The diagnosis of ovarian cancer recurrence based on vaginal cytology and immunocytochemistry: a report of two cases with initial misdiagnosis

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The liquid-based cytology test (LBC) is the most widely-used technology for gynecological cytological screening in the recent years. However, as far as we know, the immunocytochemistry (ICC) on LBC slides, especially in gynecological cytological screening test, hasn’t been widely applied and investigated yet due to the doubts of its reliability and the deficiency of experience. Here we report two cases with initial misdiagnosis, in which we applied ICC on LBC slides and successfully reported the recurrence of ovarian cancer in cytological screening test.

Clinical Presentations
Case 1: a 46-year-old woman with ovarian cancer 3 years ago, no clinical symptoms and in the latest return visit, no abnormality was reported according to B-ultrasonography and vaginal palpation.
Case 2: 61-year-old woman, with ovarian tumor of unknown type 9 years ago according to her own words, was presented with lower abdominal pain and bloody stool. CT reported a pelvic mass invading rectum and tightly adhering to the adjacent vagina, clinically diagnosed to be rectal cancer.

Cytological findings
Case 1: The slide revealed small-sized cell clusters scattered among the normal squamous cells. Some of them had papillary structure (Fig. 1a). The tightly cohesive cells in the clusters were atypical with high nuclear-to-cytoplasm (N/C) ratio. The nuclei were crowding and pleomorphism with coarse chromatin and variably prominent nucleoli (Fig. 1b). Cytoplasmic vacuolation were evident in some clusters (Fig. 1c).

Case 2: LCT slides demonstrated a bunch of papillary cell clusters with nuclear overlap and crowding (Fig. 4a). These irregular clusters were composed of atypical cells with increased nuclear size and high nuclear-to-cytoplasm (N/C) ratio. The nuclei were pleomorphism, with coarse chromatin and prominent nucleoli (Fig. 4b). Nuclear mitosis and cytoplasmic vacuolization were evident in some clusters (Fig. 4c).

ICC was performed on the unstained LCT slides for CK 7, CK 20, p53 and WT-1 by EnVision Technique. The cell clusters were cytoplasmic positive for CK7, nuclear positive for p53 and WT-1, and negative for CK20 (Fig. 2), which coincided with the immunophenotype of the primary ovarian serous adenocarcinoma (Fig. 3), supporting the diagnosis of the early recurrence of ovarian cancer on vaginal cuff.

Discussions
The two cases were initially misdiagnosed to be no recurrence and rectal cancer respectively based on the clinical and imaging findings, but eventually identified by LBC combined with ICC to be ovarian cancer recurrence. The ICC results on LBC were compared with IHC results on paraffin sections, demonstrating high consistency. ICC on LBC slide, although the stable performance is still questioned, may have a great potential as an auxiliary technique to improve the accuracy and reliability of cytological test especially when the residue cells are inadequate for cell blocks.