, including pancreatectomies, intestinal resections, and hemicolectomies. One patient with unknown primary and multiple hepatic metastases underwent tumorectomy with resection of resectable lesions. Among systemic treatments, five patients received neoadjuvant chemotherapy, three postoperative. Three patients received somatostatin analogues preoperatively and one postoperatively.In summary, our descriptive analysis of 72 patients shows that 99mTc-labeled somatostatin receptor scintigraphy (Tektrotyd®) is an effective diagnostic tool for digestive neuroendocrine tumors, particularly for well-differentiated, low-grade tumors. Results highlight superior sensitivity compared to CT in detecting primary tumors, with performance varying according to tumor grade and type.

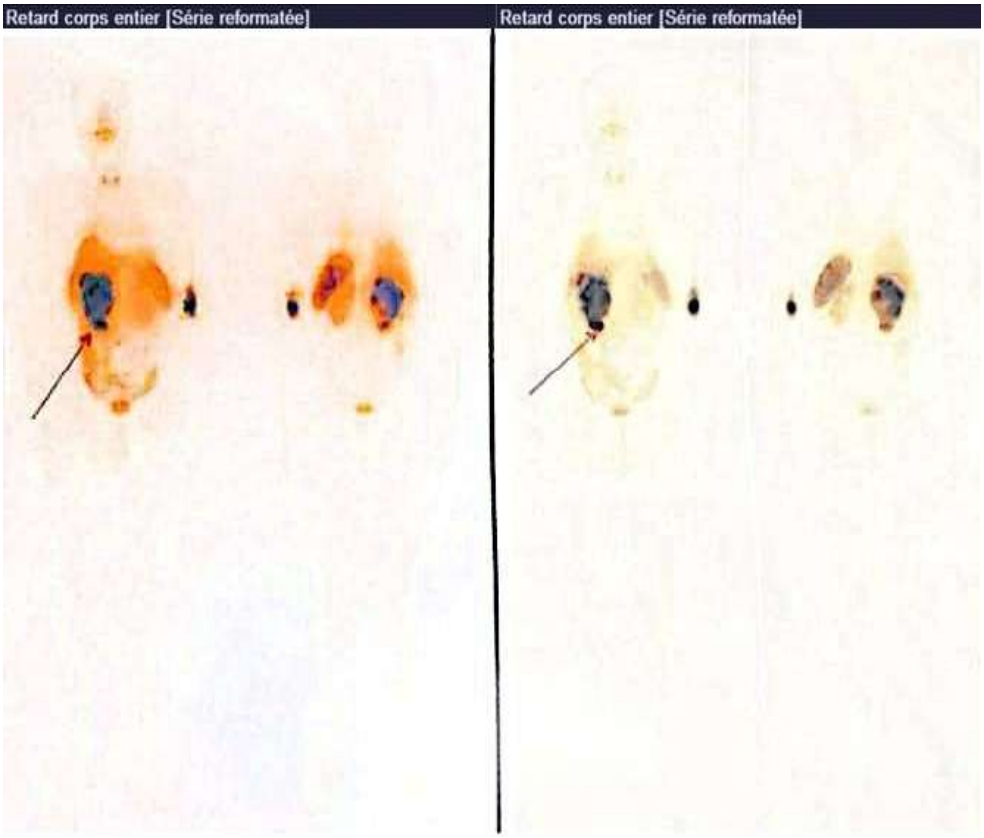

Figure 1 : Planar image of a 99mTc-Tektrotyd® scintigraphy showing a focus of hyperuptake localized in the pancreas «red arrow», with no evidence of hepatic metastatic involvement (representative case).

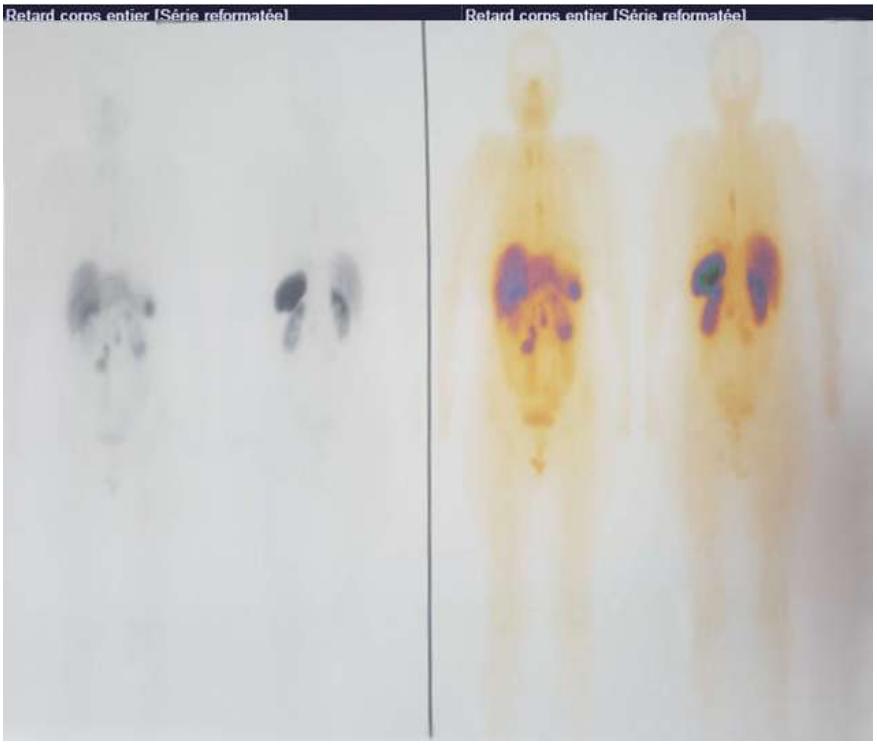

Figure 2 : Planar image of a 99mTc-Tektrotyd® scintigraphy showing multiple foci of hyperuptake localized in the umbilical region of the abdomen (representative case).

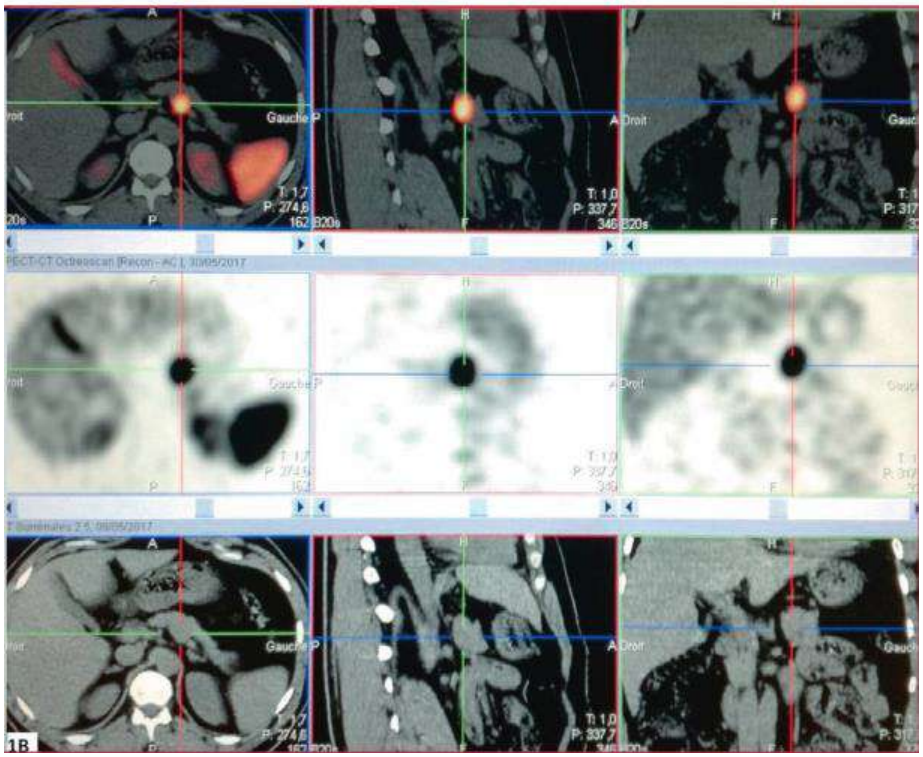

Figure 3 : SPECT/CT image of a 99mTc-Tektrotyd® scintigraphy showing a focus of hyperuptake at the junction of the isthmus and body of the pancreas, corresponding to an insulinoma (representative case).

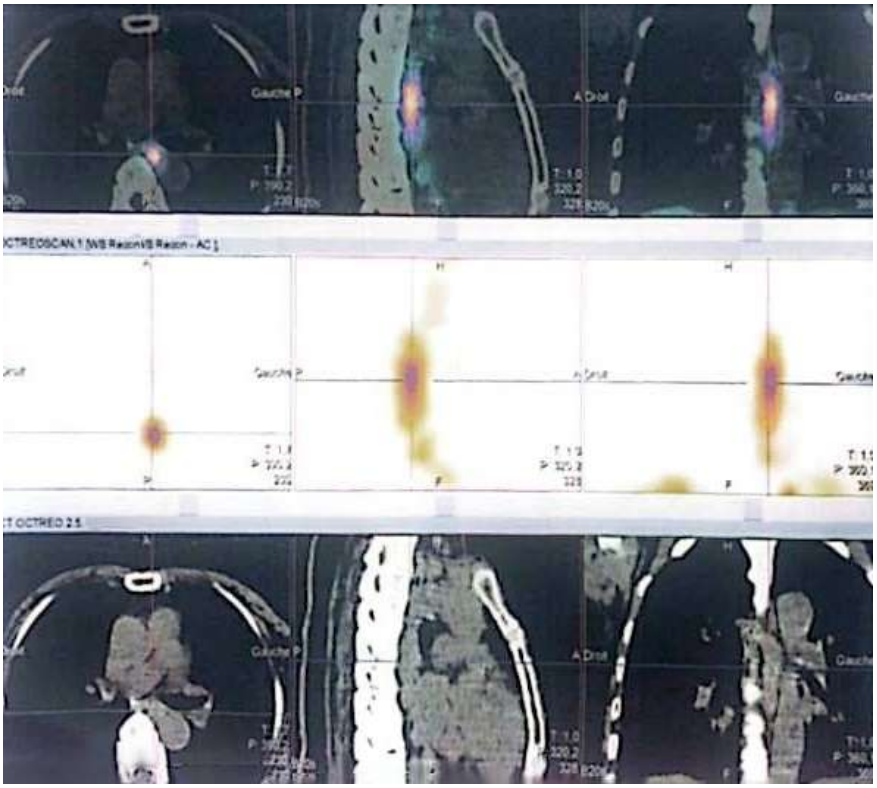

Figure 4 : SPECT/CT image of a 99mTc-Tektrotyd® scintigraphy showing tissue formations in the middle third of the esophagus (representative case).

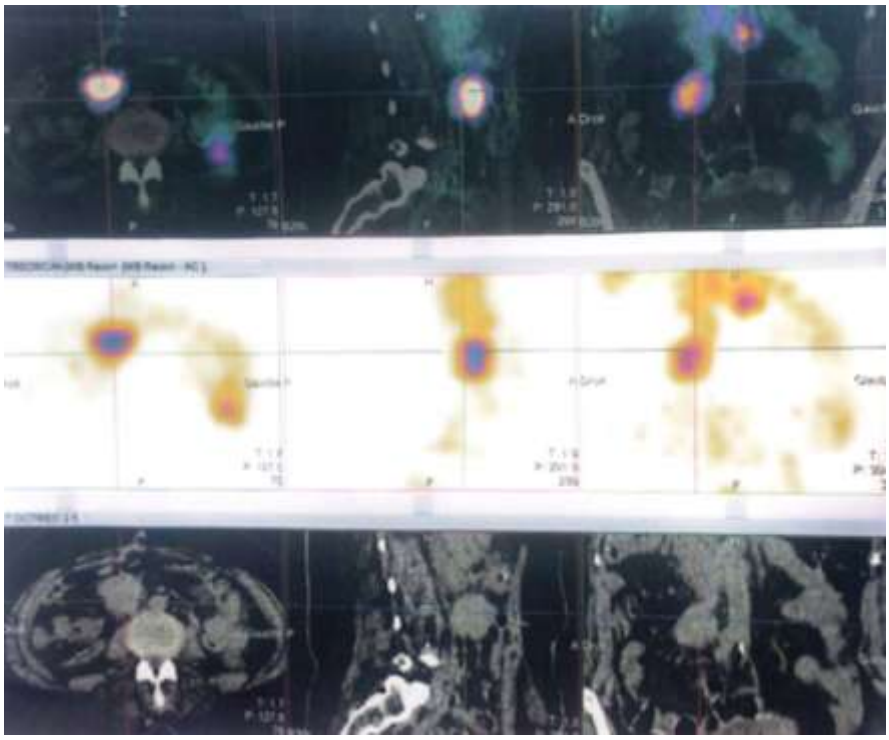

Figure 5: SPECT/CT image of a 99mTc-Tektrotyd® scintigraphy showing tissue formations in the middle third of the esophagus (representative case).

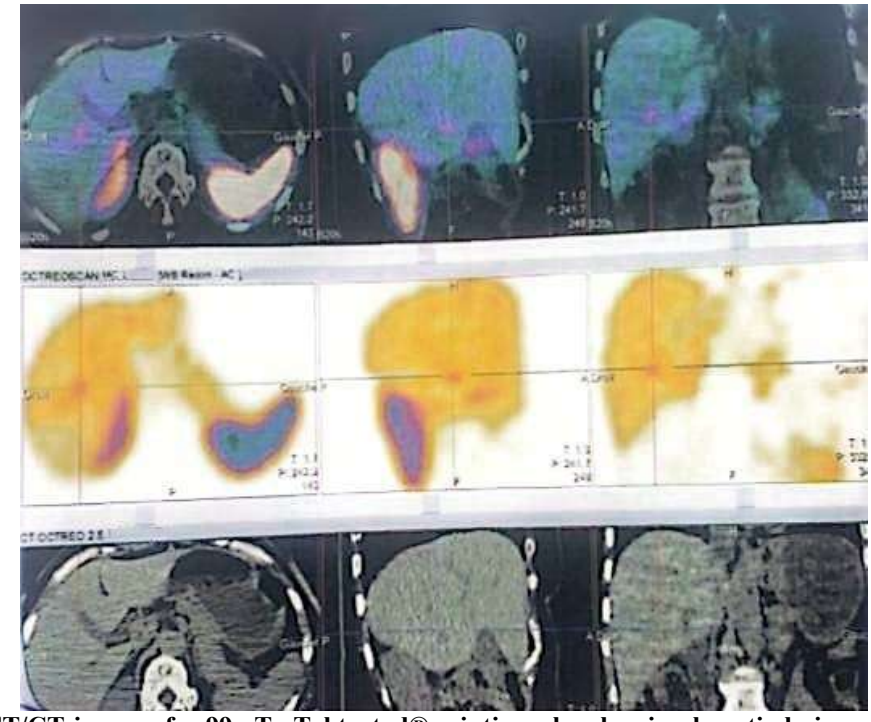

Figure 6: SPECT/CT image of a 99mTc-Tektrotyd® scintigraphy showing hepatic lesions corresponding to secondary metastases (representative case).

Discussion:-

In this single-center study of patients with digestive neuroendocrine tumors (NETs), somatostatin receptor scintigraphy using 99mTc Tektrotyd® demonstrated a significant diagnostic contribution, consistent with the

literature. The observed metastatic distribution—predominantly hepatic, followed by nodal, pulmonary, and osseous involvement—aligns with the findings of Lombard Bohas and Garcia Carbonero et al., identifying the liver as the major metastatic site [4,5].Conventional morphological imaging remains essential. Abdominal ultrasound, while accessible, has limited sensitivity (13–27 %) [6,7] and detected abnormalities in only a minority of patients. Thoraco-abdomino-pelvic CT (TAP-CT) retains a central role, with sensitivity for primary tumors ranging from 60 to 90 % and for hepatic metastases from 46 to 70 % [11,12]. Entero-CT is particularly useful for small bowel NETs not identified on standard CT, with sensitivity up to 84.7 % and specificity of 96.9 % [10]. In our cohort, it enabled localization of a mesenteric mass with small bowel thickening in one patient. MRI, particularly hepatic MRI, remains the most effective modality for detecting liver metastases, with reported sensitivity up to 95.2 % [11]. 18F-FDG PET is relevant for high-grade NETs, with average sensitivity of 58 %, reaching 78.6 % for aggressive neuroendocrine carcinomas [12,13]. Endoscopic explorations complemented the workup: 13 patients were examined, with upper GI endoscopy (FOGD) revealing duodenal NETs and polyps, and endoscopic ultrasound in three patients visualizing pancreatic nodules or a tumor process. These findings align with the literature, which reports sensitivity up to 88.5 % and specificity of 96.7 % [14,15].

From a histopathological perspective, analysis of samples in 75 % of cases revealed predominantly well-differentiated NETs, a proportion comparable to that reported by Garcia Carbonero et al. [5]. Ki-67 index, assessed in 39 patients, showed that most tumors were between 3 and 20 %, consistent with previous studies [5,16].Regarding treatment, the use of somatostatin analogues was limited, likely due to economic reasons, with only a few patients receiving pre- or post-operative therapy, in contrast to other series reporting 29 % of patients treated [5]. Nonetheless, their antisecretory and antiproliferative benefits are well established [17,18]. Chemotherapy was applied according to guidelines: streptozotocin or doxorubicin for well-differentiated tumors, cisplatin and etoposide for poorly differentiated forms [15,16].Finally, several prospects could improve diagnostic practice. Artificial intelligence applied to Tektrotyd® scintigraphy could enhance detection and interpretation, with reported sensitivity of 89.5 % and specificity of 87.8 % [19]. 68Ga-DOTATATE PET, offering higher resolution, could become the reference technique. The development of standardized protocols, the use of combined tracers, and monitoring with serum markers (chromogranin A) could further strengthen diagnostic accuracy and patient follow-up.

Conclusion:-

The diagnosis of digestive neuroendocrine tumors relies on a multidisciplinary approach integrating endocrinology, oncology, surgery, and nuclear medicine. Biological tests, although useful, lack specificity, while morphological imaging (CT, MRI) allows assessment of tumor size and extent but may be limited for slow-growing tumors. Somatostatin receptor scintigraphy represents an essential diagnostic tool, enabling localization of primary tumors and metastases, with particularly high sensitivity for tumors with a low proliferation index (Ki67 ≤ 20 %) and for gastric and pancreatic sites. In complement to conventional techniques, it contributes to early diagnosis and tailored therapeutic management, thereby optimizing patient prognosis.

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Authorship Contributions :

Medical Practices**:** S.E.A., H.A., A.A., M.A.B., A.M., Concept: S.E.A., Design: S.E.A., Data Collection or Processing: S.E.A., H.A., A.A., Analysis or Interpretation: S.E.A., H.A., A.A., M.A.B., A.M., Literature Search: S.E.A., H.A., A.A., Writing: S.E.A., H.A., A.A.,

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Declaration

Conflict of interest :

All the authors (Saad Eddine Abaid, Hamza Alaoui, Amine Azenzoul, Mohammed Aziz Bsiss, Aboubaker Matrane) declare that there is no confict of interest that could be perceived as prejudicing the impartiality of the research reported.

Informed consent: Written informed consent was obtained prospectively from the patients for the use of their clinical data.

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