Transformation of recurrent hidradenoma into a metastatic hidradenocarcinoma in a 31-year old female patient

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Hidradenocarcinoma is a rare malignant tumour of eccrine cutaneous sweat glands, accounting for less than 0.001% of all tumours and 6% of malignant eccrine tumours. It is known in the literature also as malignant nodular, clear cell hidradenoma or as malignant acrospiroma. The head and neck are the most common sites of hidradenocarcinoma. It is reported that this tumour has high recurrence and metastatic potential, and the prognosis is very poor [1, 2]. It usually arises de novo but rarely results from a pre-existing hidradenoma. There are no uniform guidelines for the treatment, but surgery is the mainstay of the treatment. The postsurgical recurrence rate is 50% [3].

A 31-year-old female was referred to the Clinic of Plastic Surgery, reporting a four-year-old history of subcutaneous tumor in her right axilla.Upon her first clinical check-up by a plastic surgeon, she presented a complete medical history of the disease. In her anamnesis, she reported no previous diseases of significance, no allergies, and a negative family history of malignancies. Her previous medical history and laboratory findings were unremarkable. The first time she noticed a painless subcutaneous lump, with no discharge, in her right axilla was back in 2018. Since then, it slowly grew and was surgically extirpated for the first time in June 2019. The histopathological finding was described as Hidradenoma nodulare cutis, 5 mm in the largest diameter, and positive resection margins. The patient reported that shortly after the first surgery, she could again palpate a lump in her right axilla and was subsequently examined by a general surgeon 2 months after her first surgery. Clinical evaluation showed a lump in the right axilla of 15 mm in the largest diameter, with local erythema and tenderness, and clinically was initially diagnosed as hidradenitis. As the local inflammatory signs resolved but the lump persisted, a check-up ultrasound of the right axilla was done on 7 February 2020. It showed a solid-cystic tumour, with vascularization in its solid part, with a diameter of 22 × 13 × 14 mm. Following such ultrasound findings, the patient was examined by a plastic surgeon, who performed a re-excision of the axillar tumefaction on 16 April 2020. Histopathological findings showed a tumour with immuno-histochemistry results: CK+, CK5/6+, p63+, Bcl2-, S100-, Ki67+ in 10% of cell nuclei, and such findings corresponded mostly to Trichoepithelioma. Resection margins were clear, with the losest one being 1 mm.

Sixteen months after the second surgery, a regular check-up ultrasound of the right axilla showed a recurrent tumor of 13 mm in size, partly cystic and partly solid in structure (Figure 1).

The patient was then examined by a dermato-oncologist, who ordered a revision of histopathological finding from the second surgery. A dermatopathologist analysed histopathological data, and immunohistochemistry finding showed Ki-67+ in less than 5% of the tumour, with proliferative index of 17.2% (counted of 2016 cells); CD31 showed no vascular invasion. Such immunohistochemistry analysis showed a proliferative index higher than the positive range of atypical hidradenoma, which may indicate incipient focal progression in hidradenocarcinoma.

Afterwards, the patient was presented to the Oncological Board, and a decision for more radical surgical treatment was brought. Re-excision of tumour and dissection of the first two levels of right axillar lymph nodes were performed. The histopathological finding of the tumour was described as cystic tumour nodules built from solid beaches of medium-sized polyhedral and rare

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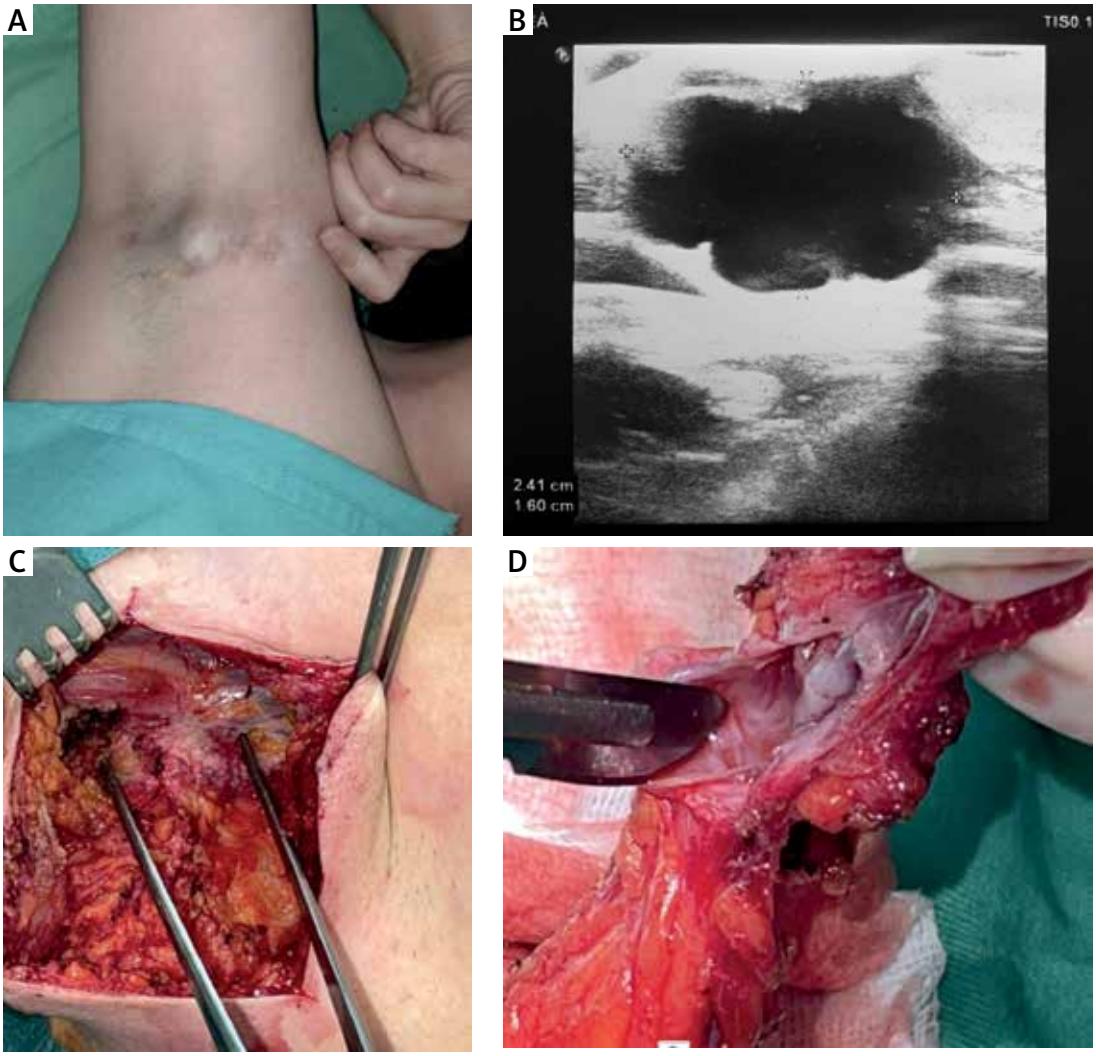

Figure 1. A – Clinical examination showing lump in the right axilla; **B** – Ultrasonography image; **C** – Intra-operative finding of the tumour; **D** – Cystic structure of the tumour

lighter cells that are uniform. Mitoses were rare, without visible pathological forms. Stroma was partly hyalinized, with no signs of necrosis. Resection margins were clear. Regarding axillar lymph nodes, 2 of 18 had secondary deposits of the previously described tumour. The pathologist's conclusion on the report indicated that since there were metastatic lymph nodes (as the only specific parameter of malignancy of such a differentiated tumour), the finding corresponded to the malignant transformation of a recurrent hidradenoma into a metastatic hidradenocarcinoma (Figure 2). Soon after, the patient pursued postoperative radiotherapy combined with chemotherapy potentiation with Capecitabine 500 mg 2 × 2 during the first and last week of radiotherapy. The patient handled postoperative radiotherapy (PORT) well during the 5 weeks and PET CT, which showed no hypermetabolic lesions.

Hidradenocarcinomas are rare malignant tumours of eccrine glands, being more common in men than women, with the age group of 50–70 years having the highest incidence [4, 5]. Most often, hidradenocarcinoma occurs de novo as an aggressive primary tumour, and significantly less often, they develop over a specific, prolonged period through a biological transformation from their benign counterpart, hidradenoma [6]. Typical localizations of hidradenocarcinoma are the head and trunk, with extremities being uncommon [7].

All the above facts considered, our patient represents a rare case regarding her age, tumour localization, and biological transformation from the benign counterpart of hidradenoma to hidradenocarcinoma. Local relapse of disease after surgical extirpation should raise suspicion of the malignant nature of the illness [8]. The histopathologic finding of well-differentiated hidradenocarcinoma (HAC) consists of cells whose cytoplasm is filled with glycogen

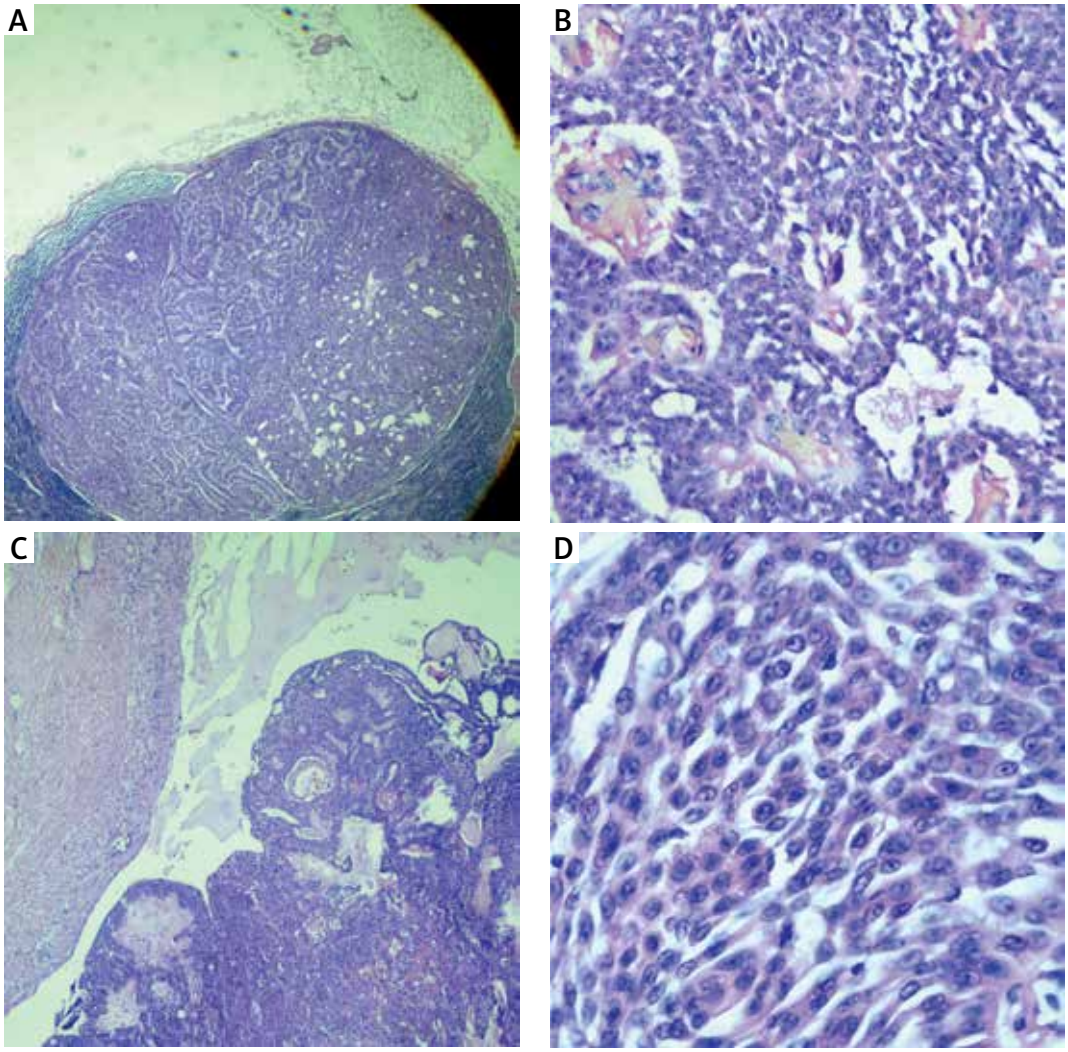

Figure 2. A – Lymph node metastasis HE (20×); **B** – Microcystic formations of tumour cells HE (400×); **C** – Intracystic proliferation of tumour tissue in the dermis; **D** – Minimal pleomorphism of tumour cells, with scarce mitosis

and presented pale. Furthermore, peripheral lobules of tumours seem irregular and invasive and may or may not have focal necrosis. The immunohistochemistry patterns may vary, but they can still provide some information. So far, Ki67, p53, S-100 protein, epithelial membrane antigen, carcinoembryonic antigen, and gross cystic disease fluid protein-15 (GCDFP-15) have been reported to be positive, but not exclusively [9]. In our patient, a recurrent hidradenoma had transformed to its malignant counterpart hidradenocarcinoma. Yet, the first pathohistological revision suggested either borderline atypical hidradenoma or a slight focus of hidradenocarcinoma in a focus of hidradenoma. Such a finding, with a mixture of malignant and benign components, makes the pathologist's job even more complex, and other invasive diagnostic approaches, such as punch biopsy and incisional biopsy, would prove an unreliable sample for pathohistological examination. The immunohistochemical staining pattern proved helpful, yet only through wide surgical resection and axillary lymph node dissection, a truly malignant, invasive nature of HAC was determined, as metastases in two regional lymph nodes were discovered. Such finding relates to a wide range of lesions, from well-differentiated hidradenoma-like tumours to invasive, poorly differentiated ones with metastatic potential [10].

Conflict of interest

The authors declare no conflict of interest.

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