INTRODUCTION: PBMAH is a rare cause of Cushing's syndrome (CS), less than 2% of endogenous CS [1,2]. CS due to PBMAH is classified as ACTH-independent CS, but cortisol secretion in PBMAH may be mediated by locally produced ACTH, in a paracrine or autocrine fashion [3]. PBMAH can be due to the aberrant hormone receptor expression [4] or it can have a genetic origin. Mutations in PKA pathway, APC, menin or FH can favor the development of PBMAH. Inactivating mutations in ARMC5, a novel tumor suppressor gene, were recently described, in up to 50% of PBMAH cases [1].

OBJECTIVE and METHODS: To describe a series of patients with CS due to PBMAH. Case series using hormonal and imaging evaluation. Cortisol stimulation testing to detect the presence of aberrant adrenal receptors using a modified version of the Lacroix protocol.

PATIENT 1, female, 66 years

- Sep. 2011: clinical suspicion of CS, morbid obesity
- Cushionoid features: BMI (kg/m²), HT, Diabetes mellitus, Osteoporosis
  - Yes
  - BMI: 45.54
  - HT: Yes
  - Diabetes mellitus: Yes
  - Osteoporosis: Nk

- 8 AM Cortisol (mcg/dL): 12.78
- Overnight 1 mg DEX (N< 1.8): 5.96
- LD DST (2x2 mg): 4.88
- UFC (x UNL): 0.7
- ACTH (pg/mL): 2.56

- Jul. 2015: Refused adrenalectomy. LOST to follow-up. Contacted by phone, re-assessed by cortisol measurement postprandially, for food induced CS

- Patient refused adrenalectomy and was again lost to follow-up

PATIENT 2, male, 61 years

- Nov. 2015: diagnosed incidentally (CT scans) with PBMAH
- Cushionoid features: BMI (kg/m²), HT, DM, Osteoporosis
  - No
  - BMI: 24.8
  - HT: No
  - DM: No
  - Osteoporosis: No

- 8 AM Cortisol (mcg/dL): 9.86
- Overnight 1 mg DEX (N< 1.8): 2.75
- LD DST (2x2): 1.8 (at dig)
- UFC (x UNL): 4.8 (Sep 17)
- ACTH (pg/mL): 7.21

- Active follow-up:
  - 30 months – no change

PATIENT 3, female, 50 years

- May 2017: high suspicion of CS
- Cushionoid features: BMI (kg/m²), HTN, Diabetes mellitus
  - Yes
  - BMI: 30
  - HTN: Stage 3 (HbA1c 11.6%)
  - Diabetes mellitus: 140 UI insulin/day
- Postural measurement: Retinopathy, neuropathy, CKD stage 4
- 8 AM Cortisol (μg/mL): 27.17
- LD DST (2x2 mg) (N< 1.8): 29.38
- UFC (x UNL): 0.86
- ACTH (pg/mL): 1.63

PATIENT 4, male, 62 years

- Jan. 2018: metabolic syndrome
- Cushionoid features: BMI (kg/m²), HT, DM, Osteoporosis
  - No
  - BMI: 29
  - HT: Yes
  - DM: Yes
  - Osteoporosis: Nk

- 8 AM cortisol: 3.37
- Overnight 1 mg DEX (N< 1.8): 2.75
- LD DST (2x2): 0.23
- UFC (x UNL): 7.94

- active follow-up by day cortisol curve

PATIENT 5, male, 62 years

- Mar 2018: CS features: round red face, abdominal obesity
- Cushionoid features: BMI (kg/m²), HT, DM, Osteoporosis
  - No
  - BMI: 36.31
  - HT: Yes
  - DM: Yes
  - Osteoporosis: Nk

- 8 AM cortisol (mcg/dL): 12.1
- Overnight 1mg DEX (N< 1.8): 11.26
- LD DST (2x2): 8.91
- UFC (x UNL): 3.01
- ACTH (pg/mL): 5.11

- Adrenalectomy delayed (dual antiplatelet TX for coronary angioplasty; on metyrapone

CONCLUSIONS: Clinical presentation in PBMAH is variable, from asymptomatic incidentalomas to severe CS. Screening for CS in patients at higher risk is warranted. UFC was within reference range in subclinical/mild CS, while DXM suppression testing and ACTH were diagnostic. Biochemical diagnostic testing for aberrant adrenal receptors has therapeutic implications and should be performed. Management should be individualized, with targeted medical therapy where appropriate and/or with steroidogenesis inhibitors. Unilateral adrenalectomy may be curative [5].