СРПСКИ АРХИВ
ЗА ЦЕЛОКУПНО ЛЕКАРСТВО
SERBIAN ARCHIVES
OF MEDICINE

Address: 1 Kraljice Natalije Street, Belgrade 11000, Serbia
☏ +381 11 4092 776, Fax: +381 11 3348 653
E-mail: office@srpskiarhiv.rs, Web address: www.srpskiarhiv.rs

Paper Accepted*

ISSN Online 2406-0895

Case Report / Приказ болесника

Ljiljana Zivgarević†, Nebojša Kozarević, Svetlana Žunić

18F-FDG PET/CT "Hepatic Superscan" in incomplete Carney's triad

18*F-FDG PET/CT* суперскен јетре у некомплетној Карнијевој тријади

Clinical Center of Serbia, Center of Nuclear Medicine, National PET Center, Belgrade, Serbia

Received: September 12, 2019
Accepted: October 23, 2019
Online First: October 30, 2019
DOI: https://doi.org/10.2298/SARH190912117Z

†**Correspondence to:**
Ljiljana ZIVGAREVIĆ
Clinical Center of Serbia, National PET Center, Višegradska 26, 11000 Belgrade, Serbia
E-mail: **ljzivgarevic@gmail.com**

18F-FDG PET/CT "Hepatic Superscan" in incomplete Carney's triad

18*F-FDG PET/CT* суперскен јетре у некомплетној Карнијевој тријади

SUMMARY

Introduction Carney triad is a rare non-hereditary condition characterized by gastrointestinal stromal tumors (GIST) – intramural mesenchymal tumors of the gastrointestinal tract with neuronal or neural crest cell origin), pulmonary chondromas and extra-adrenal paragangliomas. The term incomplete Carney Triad more precisely refers to the occurrence of at least 2 of these tumor types. Carney triad named after J. Aidan Carney is considered to be a specific type of multiple endocrine neoplasia (MEN). Less than 30 cases of complete and less than 100 cases of incomplete Carney triad have been reported worldwide. Carney's triad primarily affects young women (mean age of onset of 20 years).

Case outline A 35 years old female patient has an initial presentation at National PET Center, Clinical Center of Serbia, after the gastrectomy, with multiple hepatic metastases as well as bilateral pulmonary chondromas. 18F-FDG PET/CT scan revealed the following: 1. intense 18F-FDG uptake in the liver metastatic lesions, with reduced physiological activity in the brain and heart, bowel, and renal tracer uptakes commonly known as FDG hepatic superscan; 2. multiple irregular shaped lesions, mostly calcified in bilateral pulmonary parenchyma; 3. a nodular lesion in the left adrenal gland with accumulation 18F-FDG in its anterior part.

Conclusion The present report describes hepatic superscan in the patient with incomplete Carney Triad, including gastric GIST and pulmonary bilateral chondromas, as well as a tumor in the left adrenal gland.

Keywords: GIST; 18F-FDG PET/CT; hepatic superscan; Carney triad; tartrate-resistant acid phosphatase

САЖЕТАК

Увод Карнијева тријада је ретко нехередитарно обољење које се карактерише присуством гастроинтестиналног стромалног тумора (ГИСТ) – (интрамурални мезенхимални тумори гастроинтестиналног тракта порекла неуралног гребена), присуством хондрома у плућном ткиву и екстраадреналних параганглиома. Прецизније, медицински ентитет под називом некомплетна Карнијева тријада односи се на присутност најмање два од наведених типова тумора. Карнијева тријада је добила назив по Ј. Ејдану Карнију (*J. Aidan Carney*) и сматра се специфичним типом мултипле ендокрине неоплазије. До сада је публиковано мање од 30 случајева комплетне и мање од 100 случајева некомплетне Карнијеве тријаде. Карнијева тријада се најчешће појављује код млађих особа женског пола (просечне животне доби око 20 година).

Приказ болесника Болесница старости 35 година упућена је на испитивање у Национални *PET* центар Клиничког центра Србије, после гастректомије, са налазом бројних метастаза у јетри и билатералним плућним хондромима. 18*F-FDG PET/CT*
студијом је доказано присуство следећег: 1. интензивно везивање 18*F-FDG* у бројним метастазама у јетри, са редукованим везивањем у мозгу, срцу, цревима и бубрезима, што одговара опису *FDG* суперскена јетре; 2. мултипле лезије неправилног облика, највећим делом калцификоване, са мањим уделом мекоткивне компоненте, обострано у плућном паренхиму; 3. нодуларне лезије у левој надбубрежној жлезди која у свом антериорном делу појачано накупља 18 *FDG*.

Закључак Овај приказ описује налаз суперскена јетре код пацијенткиње са некомплетном Карнијевом тријадом која у конкретном случају укључује желудачни ГИСТ и билатералне хондроме у плућима, као и присуство тумора у левој надбубрежној жлезди.

Кључне речи: ГИСТ; 18*F-FDG PET/CT*; суперскен јетре; Карнијева тријада; тартрат-резистентна кисела фосфатаза

INTRODUCTION

Carney triad (CT) was described firstly by Carney and coworkers in 1977 [1]. This medical entity (the triad of paragangliomas, gastric stromal tumors and pulmonary chondromas), named Carney triad was latter distinguished from the dyad of paragangliomas and gastric stromal sarcomas (Carney-Stratakis syndrome) [2]. Carney triad belongs to the group of rare diseases [3, 4]. GISTs are generally Kit (CD117)-positive, mesenchymal tumors of the gastrointestinal tract [5].

The molecular basis of GIST, is important for the understanding of GIST biology [6].

GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract with malignant potential. They can be associated with synchronous tumors of different histogenesis, although uncommonly [7]. In some cases, these tumors can be of neuroendocrine origin [8].

According to the publication of Ignjatovic (2002), about 55% of GIST had malignant behavior [9]. Correct diagnosis of GIST was based on immunohistochemical studies and biological behavior upon the clinicopathological parameters in 90% of cases [9]. We report the visualization of incomplete Carney triad in 18F-FDG PET/CT study in GIST postoperative phase and try to understand the anticipated coexpression of tartrate-resistant acid phosphatase in different organs, as they are liver and lungs.

CASE REPORT

A 35 years old female patient has had an initial presentation at National PET Center, Clinical Center of Serbia. Her medical history revealed GIST which was diagnosed in 1989 and followed with surgery (subtotal gastrectomy at the age of 8, as well as total gastrectomy at the age of 23 years old). The disease has worsened in spite of surgery and chemotherapy and recent clinical examination showed multiple hepatic metastases and bilateral pulmonary chondromas.

After the patient's fasting 6 hours before the PET/CT study, and the median cubital vein cannulation, injection dose of 200 MBq 18F-FDG was applied, followed with the 90 minutes data acquisition. 18F-FDG PET/CT examination on a 64-slice hybrid PET/CT

scanner (Biograph; Siemens Medical Solutions USA Inc) was performed 90 min after tracer application. A 3-dimensional PET scan (3 min per bed position) and low-dose no enhanced CT scan was acquired from the base of the skull to the mid-thigh. MDCT was acquired with 120 kV and with automatic, real-time dose modulation amperage (CareDose4D [Siemens], with the baseline being 45 mA) (slice thickness of 5 mm; the pitch of 1.5; and a rotation time of 0.5s). CT, PET (attenuation-corrected), and combined PET/CT images were displayed for analysis on a single Multimodality Workplace (Siemens AG).

The study revealed elevated right semi-diaphragm with heart dislocation to left hemithorax (figure 1).

There are multiple irregular shaped lesions in bilateral pulmonary parenchyma, mostly calcified, a partially consisted from soft component, without increased uptake of 18F-FDG: 1. a single calcified (616 HU), diameter lesion 13x12x16mm (APxLLxKK) in apical segment of upper lobe of the right lung; 2. calcified (814 HU) lesion, soft tissue (57 HU), diameter lesion 36x33x33mm (APxLLxKK) perivascular paratracheal right at the level Th3/Th4; 3. A single calcified lesion (540 HU), soft tissue (44 HU), diameter lesion 25x25x41mm (APxLLxKK) was in the anterior segment of the upper lobe of the right lung; 4. A single calcified lesion (831 HU), soft tissue (71 HU), diameter lesion 35x30x23mm (APxLLxKK) was in a lateral segment of the middle lobe of the right lung; 5. A single calcified lesion (652 HU), soft tissue (57 HU), diameter lesion 20x18x18mm (APxLLxKK) was in the anterobasal segment of the low lobe of the left lung (figure 2).

Augmented liver 20x24x27cm (APxLLxKK) contained multiple single and confluent hypodense lesions with intense uptake of 18F-FDG (SUVmax 27.0) and lesions without any uptake of 18F-FDG reflecting areas of necrosis in the “Hepatic Superscan” (figure 1c, figure 3).

There is a nodular lesion 30x12mm (APxLL) with the intense accumulation of 18F-FDG (SUVmax 21.0) near medial contour of the anterior part of the spleen (figure 4).

The right kidney is dislocated caudally (level L3/L5) (figure 3B). There is a nodular lesion diameter 31x16x21mm (APxLLxKK) in the left adrenal gland with accumulation 18F-FDG (SUVmax 3.1), in the anterior part of the nodular lesion (figure 5).

Diffuse intense 18F-fluorodeoxyglucose (18F-FDG) uptake in the liver on positron emission tomography, with reduced physiological activity in the brain and heart, bowel, and renal tracer uptakes commonly known as FDG hepatic superscan (figure 1c) [10, 11].

DISCUSSION

Multiple neoplasia syndromes are often considered with the presentation of multiple rare primary tumors in young patients. It is important to recognize the possibility of other primary tumors when associated neoplasms are detected [12]. The term Carney triad refers to the occurrence of at least 2 of the following tumor types: gastrointestinal stromal tumor (GIST); pulmonary chondroma; extra-adrenal paraganglioma. In a small percentage of affected patients, either of these other tumors may also occur adrenocortical adenoma (a benign tumor of the adrenal gland) and esophageal leiomyoma (a benign tumor of the esophagus) [13]. The Carney triad is an extremely rare syndrome, with fewer than 30 cases reported with all three tumors present, and fewer than 100 incomplete cases having two of the three tumor types present [13]. According to Carney (1999), chondromas developed in 76% of patients [13].

The present report describes the patient with incomplete Carney Triad, including GIST and pulmonary bilateral pulmonary chondromas, as well as the tumor in the left adrenal gland. This is a demonstration of the 18F-FDG PET/CT utility in diagnosis/differential diagnosis some of the rare diseases. The hepatic superscan was demonstrated in the reported case of incomplete Carney Triad.

The multiorgan (liver, lungs) molecular coexpression of tartrate-resistant acid phosphatase (TRAP) (ACP5) in immunocytes belonging to monocyte/macrophage lineage should be anticipated as of importance in the pathogenesis of this clinical case. Physiologically, TRAP is primarily a cytochemical marker of macrophages, osteoclasts, and dendritic cells [14]. Under normal circumstances, TRAP is highly expressed by osteoclasts, activated macrophages, neurons, and by the porcine endometrium during pregnancy [15, 16]. In newborn rats, TRAP is also detectable in the spleen, thymus, liver, kidneys, skin, lung, and heart at low levels. TRAP expression is increased in certain pathological conditions. These include leukemic reticuloendotheliosis (hairy cell leukaemia), Gaucher's disease, HIV-

induced encephalopathy, osteoclastoma and osteoporosis, and metabolic bone diseases (available at https://en.wikipedia.org/wiki/Tartrate-resistant_acid_phosphatase).

Tartrate-resistant acid phosphatase is a glycosylated monomeric metalloprotein enzyme expressed in mammals [17], and characteristic for its expression in activated osteoclasts and macrophages, has proposed as a driver of metastasis and was associated with clinically relevant parameters of cancer progression and cancer aggressiveness [18].

The coexistence of an adrenal tumor with incomplete Carney triad indicates the possible neuroendocrine origin and belonging to multiple endocrine neoplasia syndromes.

Conflict of interest: None declared.

REFERENCES

1 Carney JA, Sheps SG, Go VL, Gordon H. The triad of gastric leiomyosarcoma, functioning extra-adrenal paraganglioma and pulmonary chondroma. N Engl J Med. 1977 Jun 30;296(26):1517-8. PMID: 865533; DOI:10.1056/NEJM197706302962609.

2 Stratakis CA, Carney JA. The triad of paragangliomas, gastric stromal tumours and pulmonary chondromas (Carney triad), and the dyad of paragangliomas and gastric stromal sarcomas (Carney-Stratakis syndrome): molecular genetics and clinical implications. J Intern Med. 2009;266(1):43. PMID: 19522824 doi: 10.1111/j.1365-2796.2009.02110.x

3 NCATS, GARD. [Cited 2019 Sep 05]. Available from: https://rarediseases.info.nih.gov/diseases/10924/carney-triad.

4 Nilsson B, Bümming P, Meis-Kindblom JM, Odén A, Dortok A, Gustavsson B, et al. Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era. Cancer. 2005 Feb 15;103:821–829. PMID:15648083; DOI:10.1002/cncr.20862.

5 Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. Arch Pathol Lab Med. 2006 Nov 01;130(10):1466–78. PMID: 17090188; DOI:10.1043/1543-2165(2006)130[1466:GSTROM]2.0.CO;2

6 Niinuma T, Suzuki H, Sugai T. Molecular characterization and pathogenesis of gastrointestinal stromal tumor. Transl Gastroenterol Hepatol. 2018 Jan;3:2. PMID: 29441367; PMCID: PMC5803009; doi: 10.21037/tgh.2018.01.02.

7 Kaur R, Bhalla S, Nundy S, Jain S. Synchronous gastric gastrointestinal stromal tumor (GIST) and other primary neoplasms of gastrointestinal tract: report of two cases. Annals of gastroenterology. 2013;26(4), 356–359. PMID:24714328.

8 Pusiol T, Zorzi MG, Morichetti G, Piscioli I, Scialpi M. Synchronous nonfunctional duodenal carcinoid and high risk gastrointestinal stromal tumour (GIST) of the stomach. Europ Rev Med Pharmacol Sciences. 2011;15:583–585. PMID: 21744758

9 Ignjatovic, M. Gastrointestinal stromal tumors. Vojnosanit Pregl. 2002;59(2):183-202. PMID:12053473

10 Wong SS, Yuen HY, Ahuja AT. Hepatic tuberculosis: a rare cause of fluorodeoxyglucose hepatic superscan with background suppression on positron emission tomography. Singapore Med J. 2014;55(7):e101-3. PMID: 24347039; doi: 10.11622/smedj.2013237.

11 Moriarty HK, Buckley BW, Ridge CA. "Hepatic Superscan" on a PET- CT scan of a patient with metastatic breast carcinoma. Nucl Med Biomed Imaging, 2017;2(2):1-2. DOI: 10.15761/NMBI.1000120.

12 Morales, I; Gupta, S; Gilbert, B; Thomson, N; Keshavamurthy, J. A Rare Case of Carney Triad. Chest. 2017 Oct; 152(4) Suppl: A589. DOI:http://dx.doi.org/10.1016/j.chest.2017.08.620.

13 GIST Support International. Carney Triad. [Cited 22 Apr 2019]. Available at http://www.gistsupport.org/about-gist/sdh-deficient-amp-wildtype-gist/carney-triad-summary/.

14 Lamp EC, Drexler HG. Biology of Tartrate-Resistant Acid Phosphatase, Leukemia Lymphoma. 2000;39(5-6):477-484. PMID: 11342331; DOI: 10.3109/10428190009113378.

15 Burstone MS. Histochemical demonstration of acid phosphatase activity in osteoclasts. J. Histochem. Cytochem. 1959 Jan 1;7(1):39–41. PMID 13664936; doi:10.1177/7.1.39.

16 Minkin C. Bone acid phosphatase: tartrate-resistant acid phosphatase as a marker of osteoclast function. Calcif Tissue Int. 1982;34(1):285–90. PMID 6809291; doi:10.1007/BF02411252.

17 Baumbach GA, Saunders PT, Ketcham CM, Bazer FW, Roberts RM. Uteroferrin contains complex and high mannose-type oligosaccharides when synthesized in vitro. Mol Cell Biochem. 1991;105(2):107–17. PMID 1922010; doi:10.1007/bf00227750.

18 Reithmeier A, Panizza E, Krumpel M, Orre LM, Branca RMM, Lehtiö J, et al. Tartrate-resistant acid phosphatase (TRAP/ACP5) promotes metastasis-related properties via TGFβ2/TβR and CD44 in MDA-MB-231 breast cancer cells. BMC Cancer. 2017 Sep 15;7(1):650. PMID: 28915803; PMCID: PMC5602878; doi: 10.1186/s12885-017-3616-7..

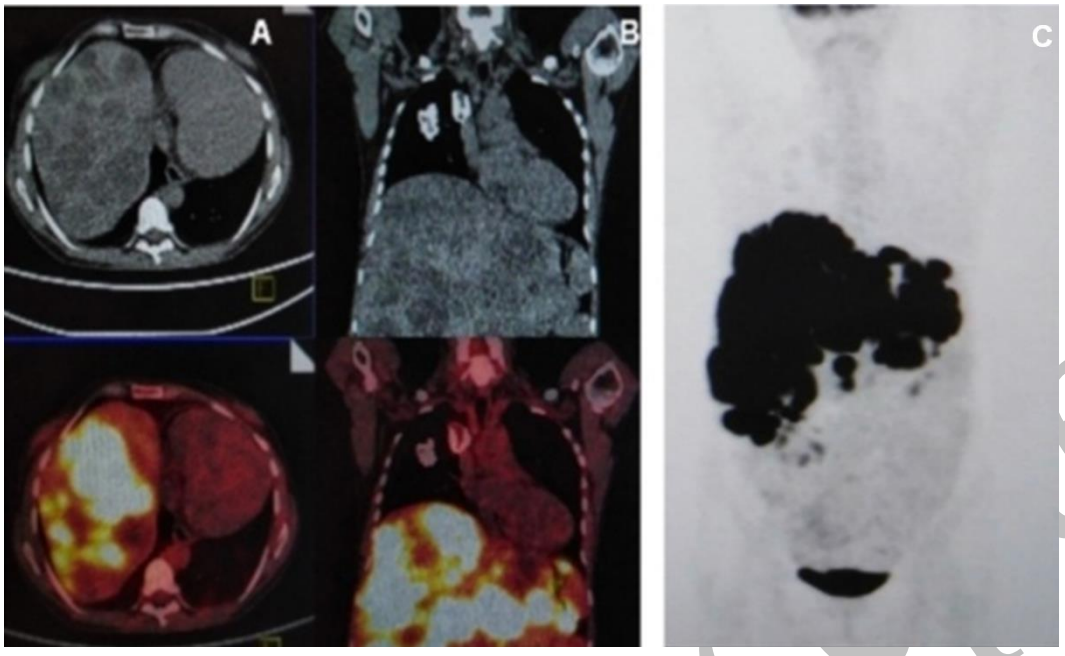

Figure 1. A – axial CT, fused PET/CT, B – coronal CT, fused PET/CT, C – (MIP) PET images of elevated right semi-diaphragm with heart dislocation to left hemithorax

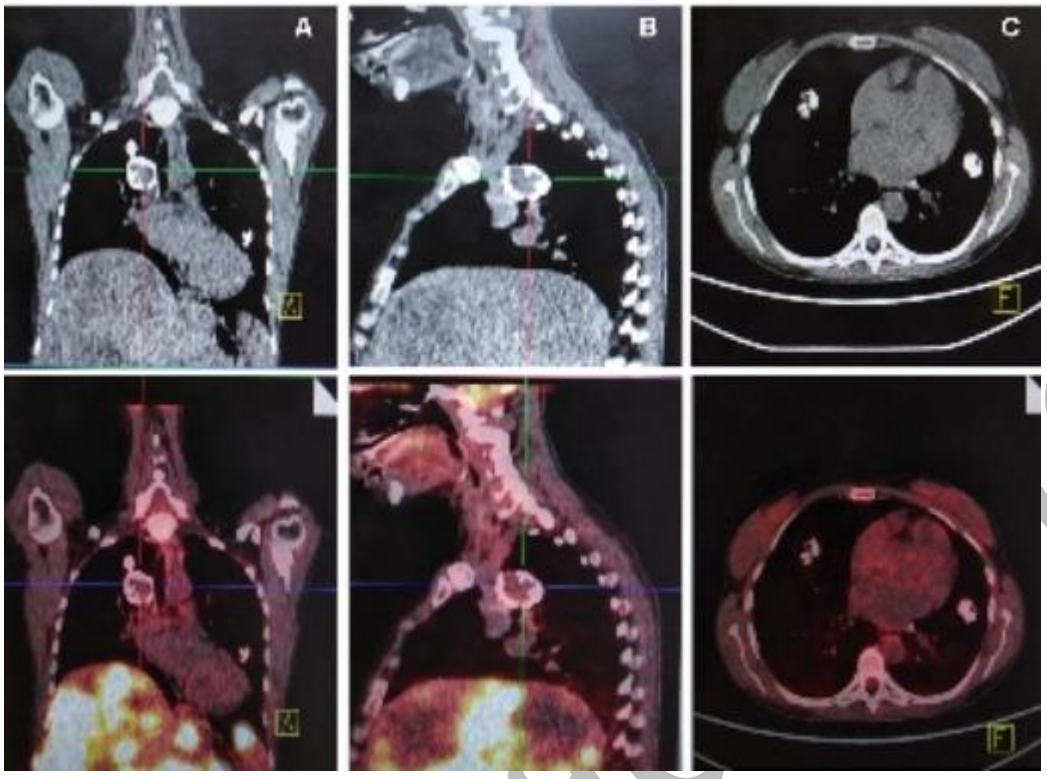

Figure 2. A – coronal, B – sagittal, C – axial CT, fused PET/CT (mediastinal window) images of bilateral pulmonary chondromas

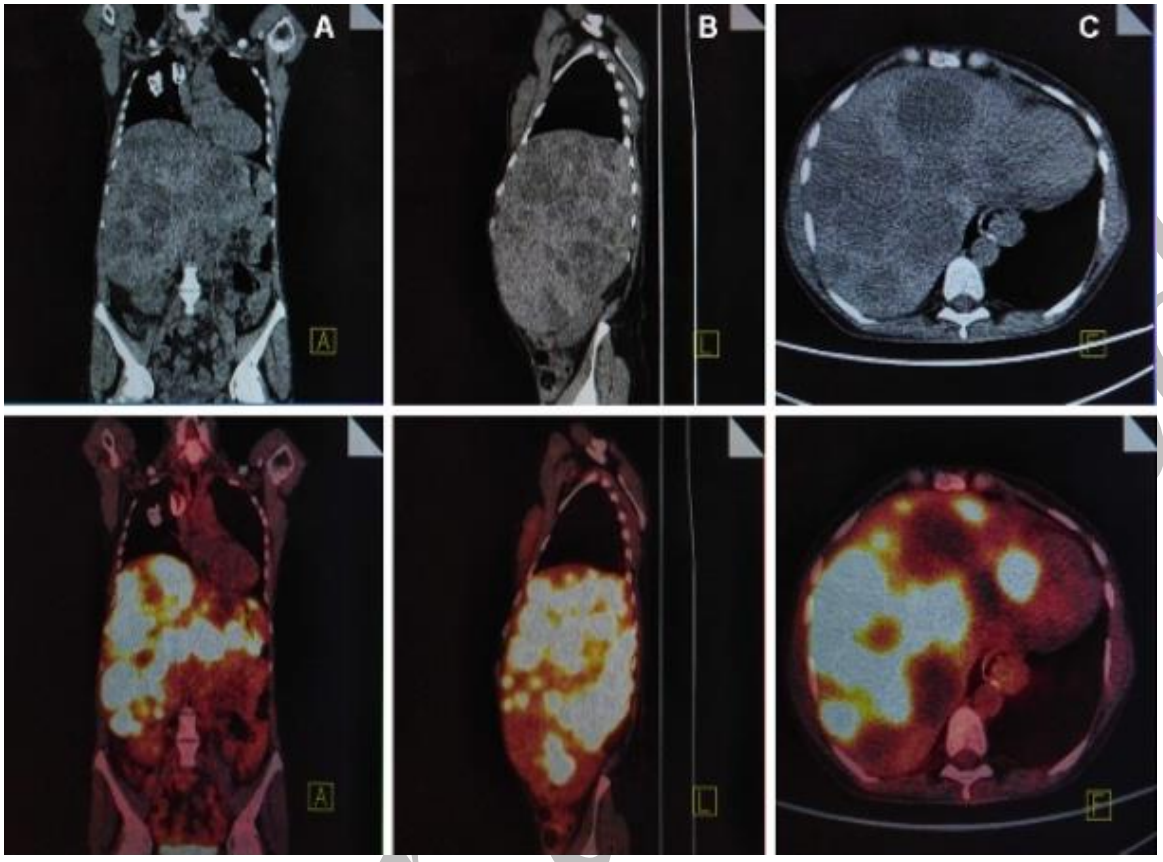

Figure 3. A – Coronal, B – Sagittal, C – Axial CT, fused PET/CT images of multiple single and confluent hypodense lesions with intense uptake of 18F-FDG; lesions without any uptake of 18F-FDG show areas of necrosis in the hepatic superscan image

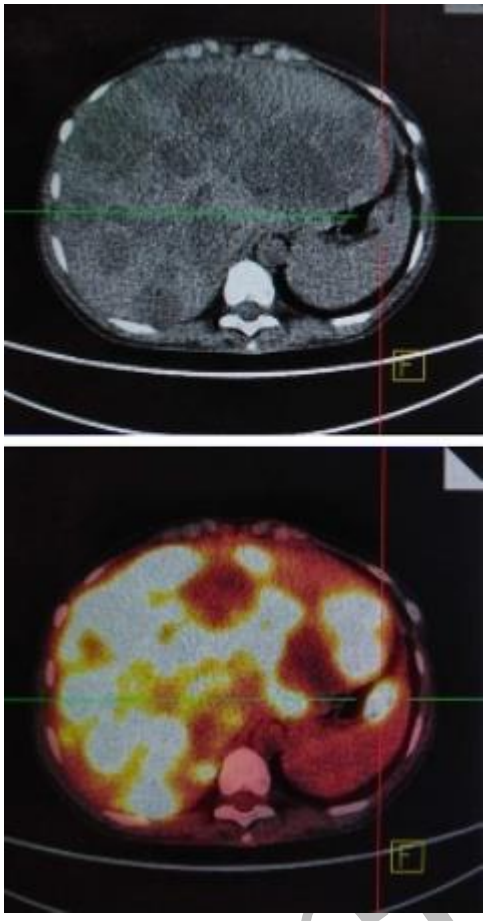

Figure 4. Axial CT, fused PET/CT images of the nodular lesion near medial contour of the anterior part of the spleen with intense uptake of 18F-FDG

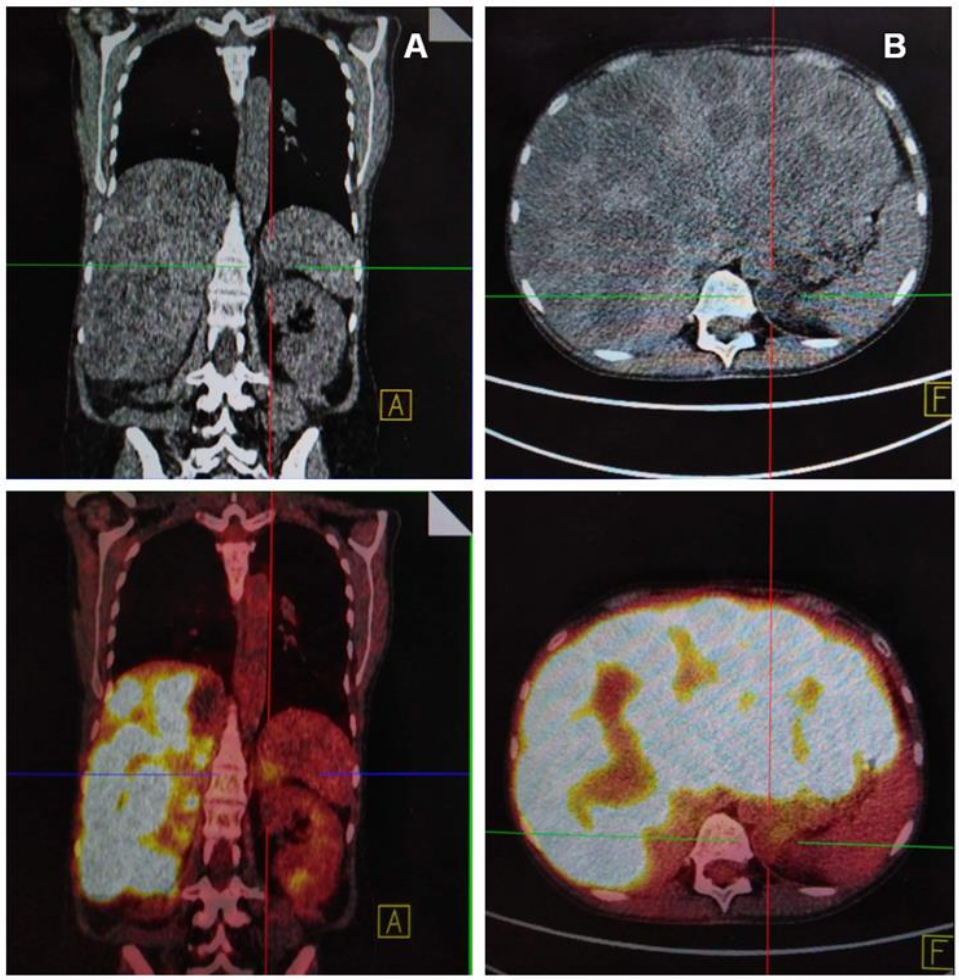

Figure 5. A – Coronal, B – Axial CT, fused PET/CT images of the nodular lesion in the left adrenal gland with accumulation 18F-FDG in the anterior part of the nodular lesion

