Squamous cell carcinoma in situ of the cervix and placental site nodule: Case report

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Abstract

An asymptomatic 24-year-old woman underwent a colposcopy, cervical biopsy, and subsequently, a conization for a cervical squamous cell carcinoma in situ with glandular extension. Simultaneously, an endometrial biopsy was carried out in which, incidentally, a placental site nodule was diagnosed, a rare non-neoplastic lesion originating in the intermediate trophoblast. Given the coexistence of these two entities, it was necessary to make a differential diagnosis between them and also with other pathologies of the trophoblast such as an exaggerated placental site, placental site trophoblastic tumor, and epithelioid trophoblastic tumor.


Introduction

Placental site nodule (PSN) is a non-neoplastic infrequent lesion originating from the intermediate trophoblast, which theoretically represents a non-involved portion of placental tissue. This lesion consists of a circumscribed nodule or plate, with abundant hyalinized stroma and trophoblastic cells of the intermediate trophoblast type. We present the case of a patient with coexistence of squamous cell carcinoma in situ with glandular extension of the cervix and PSN.

Case report

A 24-year-old female resident of a rural area of Colombia attended the local hospital in October 2013 owing to the finding of a high-grade squamous intraepithelial lesion (HSIL) on her Pap smear. She had no relevant medical history. Pregnancies 1, deliveries 1, live births 1. Date of last delivery: September 2010. She was having birth control with subdermal implant since one year prior. Physical examination was normal.

She underwent colposcopy and cervical biopsy, with a squamous cell carcinoma in situ being found, which led to the performance of a conization that confirmed the HSIL diagnosis: severe dysplasia and squamous cell carcinoma in situ with glandular extension on six out of 16 sections, with involvement of the endocervical resection margin (Fig. 1 A and B). Simultaneously, she underwent endometrial biopsy, with proliferative endometrium fragments and a PSN being observed.

By late 2014, the subdermal implant was removed and the control Pap smear reported a low grade squamous intraepithelial lesion, with cytopathic changes consistent with human papillomavirus infection, which was classified as genotype 16. Two months later, a second colposcopy and cervical biopsy were performed, with the latter being negative for squamous
Intraepithelial lesion. The patient is currently breast-feeding her second child.

Discussion

PSN occurs in childbearing age women\textsuperscript{2,3} and, usually, it is an incidental finding of endocervical curettages, cervical and endometrial biopsy and hysterectomy\textsuperscript{1,4,5}. It is mainly located at the endometrium or the cervix, and rarely at the uterine tube. It is usually detected several months or years after a pregnancy, with an average of 3 years\textsuperscript{6-8}.

When macroscopically visible, a yellow or hemorrhagic nodule is appreciated, with a diameter of 1 to 14 mm, although it rarely exceeds 4 mm; it can occur as multiple nodules\textsuperscript{2,4-6}. Microscopically, a circumscribed plaque or nodule composed of hyalinized stroma with intermediate trophoblast-type cells distributed in groups or cords, or individually displayed with absence or sparse atypical mitoses. The cells vary in size; the small ones are mono- or binucleated, with a clear, glycogen-rich cytoplasm, and the large ones have broad acidophilic or amphiphilic cytoplasms, with irregular and hyperchromatic nuclei (Fig. 2 A). Multinucleated trophoblastic cells can occasionally be observed. Towards the periphery, there is a circumferential inflammatory infiltrate composed of lymphocytes and plasmocytes\textsuperscript{2,3,5-8} (Fig. 2 B).

PSNs are positive for PLAP, p63, inhibin $\alpha$ and cytokeratin 18, with focal or negative expression for hPL and CD146 (Mel-CAM). They are usually negative for $\beta$-hCG and their Ki67 proliferation index ranges between 1 and 5\% (Fig. 3 A and E). Given their morphology and immunohistochemical (IHC) characteristics, PSNs originate from the intermediate trophoblast of the chorionic type, and it is suggested that they are the benign counterpart of the epithelioid trophoblastic tumor (ETT)\textsuperscript{1,2,8,9}.

Most important differential diagnoses include exaggerated placental site (EPS), placental site trophoblastic tumor (PSTT), ETT and squamous cell carcinoma of the cervix\textsuperscript{5,8-10} (Table 1). EPS is diagnosed after a normal pregnancy, an ectopic pregnancy or a
Figure 3. PSN trophoblastic cells are positive for P63 (IHC, x20) (A), PLAP (IHC, x40) (B), inhibin (IHC, x40) (C) and keratin (IHC, x40) (D). E: Ki67 proliferation index is lower than 1% (IHC, x40).

Table 1. PSN differential diagnoses

<table>
<thead>
<tr>
<th>EPS</th>
<th>PSN</th>
<th>PSTT</th>
<th>ETT</th>
<th>SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histogenesis</strong></td>
<td>Implantation site intermediate trophoblast</td>
<td>Chorionic type intermediate trophoblast</td>
<td>Implantation site intermediate trophoblast</td>
<td>Chorionic type intermediate trophoblast</td>
</tr>
<tr>
<td><strong>Morphological findings</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Growth pattern</strong></td>
<td>Not arranged in nodules</td>
<td>Circumscribed nodule(s)</td>
<td>Poorly-defined and infiltrating mass</td>
<td>Falsely circumscribed mass with focal infiltration</td>
</tr>
<tr>
<td><strong>Cellularity</strong></td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td><strong>Cytological atypia</strong></td>
<td>Generalized</td>
<td>Focal/sparse</td>
<td>Generalized</td>
<td>Generalized</td>
</tr>
<tr>
<td><strong>Mitotic figures</strong></td>
<td>Absent</td>
<td>Absent to rare</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Stroma</strong></td>
<td>Fibrin deposit</td>
<td>Abundant hyalinization</td>
<td>Deposit of fibroid material</td>
<td>Deposit of hyaline material</td>
</tr>
<tr>
<td><strong>Necrosis</strong></td>
<td>Absent</td>
<td>Occasional, central</td>
<td>Common, coagulative</td>
<td>Geographic and extensive</td>
</tr>
<tr>
<td><strong>Chorionic villi</strong></td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Immunohistochemistry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD146 (Mel-CAM)</td>
<td>Positive. Diffuse</td>
<td>Negative/positive focal</td>
<td>Positive. Diffuse</td>
<td>Negative/positive focal</td>
</tr>
</tbody>
</table>

(Continue)
EPS PSN PSTT ETT SCC
PLAP Negative Positive. Diffuse Negative Positive. Diffuse Negative
Inhibin alpha Positive Positive. Diffuse Positive Positive Positive
hPL Positive. Diffuse Negative/positive focal Positive. Diffuse Negative/positive focal Negative
P63 Negative Positive. Diffuse Negative Positive. Diffuse Positive. Diffuse
P16 (nuclear) Negative Negative Negative Negative Positive
Ki-67 < 1% 1-5% > 10% 10-25% 10-50%

EPS: exaggerated placental site; PSN: placental site nodule; PSTT: placental site trophoblastic tumor; ETT: epithelioid trophoblastic tumor; SCC: squamous cell carcinoma.

molar pregnancy; it doesn’t arrange in nodules, it is usually associated with chorionic villi and its Ki-67 proliferation index is lower than 1%5,10. PSTT is macroscopically visible, and its histology is characterized by myometral infiltration, areas of coagulation necrosis, tumor cells with atypical nuclei, frequent mitosis and Ki-67 proliferation index higher than 10%5,7,8,10. Both EPS and PSTT are negative for p63 and diffusely positive for hPL11. ETT shows IHC findings similar to those of PSN; however, they are neoplasms of larger size, infiltrating growth with high cellularity, pleomorphism, atypical mitoses, geographic necrosis and high cell proliferation index (10-25%)1,5,8,10,11.

In our case, the most important differential diagnosis is cervical squamous cell carcinoma. Some patients assessed for cervical dysplasia or carcinoma in situ with a concomitant PSN can be wrongly diagnosed with infiltrating squamous cell carcinoma. In this case, IHC is useful because antibodies against HLA-G and CK18 are diffusely positive in trophoblastic lesions and negative in squamous cell carcinoma. Inhibin alpha is positive in PSN and negative in squamous cell carcinoma6.

PSNs are lesions that do not require treatment in addition to initial surgical resection10.

Conclusion

PSNs are sometimes diagnosed in women with Pap smear abnormal findings1. In a study by Shih et al.6, this condition was observed in 29% of patients. Although PSN is infrequent, pathologists should recognize its morphological features and obtain the necessary IHC markers to differentiate it in patients with concomitant HSIL, in order to avoid the infiltrating squamous cell carcinoma of the cervix misdiagnosis.

References