

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

May an adrenal incidentaloma change its nature?

This is the author's manuscript

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1742717> since 2021-02-01T11:36:00Z

Published version:

DOI:10.1007/s40618-020-01219-3

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

May an adrenal incidentaloma change its nature?

1 **Alessandra Müller¹, Elisa Ingargiola¹, Federica Solitro², Enrico Bollito³, Soraya Puglisi^{1*},**
2 **Massimo Terzolo¹, Anna Pia^{1**}, Giuseppe Reimondo^{1**}.**

3 ** have equally contributed as senior authors

4 ¹ *Internal Medicine, Department of Clinical and Biological Sciences, San Luigi Gonzaga Hospital, University of Turin,*
5 *Orbassano, Italy*

6 ² *Radiology, Department of Oncology, San Luigi Gonzaga Hospital, University of Turin, Orbassano, Italy*

7 ³ *Pathology, Department of Oncology, San Luigi Gonzaga Hospital, University of Turin, Orbassano, Italy*

8

9 * Corresponding Author: **Soraya Puglisi**

10 Internal Medicine, Department of Clinical and Biological Sciences, San Luigi Gonzaga Hospital,

11 Regione Gonzole 10, 10043 Orbassano, Italy; tel: +39 011 9026292, fax: +39 011 6705456

12 e-mail: sorayapuglisi@yahoo.it ORCID: 0000-0002-2883-6139

13

14 **Keywords:** incidentaloma, adrenal tumor, metastasis, PET, uptake, adrenalectomy, follow-up, lung
15 cancer.

16

17 **Author Contributions:** Clinical management of the patient: AP; Imaging review: FS; Pathological
18 review: EB; Drafting of the Manuscript: AM, EI; Critical Review of the Manuscript: SP, AP, GR,
19 MT; Supervision: AP, GR, MT.

20 **Abstract**

21 Up to 70% of adrenal masses detected in patients affected by extra-adrenal malignancy are metastatic
22 lesions. Therefore, detection of an adrenal mass in patients with active or previous malignancy
23 requires a careful differential diagnostic work-up. ^{18}F -Fluorodeoxyglucose-positron emission
24 tomography/computed tomography (^{18}F -FDG-PET/CT) is increasingly used to determine the
25 malignant potential of adrenal lesions.

26 We report the case of a 64-year-old man who had a single adrenal metastasis due to non-small-cell
27 lung carcinoma developing on a pre-existing benign adrenal lesion. This metastasis occurred in a
28 phase of perceived oncological remission and was detected thanks to ^{18}F -FDG-PET/CT showing a
29 focal adrenal uptake. Contrast-enhanced computed tomography (CT), performed as part of
30 oncological follow-up, and MRI with chemical shift sequences did not lead to the correct diagnosis.
31 The patient underwent laparoscopic adrenalectomy and the pathological evaluation confirmed a lung
32 carcinoma metastasis.

33 The present case highlights the peculiarity of the follow-up of adrenal masses in cancer patients and
34 the primary role of ^{18}F -FDG-PET/CT in the management of such patients.

35

36 **Background**

37 About 2% of all incidentally detected adrenal masses are of metastatic nature. This percentage rises
38 to 30-70% in patients affected by an extra-adrenal malignancy [1] . The adrenal gland represents
39 indeed a frequent site of metastasis, due to its rich sinusoidal vascularization. Lung cancer followed
40 by breast cancer and melanoma are most likely to spread to the adrenal gland [2] . Rare cases of
41 collision tumors, defined as the coexistence of two different tumors in an adrenal gland, such as an
42 adrenal adenoma and an adrenal cancer or a metastatic tumor, have been described [3].

43 Although no randomized study comparing imaging tests has been performed, non-contrast computed
44 tomography (CT) is generally considered as the first-line imaging test to make a differential
45 diagnosis between benign and malignant adrenal masses. Whenever the mass is considered of
46 indeterminate nature after non-contrast CT, second-line imaging tests, including CT with delayed
47 contrast media washout, chemical shift MRI, and ¹⁸F-FDG-PET/CT, are needed to define the
48 diagnosis [4]. Once that an adrenal incidentaloma is considered to be a benign lesion after an
49 appropriate work-up, it is not recommended to pursue a specific follow-up with repeated imaging
50 studies [4]. The recommendation is based on the very low chance that a benign adrenal lesion may
51 turn in a malignant one during follow-up [5].

52 We report here in a case that represents an exception to this general rule and underlines the
53 challenges that may arise in the diagnosis of adrenal metastases.

54

55 **Case presentation**

56 The patient is a 64-year-old man, ex-smoker (10 cigarettes/day), with an occupational exposure to
57 silica dust and asbestos and a clinical history of chronic obstructive pulmonary disease and arterial
58 hypertension. In 2008, a left adrenal nodule was occasionally detected and investigated with

59 endocrinological workup and non-contrast CT, which were suggestive for a benign, non-functioning,
60 adrenal adenoma. The lesion was of 30 mm in size with a density < 0 Hounsfield Units (HU) [Figure
61 1].

62 In August 2015, a squamous cell carcinoma of the upper lobe of the right lung with mediastinal
63 lymphadenopathy was diagnosed. The patient was treated with chemo- and radiotherapy with
64 complete disease response and subsequent negative radiological follow-up.

65 In September 2017, a follow-up total body contrast-enhanced CT scan showed multiple pulmonary
66 lesions and a slight enlargement of the known left adrenal nodule (37 mm diameter) [Figures 2a and
67 2b]. Hounsfield Units and morphological characteristics were not reported. Due to the suspect of
68 disease recurrence a ¹⁸F-FDG-PET/CT scan was performed and it showed a focal pathological uptake
69 in the left adrenal region without relevant uptakes in other sites (absolute SUV value 7.8,
70 adrenal/liver ratio 3.5) [Figure 2c], while the pulmonary lesions resolved after antibiotic therapy.

71 The patient was then referred to our outpatient unit. A hormonal workup was negative for
72 hypercortisolism, primary hyperaldosteronism and catecholamine excess. All the available CT scans
73 were re-evaluated by an expert radiologist, who confirmed the increase in size (7 mm) and described
74 the adrenal mass as inhomogeneous with faintly irregular borders. Due to the changed radiological
75 characteristics an adrenal magnetic resonance imaging (MRI) with chemical shift sequences was
76 performed but was not conclusive in the differential diagnosis between a lipid-poor adenoma and a
77 malignant lesion, showing incomplete, inhomogeneous signal intensity loss in out-of-phase
78 sequences [Figures 3a and 3b].

79 Following the pathological adrenal uptake at FDG-PET scan, not justified by an autonomous
80 hormone production, and the undetermined radiological characteristics at MRI the patient underwent
81 left laparoscopic adrenalectomy with an uneventful course. The pathological exam revealed that the
82 adrenal parenchyma was completely replaced by squamous carcinoma cells, with typical
83 adenomatous cells surrounding the central neoplastic core [Figures 4a and 4b].

85 Discussion

86 Whether most adrenal masses detected in patients affected by extra-adrenal malignancies are of
87 secondary nature, adrenal metastases are rarely found in non-oncological patients [1]. Therefore, a
88 history of known extra-adrenal malignancy requires a particular attention to the possibility of an
89 adrenal metastasis. A new adrenal lesion developing during oncological follow-up should also be
90 viewed as suspicious.

91 In clinical practice, the most commonly used imaging techniques to assess the risk of malignancy are:
92 non-contrast CT, MRI with chemical shift sequences, and ^{18}F -FDG-PET/CT. The recent
93 ESE/ENSAT guidelines on the management of adrenal incidentalomas recommended non-contrast
94 CT as the first radiological test [4]. Adrenal lesions that are homogeneous, smaller than 4 cm, with
95 density < 10 Hounsfield units (HU) are considered benign, lipid-rich adenomas. However, about 30%
96 of adrenal adenomas are lipid-poor and show an attenuation value > 10 HU that overlaps with
97 malignant lesions and pheochromocytomas [6-8]. The use of MRI with chemical shift sequences is
98 based on the typical loss of signal intensity shown by intracellular lipid-rich lesions in out-of-phase
99 sequences, while lipid-poor adenomas, malignant lesions and pheochromocytomas remain unchanged
100 [9-11]. In patients with history of extra-adrenal malignancy, the ESE/ENSAT guidelines suggest the
101 use of ^{18}F -FDG-PET/CT performed as part of oncological follow-up [4]. ^{18}F -FDG-PET/CT has the
102 advantage of being able to detect malignant adrenal lesions with a low rate of false negatives (mainly
103 metastases from tumors with low FDG-uptake, i.e. kidney cancer [12]) and a certain rate of false
104 positives (i.e., functional adenomas [13]) [14]. Routine use of ^{18}F -FDG-PET/CT in patients without
105 history or suspect of malignancy is currently not recommended, but a recent prospective study
106 showed that it has an excellent negative predictive value in the characterization of indeterminate
107 and/or large adrenal masses in non-cancer patients [15].

108 In our patient, the contrast-enhanced CT performed during the oncological follow-up reported only a
109 slight enlargement of the known adrenal lesion and only the radiological revision, requested after the
110 ¹⁸F-FDG-PET/CT, showed changes of the lesion's features. The ¹⁸F-FDG-PET/CT was done
111 primarily for the suspect of pulmonary progression of disease but showed a single, focal uptake of
112 the known adrenal lesion. Since the mass has been previously recognized as benign, further
113 diagnostic tests were done. Hormone assessment was unrewarding, and MRI was still compatible
114 with a lipid-poor adenoma. Our case represents a “real-life” demonstration of the limits of
115 radiological and functional imaging in defining adrenal masses nature, especially in patients with
116 known oncological history. These limits have been widely analyzed in a systematic review and meta-
117 analysis [16] which laid the groundwork for the recommendations given by the ESE/ENSAT
118 guidelines, especially when second-line imaging techniques are used in indeterminate adrenal
119 masses. Despite the great potential of available radiological and functional imaging, there are not
120 only difficulties related to the heterogeneity of both benign and malignant adrenal lesions and to the
121 frequent overlap in imaging features [17], but also the expertise of the single radiologist and clinician
122 influence the patient's diagnostic pathway in clinical practice.

123 In our patient, since radiological and functional imaging were not conclusive in defining the nature of
124 the adrenal lesion's changes, a histopathological evaluation was considered essential. The
125 multidisciplinary team discussion considered the adrenal biopsy a possible choice, but since we had
126 a consistent suspicion of malignancy and the patient was in excellent clinical conditions with a
127 prolonged disease-free interval following oncological treatment of his non-small cell lung cancer
128 (NSCLC), we decided to be proactive and recommended surgical removal of the adrenal lesion. Our
129 choice was also supported by the expertise of our surgeon and the notion of a favorable outcome of
130 patients who underwent removal of solitary adrenal metastases from different cancer types, including
131 NSCLC.

132 Since the first description of adrenalectomy for isolated metastasis in 1982 [18], many retrospective
133 series showed a potential benefit in survival in well-selected patients undergoing surgical treatment
134 [19-26].

135 In recent years, there is growing evidence in support of use of laparoscopic approach in malignant
136 adrenal lesions ensuring an adequate oncologic result, in addition to the advantages of mini-invasive
137 surgery in terms of safety and post-operative recovery [27-30]. Therefore, laparoscopic
138 adrenalectomy represents the first-choice surgical option in these patients.

139 Given the low probability that a benign adrenal lesion becomes malignant during follow-up [5], an
140 active imaging surveillance of adrenal incidentalomas that are characterized to be benign is currently
141 not recommended [4, 31]. However, oncological patients may represent a possible exception to the
142 rule because neoplastic cells may be seeded in a pre-existing benign lesion. **Whether the coexistence
143 of a metastasis in an adrenal benign lesion is an incidental occurrence or represents the result of
144 changes in the local environment that may favor hematogenous metastatization in an adrenal
145 adenoma is not still clear. In 2014, Untch and colleagues [3] reviewed 11 histopathologically-proved
146 adrenal collision tumors described in literature. In the last five years other 14 case reports of adrenal
147 collision tumors have been published [3, 32-51]. The 25 cases are summarized in Table 1. In 18
148 cases, an adrenal adenoma was present. In 17 cases a malignant component was described, in 6 cases
149 of primitive adrenal origin, in 11 cases of metastatic nature. 3 cases were lung cancer metastases, one
150 small cell lung carcinoma (SCLC) and two NSCLC.**

151

152 **Conclusions**

153 In conclusion, we have reported the development of a solitary adrenal metastasis on a pre-existing
154 benign adrenal lesion in a patient with a NSCLC in apparent clinical remission. **Although oncologists**

155 and pneumologists, familiar with the way of metastatic spreading of lung carcinoma, are used to
156 follow up patients with total body CT, this case report highlights the peculiarity of the follow-up of
157 adrenal masses in cancer patients. While imaging follow-up of adrenal incidentalomas is seldom
158 recommended [4, 5, 31] any adrenal lesion in a patient with known oncological disease should be
159 carefully evaluated at any restaging, even if the mass has been previously labelled as benign. This is
160 of utmost importance when a complete response of the primary cancer has been obtained after
161 treatment, since the detection of new adrenal metastasis may change the management plan. In this
162 clinical scenario, ¹⁸F-FDG-PET/CT represents a valid tool to guide clinicians in the decision-making
163 process [52].

164

165 **Conflict of Interest**

166 On behalf of all authors, the corresponding author states that there is no conflict of interest.

167

168 **REFERENCES**

- 169 1. Terzolo M, Stigliano A, Chiodini I, Loli P, Furlani L, Arnaldi G et al. (2011) AME position statement on adrenal
170 incidentaloma Eur J Endocrinol 164:851-70.
- 171 2. Cingam SR, Karanchi H (2019) Cancer, Adrenal Metastasis. StatPearls Publishing
- 172 3. Untch BR, Shia J, Downey RJ, Carrasquillo JA, Panicek DM, Strong VE (2014) Imaging and management of a
173 small cell lung cancer metastasis/adrenal adenoma collision tumor: a case report and review of the literature.
174 World J Surg Oncol 12:45.
- 175 4. Fassnacht M, Arlt W, Bancos I, Dralle H, Newell-Price J, Sahdev A et al. (2016) Management of adrenal
176 incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the
177 European Network for the Study of Adrenal Tumors Eur J Endocrinol 175:G1-G34.
- 178 5. Elhassan YS, Alahdab F, Prete A, Delivanis DA, Khanna A, Prokop L et al. (2019) Natural History of Adrenal
179 Incidentalomas With and Without Mild Autonomous Cortisol Excess: A Systematic Review and Meta-analysis
180 Ann Intern Med 171:107-116.

- 181 6. Caoili EM, Korobkin M, Francis IR, Cohan RH, Dunnick NR (2000) Delayed enhanced CT of lipid-poor adrenal
182 adenomas *AJR Am J Roentgenol* 175:1411-5.
- 183 7. Peña CS, Boland GW, Hahn PF, Lee MJ, Mueller PR (2000) Characterization of indeterminate (lipid-poor)
184 adrenal masses: use of washout characteristics at contrast-enhanced CT *Radiology* 217:798-802.
- 185 8. Zhang HM, Perrier ND, Grubbs EG, Sircar K, Ye ZX, Lee JE, et al. (2012) CT features and quantification of the
186 characteristics of adrenocortical carcinomas on unenhanced and contrast-enhanced studies *Clin Radiol* 67:38-46.
- 187 9. Dunnick NR, Korobkin M (2002) Imaging of adrenal incidentalomas: current status *AJR Am J Roentgenol*
188 179:559-68.
- 189 10. Haider MA, Ghai S, Jhaveri K, Lockwood G (2004) Chemical shift MR imaging of hyperattenuating (>10 HU)
190 adrenal masses: does it still have a role? *Radiology* 231:711-6.
- 191 11. Bharwani N, Rockall AG, Sahdev A, Gueorguiev M, Drake W, Grossman AB, et al. (2011) Adrenocortical
192 carcinoma: the range of appearances on CT and MRI *AJR Am J Roentgenol* 196:W706-14.
- 193 12. Zukotynski K, Lewis A, O'Regan K, Jacene H, Sakellis C, Krajewski K, et al. (2012) PET/CT and renal
194 pathology: a blind spot for radiologists? Part 1, primary pathology *AJR Am J Roentgenol* 199:W163-7.
- 195 13. Alencar GA, Fragoso MC, Yamaga LY, Lerario AM, Mendonca BB (2011) (18)F-FDG-PET/CT imaging of
196 ACTH-independent macronodular adrenocortical hyperplasia (AIMAH) demonstrating increased (18)F-FDG
197 uptake *J Clin Endocrinol Metab* 96:3300-1.
- 198 14. Ansquer C, Scigliano S, Mirallié E, Taïeb D, Brunaud L, Sebag F, et al. (2010) 18F-FDG PET/CT in the
199 characterization and surgical decision concerning adrenal masses: a prospective multicentre evaluation *Eur J*
200 *Nucl Med Mol Imaging* 37:1669-78.
- 201 15. Guerin C, Pattou F, Brunaud L, Lifante JC, Mirallié E, Haissaguerre M, et al. (2017) Performance of 18F-FDG
202 PET/CT in the Characterization of Adrenal Masses in Noncancer Patients: A Prospective Study *J Clin*
203 *Endocrinol Metal* 102:2465-72.
- 204 16. Dinnes J, Bancos I, Ferrante di Ruffano L, Chortis V, Davenport C, Bayliss S, et al (2016) Imaging for the
205 diagnosis of malignancy in incidentally discovered adrenal masses – a systematic review and meta-analysis *Eur*
206 *J Endocrinol* 175: R51-64.
- 207 17. Albano D, Agnello F, Midiri F, Pecoraro G, Bruno A, Alongi P et al. (2019) Imaging features of adrenal masses.
208 *Insights Imaging* 10:1.
- 209 18. Twomey P, Montgomery C, Clark O (1982) Successful treatment of adrenal metastases from large-cell
210 carcinoma of the lung *JAMA* 248:581-3.
- 211 19. Vazquez BJ, Richards ML, Lohse CM, Thompson GB, Farley DR, Grant CS, et al. (2012) Adrenalectomy
212 improves outcomes of selected patients with metastatic carcinoma *World J Surg* 36:1400-5.

- 213 20. Higashiyama M, Doi O, Kodama K, Yokouchi H, Imaoka S, Koyama H (1994) Surgical treatment of adrenal
214 metastasis following pulmonary resection for lung cancer: comparison of adrenalectomy with palliative therapy
215 *Int Surg* 79:124-9.
- 216 21. Kim SH, Brennan MF, Russo P, Burt ME, Coit DG (1998) The role of surgery in the treatment of clinically
217 isolated adrenal metastasis *Cancer* 82:389-94.
- 218 22. Porte H, Siat J, Guibert B, Lepimpec-Barthes F, Jancovici R, Bernard A, et al. (2001) Resection of adrenal
219 metastases from non-small cell lung cancer: a multicenter study *Ann Thorac Surg* 71:981-5.
- 220 23. Pfannschmidt J, Schlolaut B, Muley T, Hoffmann H, Dienemann H (2005) Adrenalectomy for solitary adrenal
221 metastases from non-small cell lung cancer *Lung Cancer* 49:203-7.
- 222 24. Tanvetyanon T, Robinson LA, Schell MJ, Strong VE, Kapoor R, Coit DG, et al. (2008) Outcomes of
223 adrenalectomy for isolated synchronous versus metachronous adrenal metastases in non-small-cell lung cancer: a
224 systematic review and pooled analysis *J Clin Oncol* 26:1142-7.
- 225 25. Raz DJ, Lanuti M, Gaissert HC, Wright CD, Mathisen DJ, Wain JC (2011) Outcomes of patients with isolated
226 adrenal metastasis from non-small cell lung carcinoma *Ann Thorac Surg* 92:1788-93.
- 227 26. Ramsingh J, O'Dwyer P, Watson C (2019) Survival outcomes following adrenalectomy for isolated metastases
228 to the adrenal gland *Eur J Surg Oncol* 45:631-4.
- 229 27. Marangos IP, Kazaryan AM, Rosseland AR, Røsok BI, Carlsen HS, Kromann-Andersen B, et al (2009) Should
230 we use laparoscopic adrenalectomy for metastases? Scandinavian multicenter study *J Surg Oncol* 100:43-7.
- 231 28. Moreno P, de la Quintana Basarrate A, Musholt TJ, Paunovic I, Puccini M, Vidal O, et al. (2013)
232 Adrenalectomy for solid tumor metastases: results of a multicenter European study *Surgery* 154:1215-23.
- 233 29. Puccini M, Panicucci E, Candalise V, Ceccarelli C, Neri CM, Buccianti P, et al. (2017) The role of laparoscopic
234 resection of metastases to adrenal glands *Gland Surg* 6:350-4.
- 235 30. Drake FT, Beninato T, Xiong MX, Shah NV, Kluijfhout WP, Feeney T, et al. (2019) Laparoscopic
236 adrenalectomy for metastatic disease: Retrospective cohort with long-term, comprehensive follow-up *Surgery*
237 165:958-64.
- 238 31. Terzolo M, Reimondo G (2019) Insights on the Natural History of Adrenal Incidentalomas *Ann Intern Med*
239 171:135-136.
- 240 32. Pakalniskis MG, Ishigami K, Pakalniskis BL, Fujita N (2019). Adrenal collision tumour comprised of
241 adrenocortical carcinoma and myelolipoma in a patient with congenital adrenal hyperplasia. *J Med Imaging*
242 *Radiat Oncol*.
- 243 33. Foresti M, Parmiggiani A (2019) Adrenal Adenoma-Hemangioma Collision Tumor: Description of Two Cases. *J*
244 *Radiol Case Rep* 13:1-12.
- 245 34. Khorsand A, Khatami F, Sefidbakht S, Saffar H, Sadeghipour A, Tavangar SM (2018)
246 Adrenal Collision Tumor Composed of Pheochromocytoma and Diffuse Large B-Cell Lymphoma: A Case Report.
247 *Int J Hematol Oncol Stem Cell Res* 12:249-252.

- 248 35. Lai Y, Zhou L, Hu J, Li W, Cui L, Lai Y, Ni L (2018) Erratum: Adrenal collision tumor (parachordoma and
249 ganglioneuroma): A case report. *Mol Clin Oncol* 9:238.
- 250 36. Zhang CX, Tian Y (2018) Adrenal Collision Tumor Composed of Adrenocortical Adenoma and
251 Pheochromocytoma. *Chin Med J (Engl)*. 131:374-375.
- 252 37. Liu D, Kumar SA (2017) An exceedingly rare adrenal collision tumor: adrenal adenoma-metastatic breast
253 cancer-myelolipoma. *J Community Hosp Intern Med Perspect* 7:241-244.
- 254 38. Takizawa K, Kohashi K, Negishi T, Taguchi K, Yamada Y, Nakamura M, et al (2017) A
255 exceptional collision tumor of primary adrenal angiosarcoma and non-functioning adrenocortical adenoma.
256 *Pathol Res Pract* 213:702-705.
- 257 39. Lee HS, Choi YJ, Kim C, Kim BH (2016) Adrenal Collision Tumor: Coexistence of Pigmented Adrenal Cortical
258 Oncocytoma and Ganglioneuroma. *Case Rep Surg* 5790645.
- 259 40. Piotrowski Z, Tomaszewski JJ, Hartman AL, Edwards K, Uzzo RG (2015) Renal cell carcinoma and an
260 incidental adrenal lesion: adrenal collision tumors. *Urology* 85:e17-8.
- 261 41. Hayashi T, Gucer H, Mete O (2014) A mimic of sarcomatoid adrenal cortical carcinoma: epithelioid
262 angiosarcoma occurring in adrenal cortical adenoma. *Endocr Pathol* 25:404-9.
- 263 42. Wang JI, Fisher CI, Thway K2 (2014) "Dominant" myelolipoma encasing adrenal cortical carcinoma: an
264 unusual variation of myelolipoma occurring as a synchronous and predominant neoplasm *Int J Surg Pathol*
265 22:731-5.
- 266 43. Abdullazade I. S., Tezel G (2012) A rare case of collision tumor: coexistence of adrenocortical adenoma and
267 pheochromocytoma in the same adrenal gland *Journal of Medical Cases* 3:63–67.
- 268 44. Siddiqi AJ, Miller FH, Kasuganti D, Nikolaidis P (2009) Adrenal hemangioma-adenoma: an exceedingly
269 rare adrenal collision tumor. *J Magn Reson Imaging* 29:949-52.
- 270 45. Bertolini F, Rossi G, Fiochhi F, Giacometti M, Fontana A, Gibertini MC, et al. (2011) Primary adrenal gland
271 carcinosarcoma associated with metastatic rectal cancer: a hitherto unreported collision tumor *Tumori* 97:27e–
272 30e.
- 273 46. Thorin-Savoure A, Tissier-Rible F, Guignat L, Pellerin A, Bertagna X, Bertherat J, et al. (2005)
274 Collision/composite tumors of the adrenal gland: A pitfall of scintigraphy imaging and hormone assays in the
275 detection of adrenal metastasis *J Clin Endo Metabol* 90:4924–4929.
- 276 47. Hagspiel KD (2005) Manifestation of Hodgkin’s lymphoma in an adrenal myelolipoma *Eur Radiol* 15:1757–
277 1759.
- 278 48. Blake MA, Sweeney AT, Kalra MK, Maher MM (2004) Collision adrenal tumors on PET/CT *AJR Am J*
279 *Roentgenol* 183:864–865.
- 280 49. Otal P, Escourrou G, Mazerolles C, Janne d’Othee B, Mezghani S, Musso S, et al. (1999) Imaging features of
281 uncommon adrenal masses with histopathologic correlation *Radiographics* 19:569–581.
- 282 50. Schwartz LH, Macari M, Huvos AG, Panicek DM (1996) Collision tumors of the adrenal gland: demonstration
283 and characterization at MR Imaging. *Radiology* 201:757–760.
- 284 51. Hoshi H, Jinnouchi S, Ono S, Kihara Y, Arakawa K, Takeuchi M, et al. (1984) Scintigraphic demonstration of
285 coexisting adenoma and metastasis of the adrenal gland in a patient with bronchogenic carcinoma. *Clin Nucl*
286 *Med* 9:717–718.

- 287
288
289
290
52. Kandathil A, Wong KK, Wale DJ, Zatelli MC, Maffione AM, Gross MD, et al. (2015) Metabolic and anatomic characteristics of benign and malignant adrenal masses on positron emission tomography/computed tomography: a review of literature *Endocrine* 49:6-26.