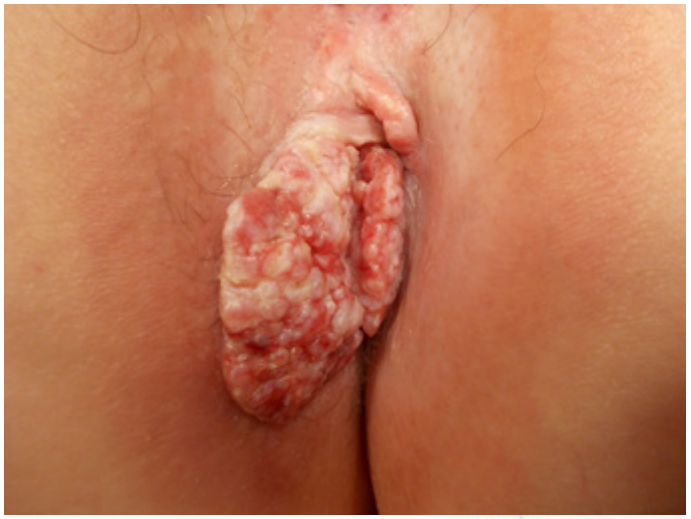
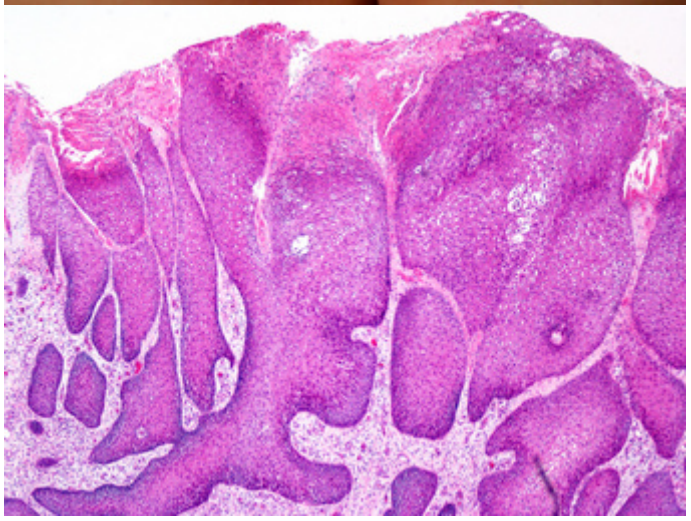
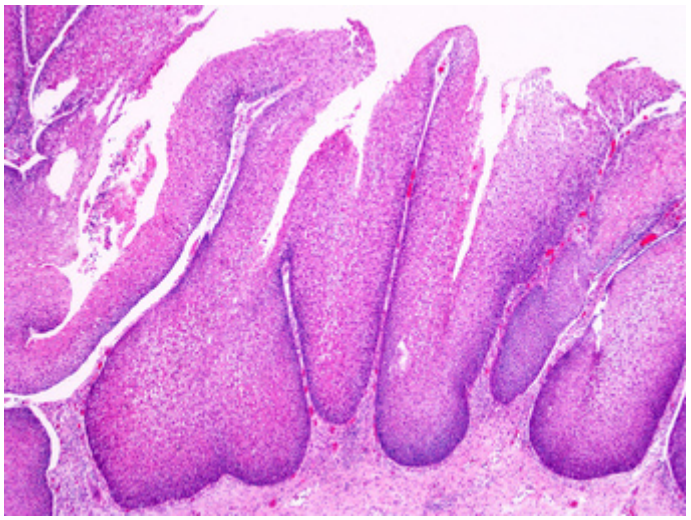
September 2019

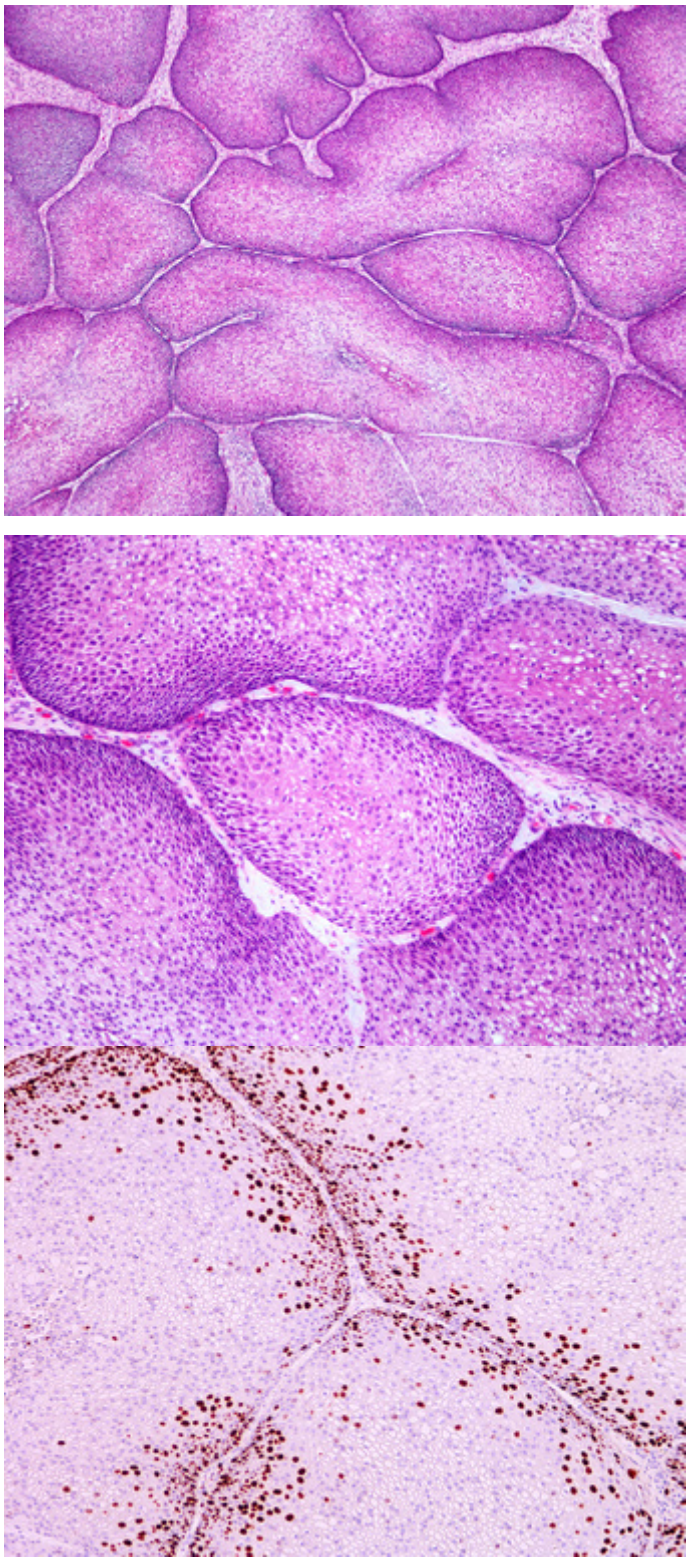
A slowly growing anal tumor in a 60-year-old female.

What is your diagnosis?









Diagnosis:

Anal verrucous carcinoma.

Comment:

Macroscopically, tumor measured 4 x 3.5 cm and was broad based, exophytic, with a warty surface (Panel A). Microscopically, it was composed of thickened projections and islands of well differentiated squamous epithelium with focal surface keratinization, with no atypia. It invaded the subjacent stroma with well-defined pushing borders (Panels B-E). Mitoses were present only in the suprabasal layer, Ki67 stained only basal and parabasal cells (Panel F). Immunohistochemistry for p16 and in situ hybridization for HPV 16/18 and HPV 6/11 were negative. The tumour was excised, with clean surgical margins, and has not recurred.

Verrucous carcinoma (VC) is a rare variant of well differentiated squamous cell carcinoma (SCC) that can occur in various sites of the body including the anal mucosa and skin. It is characterised by slow but locally invasive growth. Pure VC does not metastasize. Hybrid (mixed) tumours also exist, composed of VC and conventional SCC which can metastasize and should be treated as conventional SCC. It is widely believed that VC is aetiologically related to infection with HPV. However, recent studies using highly sensitive and specific molecular methods suggest that VC is not associated with HPV infection.

VC is characterised by a high frequency of initial misdiagnosis. An adequate, full-thickness biopsy must be obtained, when a clinician suspects VC; moreover, multiple biopsies may be needed to rule out a conventional SCC component in VC.

Differential diagnosis includes conventional SCC and giant condyloma. Lack of atypia helps to rule out conventional SCC. VC must be distinguished from giant condyloma which is an HPV-related tumour, composed of well-formed papillary fronds; it usually shows koilocytosis and is caused by HPV 6/11 or other HPV types which can be proven by in situ hybridization or PCR.

VC may be treated by excision or by radiotherapy, and has an excellent prognosis.

For further reading:

- Fléjou JF. An update on anal neoplasia. Histopathol. 2015; 66: 147–160.
- Patel KR, Chernock RD, Zhang TR et al. Verrucous carcinomas of the head and neck, including those with associated squamous cell carcinoma, lack transcriptionally active high-risk human papillomavirus. Hum Pathol 2013; 44: 2385–2392.
- Shia J. An update on tumors of the anal canal. Arch Pathol Lab Med. 2010; 134: 1601–1611. Graham RP. Anal squamous cell carcinoma. In: WHO classification of tumours. Digestive system tumours. 5th ed. Lyon: IARC; 2019; p. 205–207.
- Zidar N, Langner C, Odar K et al. Anal verrucous carcinoma is not related to infection with human papillomaviruses and should be distinguished from giant condyloma (Buschke-Löwenstein tumor). Histopathol. 2017; 70: 938–945.

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