Background
PTEN hamartoma tumor syndrome (PHTS) encompasses rare disorders linked to PTEN gene's mutations including Cowden Disease (CD), Bannayan-Riley-Ruvalcaba syndrome (BRRS), and adult Lhermitte-Duclos disease (LDD) and autism spectrum disorders associated with macrocephaly.

CD is a rare, multisystem disease that causes an increased risk of malignancies (breast, thyroid and endometrial) as well as a benign hamartomatosus overgrowth of tissues (such as skin, colon and thyroid). BRRS is a rare congenital disorder whose primary clinical features include macrocephaly, hamartomatosus intestinal polyps, lipomas and pigmented macules on the penis. Other features include developmental delay, vascular anomalies, large birth weight and joint hyperextensibility.

Objectives
To present a case series of PHTS patients. The secondary aim is to stimulate clinicians to perform an accurate oral examination focusing mainly on the gingival, lingual and buccal mucosa and to investigate the differential diagnosis of widespread oral papillomatous lesions carefully. The dermatological examination is a key point to improve the achievement of the diagnosis. Diagnosis and management of these rare entities are summarized in Table 2 and Table 3.

Materials and methods
Clinical records between 1980-2014 of patients were retrospectively analyzed in a south Italian hospital. We selected the clinical data of PHTS patients from the archives of the outpatient clinic of the Oral Medicine Unit, Department of Head and Neck Diseases, Federico II University of Naples.

Our single center case series revealed 5 PHTS patients (Table 1), 3 male (60%) and 2 female (40%), treated between 1995 and 2013, three of whom affected by CD and two by BRRS. Their mean (+ SD) age at the time of diagnosis was 35.8 (+ 13.83) years.

The five patients were referred to the oral medicine unit because of asymptomatic lesions of the oral mucosa, and four of them underwent incisional biopsy.

Most commonly affected oral site was the alveolar gingiva (4 patients, 80%) followed by tongue and buccal mucosa. The most common clinical presentation was a widespread oral papillomatosis (6 patients, 100%) and concomitant cutaneous lesions were present in the 100% of cases.

Conclusions
To suspect the presence of a PTEN-related syndrome, or more generally of a multiple hamartoma syndrome, should request from specialists a better screening of their patients to meet major and minor diagnostic criteria before resorting to genetic investigation, which is expensive.

The most important clinical sign of the oral examination are an accurate anamnestic evaluation, an accurate total-body dermatological examination, a breast and thyroid ultrasound imaging, a genitourinary screening, gastroscopy and coloscopy.

The oral manifestations may represent one of the primary clinical detectable manifestations of these rare systemic diseases, for which early diagnosis could decrease the associated mortality and morbidity. The knowledge of these diseases and their clinical features, associated with a multidisciplinary approach, allows to achieve a remarkable diagnostic success.