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A case of placental site nodule associated with cervical high-grade squamous intraepithelial lesion

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Summary

Introduction: A placental site nodule (PSN) is a remnant of intermediate trophoblast (extravillous trophoblast, EVT) from a previous pregnancy. Usually, this a benign lesion, which once removed, does not require any treatment and does not recur. Although this lesion is related to pregnancy, it may be detected many months or several years after the pregnancy from which it resulted. The lesion represents a degenerative process of EVT. Especially in tissue obtained from curettage, can microscopically mimic aggressive lesions of intermediate trophoblast, such as placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor (ETT), and in an unusual location can pose problems in differential diagnosis with other malignancies, as in the present cervical example. *Case Report:* A 36-year-old female, gravida 2, para 1, with a history of early spontaneous abortion two years prior, was submitted to a cervical smear for abnormal uterine bleeding, which showed a cervical high squamous intraepithelial lesion (HSIL) with extension to the endocervical cells. Histologic examination of the endocervical curettage revealed haphazardly distributed fragments of tissue, showing extensive hyalinization and cells of different size with indistinct outlines, organized in small groups, singly, or in cords. Mitotic figures were absent. Immunohistochemical analysis revealed focal positivity to cytokeratin 8 (CK8) and placental alkaline phosphatase and negativity to high molecular weight cytokeratin. The Ki-67 index was low. As a result, the morphological and immunohistochemical findings led to the diagnosis of a PSN. *Conclusion:* Diagnosis of a PSN in an unusual location also can pose problems in differential diagnosis with other malignancies, as in the present cervical example. In the present case, the cervical location and the association with HSIL might suggest an erroneous diagnosis of cervical invasive squamous carcinoma. Clinical and pathological data, with immunohistochemical study, are mandatory for a correct diagnosis of this lesion.

Key words: Intermediate trophoblast; Placental site nodule; Cervical high-grade squamous intraepithelial neoplasm.

Introduction

A placental site nodule (PSN) is the remnant of an intermediate trophoblast (extravillous trophoblast, EVT) and may be detected many months or several years after a preceding pregnancy [1, 2]. The lesion represents a degenerative process of EVT that mainly involves the endometrium [3], is usually benign, and once removed, does not require any treatment and does not recur. Microscopically, it could mimic aggressive intermediate trophoblastic lesions, such as a placental site trophoblastic tumor (PSTT) or an epithelioid trophoblastic tumor (ETT), but also non-trophoblastic malignant neoplasms.

In this paper, the authors report a case of a PSN with a synchronous cervical intraepithelial neoplasm; in this unusual location and in this association, it can pose problems in differential diagnosis with primary cervical squamous carcinoma.

Case Report

A 36-year-old female, gravida 2, para 1, with a history of early spontaneous abortion two years prior, was submitted to a cervical smear for abnormal uterine bleeding, which showed a cervical high squamous intraepithelial lesion (HSIL) with extension to the endocervical cells. This was confirmed by a subsequent cervical biopsy. Contextually, an endocervical curettage was also performed. All specimens were submitted for Haematoxylin and Eosin (H&E) staining and immunohistochemical studies with standard methods, following the supplier's instructions. On microscopic examination, a cervical biopsy confirmed HSIL (Figure 1A) with extension to the endocervical cells (Figure 1B). In the endocervical curettage there were present haphazardly distributed fragments of tissue (Figure 2A), showing extensive hyalinization and cells of different size with indistinct outlines, organized in small groups, singly, or in cords (Figure 2B). Mitotic figures were absent.

Immunohistochemical analysis revealed focal positivity to cytokeratin 8 (CK8) (Figure 3A) and placental alkaline phosphatase (PLAP) (Figure 3B) and negativity to high molecular weight cytokeratin (Figure 3C). The Ki-67 index was low (Figure 3D). As a result, the morphological and immunohistochemical findings led to the diagnosis of a PSN. Subsequent cervical smears revealed no recurrence of the disease.

Discussion

A PSN develops from retained placental tissue in utero which does not undergo involution after pregnancy. It is an incidental finding observed in the evaluation of uterine bleeding or post-coital bleeding [1].

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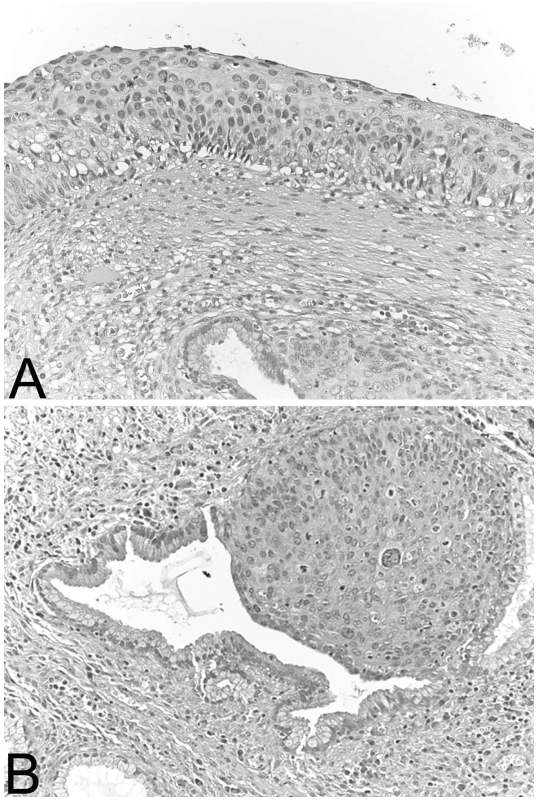

Figure 1. — A cervical biopsy showing a cervical high squamous intraepithelial lesion (HSIL)(A: H&E, x200) with extension to the endocervical cells; B: H&E, x200).

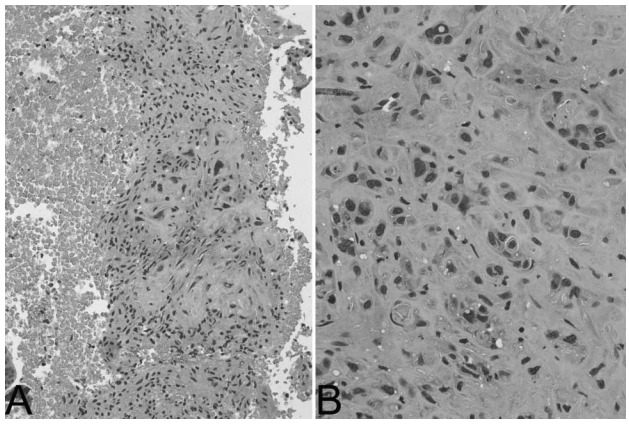

Figure 2. — Endocervical curettage showing haphazardly distributed fragments of tissue (A: H&E, x100) with extensive hyalinization and cells of different size with indistinct outlines, organized in small groups, singly, and absence of mitotic figures; B: H&E x400).

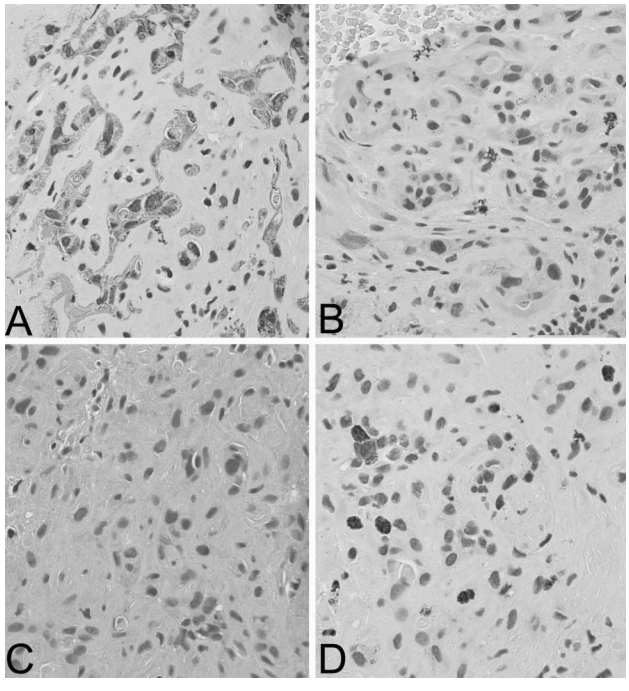

Figure 3. — Immunohistochemical analysis revealed focal positivity to cytokeratin 8 (A: x400), placental alkaline phosphatase (PLAP) (B: x400), and negativity to high molecular weight cytokeratin (C: x400). The Ki-67 index was low (D: x400).

Usually, in the endometrium, PSN is a very small lesion, with microscopic size, but when evident grossly, it appears as yellowish or tan surface nodules in the endometrium [2, 3].

PSN can occasionally be observed in the cervix [4-6] and, more rarely, in the fallopian tube [7, 8] and ovary [9]. In the endometrium, a PSN can mimic aggressive intermediate trophoblastic lesions, such as ETT and PSTT, which are neoplasms with a potential for local invasion and metastasis. Thus, a correct differential diagnosis is important because each disease entity requires a different therapeutic approach. [3, 10-14].

ETT is an unusual trophoblastic tumor which is composed by chorionic-type intermediate trophoblastic elements. This neoplasms is a large solid / cystic lesion that microscopically resembles carcinoma due to cords, nests, and sheets containing hyaline material and necrotic debris. The differential diagnosis from PSN and ETT is suggested by the presence of extensive hyalinization low cellularity and low Ki- 67 index in the former [2, 11]. Moreover, clinical data in cases of ETT reports usually elevated beta hCG.

PSTT is composed of neoplastic implantation site intermediate trophoblastic cell, usually is a large lesion, with monomorphic cells. PSTT can be associated with malignant behavior, when neoplastic elements invade singly or in cords and nests, muscle fibers of the myometrium causing tissue destruction and necrosis [2, 11].

The differential diagnosis PSN can be differentiated from PSTT because of its small sizes, presence of extensive hyalinization lower cellularity, and lower Ki- 67 index [2, 11].

Diagnosis of a PSN in an unusual location can also pose problems in differential diagnosis with other malignancies, as in the present cervical example. In the present case, the cervical location and the association with HSIL might suggest an erroneous diagnosis of cervical invasive squamous carcinoma. Confusion with invasive squamous carcinoma can be made because of nuclear atypia, which is also present in a PSN. Moreover, the hyalinized stroma in a PSN can be mistaken for keratin. A correct diagnosis derives from the fact that a PSN presents only nuclear atypia, but mitoses are absent.

Immunohistochemical analysis is very useful to differentiate a PSN from squamous cell carcinoma. In fact, squamous cell carcinoma shows immunoreactivity to cytokeratin of high weight (CHW), high index Ki 67, plus negativity to CK8 and PLAP. On the contrary, on immunohistochemical studies, a PSN reveals negativity to CHW, low Ki 67 index, and positivity to CK8, and PLAP.

Conclusion

In conclusion, because of the bizarre histological features of a PSN, for accurate diagnosis, clinical and pathological data with accurate immunohistochemical analysis are mandatory.

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