Basaloid squamous cell carcinoma of the uterine cervix with an uncommon metastasis to the left iliac region - case report

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Summary

We describe a rare and interesting case of a basaloid squamous cell carcinoma (BSC) of the uterine cervix with metastasis in the left iliac region diagnosed by fine needle aspiration (FNA).

A 54-year-old woman underwent FNA because of a mass in the left iliac region. The material was processed by conventional liquid based cytology (ThinPrep), and by the cell-block technique and diagnosis was based on the cytomorphologic and immunochemical characteristics as well as the patient's history. The cytologic diagnosis concerned a poorly differentiated squamous cell carcinoma. After a laborious search, we found out that the patient had undergone a total hysterectomy almost 15 years before. The histological diagnosis then was an "infiltrative squamous cell carcinoma of basaloid type" of the uterine cervix.

Our case is of particular interest because it is a rare type of neoplasm with an unusual site of metastasis after a long disease-free period.

Key words: Basaloid squamous cell carcinoma; Cervix; Squamous cell carcinoma.

Introduction

Basaloid squamous carcinoma (BSC) was first identified and described by Wain *et al.* in 1986 [1].

Carcinomas of this type are rare and can arise from different anatomic sites, including usually the upper aerodigestive tract, esophagus, lung, and thymus [1, 2] and less frequently anus, vagina, uterine cervix, liver, maxilla and others [1, 3, 4]. It demonstrates characteristic cytomorphological, immunochemical and ultrastructural features, which make the diagnosis rather easy [1]. The differential diagnosis includes small cell neuroendocrine carcinoma, basal cell carcinoma and adenoid cystic carcinoma [1, 4, 5]. The accurate diagnosis of these neoplasms is important because of differences in biological behaviour, clinical management and prognosis [1].

Basaloid squamous cell carcinoma of the uterine cervix is a rare variant of squamous cell carcinoma, which is supposed to have an aggressive biologic behaviour [6].

Our case is of particular interest for two reasons: it is a basaloid squamous cell carcinoma with an unusual metastasis and, moreover, there was a long disease-free period up to the occurrence of metastasis.

Case Report

A 54-year-old woman underwent a fine needle aspiration (FNA) because of a mass in the left iliac region. The material was prepared by a conventional and liquid based cytology technique (ThinPrep – an automated thin layer method for preparation of cytological smears), as well as by the cell block technique.

In addition to the conventional stains (Papanicolaou, Haematoxylin & eosin), immunocytohistochemical stains were performed in cytologic smears as well as in cell-block preparations, using the avidin-biotin complex technique, with appropriate positive and negative controls. The following antibodies were used: anticytokeratins AE1/AE3 (Dako, 1:50), pancytokeratin (Novocastra, 1:100)], EMA (Dako, 1:100), vimentin (Dako, 1:100) and HMB45 (Novocastra, 1:50).

Microscopic findings

The cytological examination of the conventional and ThinPrep smears revealed a haemorrhagic and degenerative background, containing some malignant cells of squamous differentiation with obvious keratinisation of the cytoplasm and hyperchromatic nuclei (Figure 1). In addition, a few islands of small hyperchromatic, malignant, neoplasmatic cells were observed. The cells appeared basaloid with small hyperchromatic nuclei, small but distinct nucleoli and scant cytoplasm. No mitoses were evident. Finally, the cell-block smears showed a few compact sheets of large malignant cells with clear cytoplasm focally, nuclear pleomorphism and atypia. There was also peripheral palisading (Figure 2). The neoplastic cells expressed strong cytokeratin (AE1/AE3) staining (Figure 3) and EMA positivity (Figure 4), while there was negative expression of vimentin and HMB45.

According to these findings, our diagnosis concerned a poorly differentiated, squamous cell carcinoma.

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Fig. 1

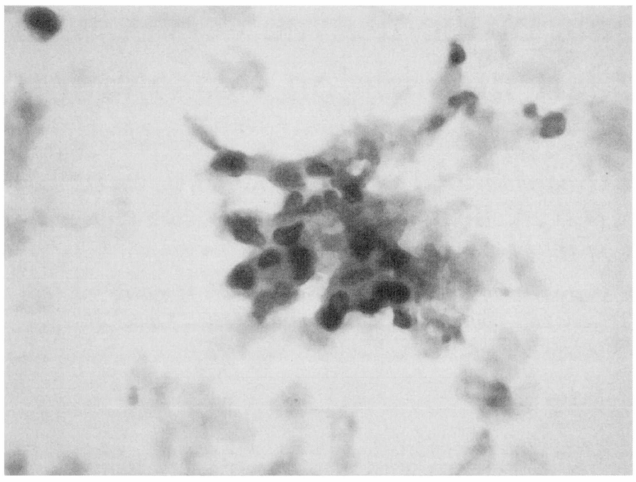


Fig.

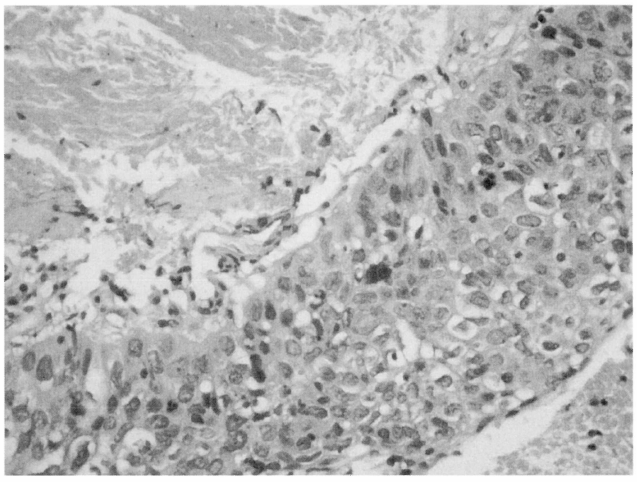
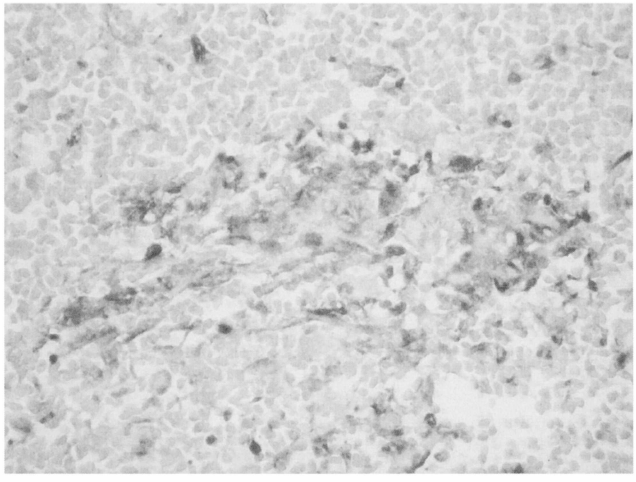


Fig. 3



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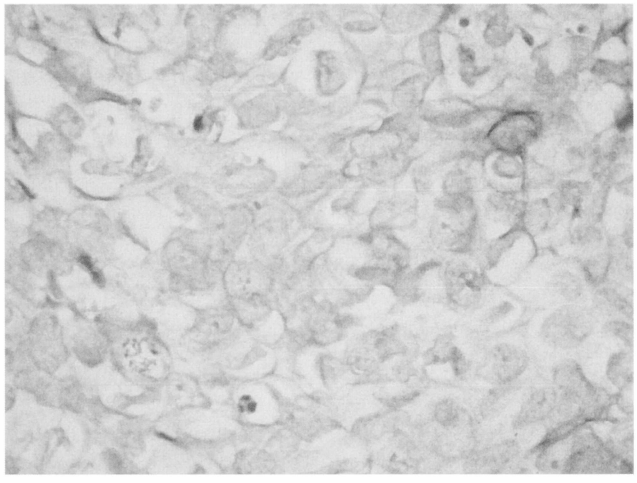

Figure 1. — Basaloid squamous cell carcinoma, keratinised cells, ThinPrep technique (Papanicolaou x 400).
Figure 2. — Basaloid squamous cell carcinoma, cell-block technique (haematoxylin & eosin x 250).
Figure 3. — Basaloid squamous cell carcinoma, cell-block technique (Cytokeratin AE1/AE3 positivity x 250).
Figure 4. — Basaloid squamous cell carcinoma, cell-block technique (EMA positivity x 600).

Clinical history

After a laborious search, we found out that the patient had undergone a total hysterectomy almost 15 years before. The histological diagnosis then was an "infiltrative squamous cell carcinoma of basaloid type" of the uterine cervix.

Consequently, we concluded that the mass appearing in the left iliac region was in fact a metastasis of the referred primary basaloid squamous cell carcinoma. The patient underwent eight cycles of chemotherapy after the cytologic diagnosis. The tumour has remained unchanged upto now (four years) and the patient is in good health, complaining only of leg pain.

Discussion

BSC is considered a rather aggressive tumour with a poor prognosis, often presenting at an advanced stage with lymph node or distant metastases [1]. This specific type of neoplasm and other basaloid tumors are supposed to share origin from pluripotent reserve cells, which are epithelial stem cells. Thus, this theory would explain the divergent differentiation seen in some of these tumors [6, 7].

Moreover, BSC of the cervix consists of a rare high-grade malignant tumour [8, 9]. It is supposed to be a poorly differentiated variant of squamous cell carcinoma (SCC) and belongs to a recently discribed group of 'basaloid cervical neoplasms'of putative 'reserve cell' origin, which include a broad spectrum of tumours: at one end of the spectrum, there are low-grade lesions such as adenoid basal carcinomas, while at the opposite end, there are aggressive tumours including adenoid cystic carcinoma, large cell neuroendocrine carcinoma and BSC [6].

This report documents a case of BSC of the cervix, identified by cytology, but with an unusual site of metastasis in the soft tissue of the left iliac region; this type of neoplasm shows as a first manifestation of metastasis to the regional lymph nodes [1, 5, 9].

Additionally, the initial BSC of the cervix exhibited an unexpected favourable biologic behaviour in our case giving metastasis after a 15-year disease-free period. Also, the fact that the patient is in good general health with an unchanged metastatic tumour, four years now, is

also of particular interest. This is in agreement with a few similar cases discribed by others of BSCs with a similar biological outcome as conventional SCCs when matched for stage, but these reports concerned the head and neck region [10-13]. Moreover, Zbaren *et al.* in their review of BSC of the head and neck concluded that the biological behaviour of this rare tumour remains controversial [14].

To the best of our knowlegde, while references of BSC diagnosed by cytology have been relegated to rare comments (5), no reports could be detected describing a BSC of the cervix diagnosed by FNA.

Our smears contained small groups of basaloid appearing cells with small nucleoli in the ThinPrep preparations, intermingled with pure malignant keratinised squamous cells, while islands of medium-sized cells, with more abundant cytoplasm and peripheral palisading of basaloid cells were evident in the cell-block smears. Our findings are in agreement with the cytologic picture described in the literature. Banks *et al.* describe the tumour cells as small or medium-sized with small round to oval hyperchromatic nuclei, pale nucleus, small nucleoli and scant cytoplasm. The cells form fragments of cohesive cells, large clusters and single cells. Nuclear moulding is often seen but single keratinised cells are rarely seen (5). In contrast, in our case, no moulding was evident and the keratinised cells were abundant, possibly because the tumour was metastatic.

Sometimes large, pleomorphic cells with small eosinophilic nucleoli are present. Mitoses are occasionally numerous [1, 7, 9], a finding that we could not observe in our case. Sheets with peripheral palisading seem to be a clue in histologic specimens and cell-block preparations rather than in cytologic smears [15].

BSC is often reported in association with squamous dysplasia, in situ SCC or invasive SCC [7-9, 16, 17].

Immunocytochemistry was very helpful in our case identifying the epithelial origin of this neoplasm (positive expression for keratin and EMA). The immunophenotype of BSC seems to be controversial in a way, because some studies suggest that all neoplastic cells show strong positivity for high-molecular weight cytokeratin antibody 34βE12 (100%), as well as AE1/AE3 or CAM 5.2 [1, 4, 16]. Also CK 14 seems to be positive in basaloid cells of BSC [2]. On the other hand, some authors refer to a low or no expression of cytokeratins in basaloid cells [8, 9, 15]. EMA is usually positive, while vimentin, smooth muscle actin, desmin and neuroendocrine markers show no or weak reactivity in most of the studies. In a small number of cases positive expression can be seen for the above-mentioned markers as well [1, 4, 8, 9, 16]. NSE (weak, 75%) and CEA (53%) can also exhibit positive staining. This different immunochemical phenotype also reflects the possible origin of the tumour from a pluripotent cell of origin.

The differential diagnosis includes variants of basaloid tumors, especially adenoid cystic carcinoma and small cell neuroendocrine carcinoma [1, 4, 5, 8, 9, 16]. It can be very difficult to differentiate BSC from the solid variant of adenoid cystic carcinoma. Both represent carcinomas that are characterised by a complete loss of differentiation but mitoses, necrosis and nuclear pleomorphism are more prominent in BSC than in adenoid cystic carcinoma [8]. On the other hand, small cell carcinoma does not exhibit large tissue fragments and, at times, pseudoglandular spaces and single keratinised cells are found. Sometimes though, differentiating BSC from small cell carcinoma can be difficult or even impossible [5]. Distinction is important as the biological behaviour, clinical management and prognosis of BSC are different [1, 5, 8, 16, 18]. Apart from the cytomorphologic differences, the most important differential criterion, though, is the identification of a dual population of basaloid and squamous cells, as was obvious in our case, in order to make the accurate diagnosis [17].

The liquid-based cytology technique (ThinPrep) contributed to the diagnosis by providing superior slide quality, with no excess of blood and debris, as observed by others in the literature as well [19, 20]. This resulted in straightforward identification of both cell types. Moreover, application of conventional staining and immunocytochemistry was quite easy and reproducible [19].

The FNA of BSC in our case, using liquid based cytology, contributed to the diagnosis, based both on cytomorphological features and on immunocytohistochemical investigation, in association with the patient's history.

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