

Malignant cylindroma in a patient with Brooke-Spiegler syndrome

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ABSTRACT Malignant cylindroma (cylindromatous carcinoma, cylindrocarcinoma) is the malignant counterpart of benign cylindroma. It is a rare neoplasm, more often developing in the setting of multiple pre-existing benign neoplasms. Herein we present an additional case of malignant transformation of the cylindroma diagnosed in an 83-year-old patient with known Brooke-Spiegler syndrome.

Case presentation

An 83-year-old patient presented to the dermatologist numerous times with multiple lesions on the face, scalp and ears (Figure 1). Lesions were gradually excised (11 lesions were excised and studied from 2011-2013). Histopathologically, two of the lesions were benign cylindromas, four were spiradenomas, and four others were combined lesions (cylindromas in conjunction with spiradenomas). The patient was diagnosed with Brooke-Spiegler syndrome. At the time of this biopsy, the patient presented with a rapidly enlarging nodule on the scalp.

The biopsy of the scalp showed an adnexal neoplasm with poor circumscription, irregular borders and infiltrative growth pattern at the base (Figure 2). It was composed of small irregular cylindroma-like aggregates, which had almost lost their



Figure 1. Multiple nodules in the central face. [Copyright: ©2015 Kazlouskaya et al.]

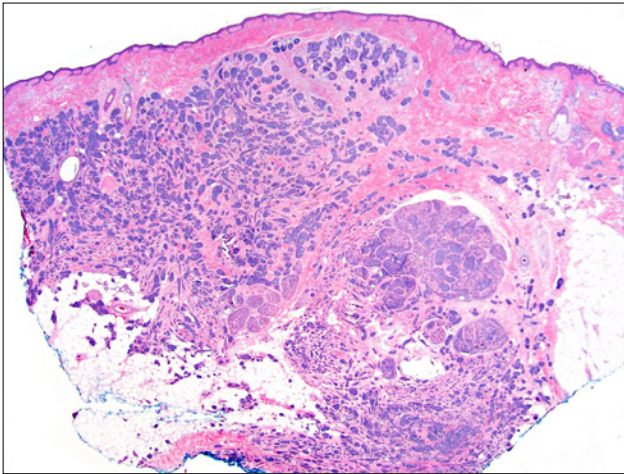


Figure 2. A cylindroma-like adnexal neoplasm with an irregular, infiltrative pattern. Hematoxylin and eosin (H&E) stained sections, $\times 40$. [Copyright: ©2015 Kazlouskaya et al.]

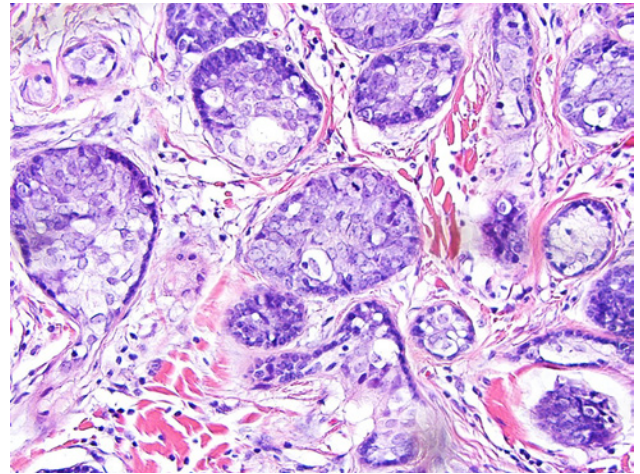


Figure 4. Tumor aggregates composed of mostly enlarged cells with mitotic figures. Lack of hyaline sheath around them. H&E stained sections, $\times 400$. [Copyright: ©2015 Kazlouskaya et al.]

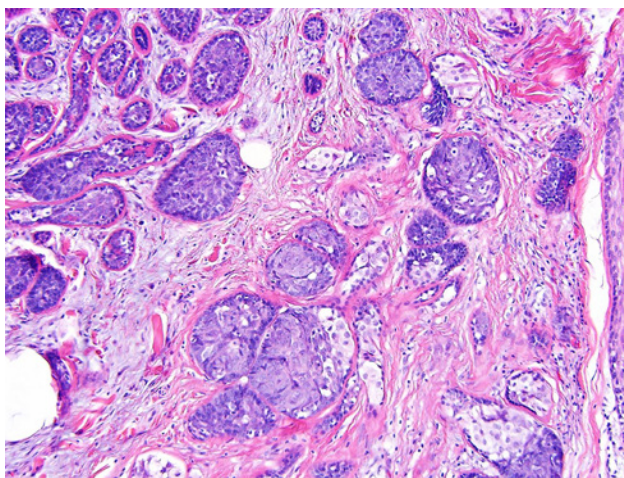


Figure 3. Small irregular aggregates of the cylindrocarcinoma, some are without hyaline sheath. Loss of jigsaw pattern. H&E stained sections, $\times 100$. [Copyright: ©2015 Kazlouskaya et al.]

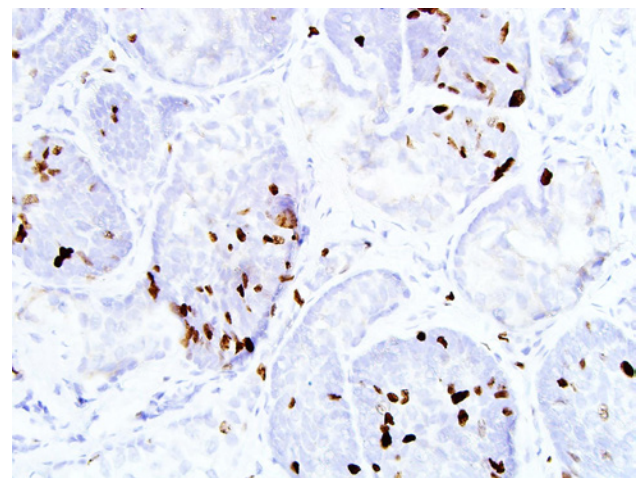


Figure 5. Ki-67 immunostain in cylindrocarcinoma. [Copyright: ©2015 Kazlouskaya et al.]

jigsaw pattern. Hyaline sheaths were lost around some aggregates (Figure 3). The cells of the tumor were mostly enlarged with striking nuclear pleomorphism. There was individual cell necrosis, but no necrosis en masse (Figure 4). Focal clear cell change was seen. S100 immunostain showed a patchy staining and was inconclusive. Ki-67 immunostain showed relatively high proliferation rate (Figure 5). The diagnosis of cylindrocarcinoma was made and the complete excision of the tumor was recommended. On the re-excision, the tumor showed the same pattern with the involvement of the fat with the small aggregates of the tumor (Figure 6). A focus of spiradenoma was revealed in one of the sections of the re-excision specimen (Figure 7A and B). No recurrences or metastases were observed in this patient after 12 months of follow up.

After a year of follow up, the patient presented with two additional enlarging nodules on the scalp (different locations from the first one). Both of tumors showed unusual features, including infiltrative growth pattern, asymmetry,

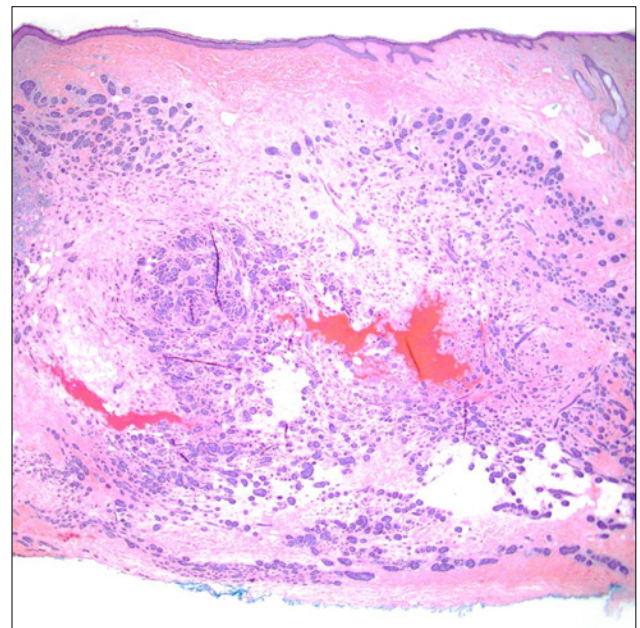


Figure 6. Re-excision of cylindrocarcinoma showed infiltrative pattern with the involvement of the fat tissue and underlying structures. H&E stained section, $\times 20$. [Copyright: ©2015 Kazlouskaya et al.]

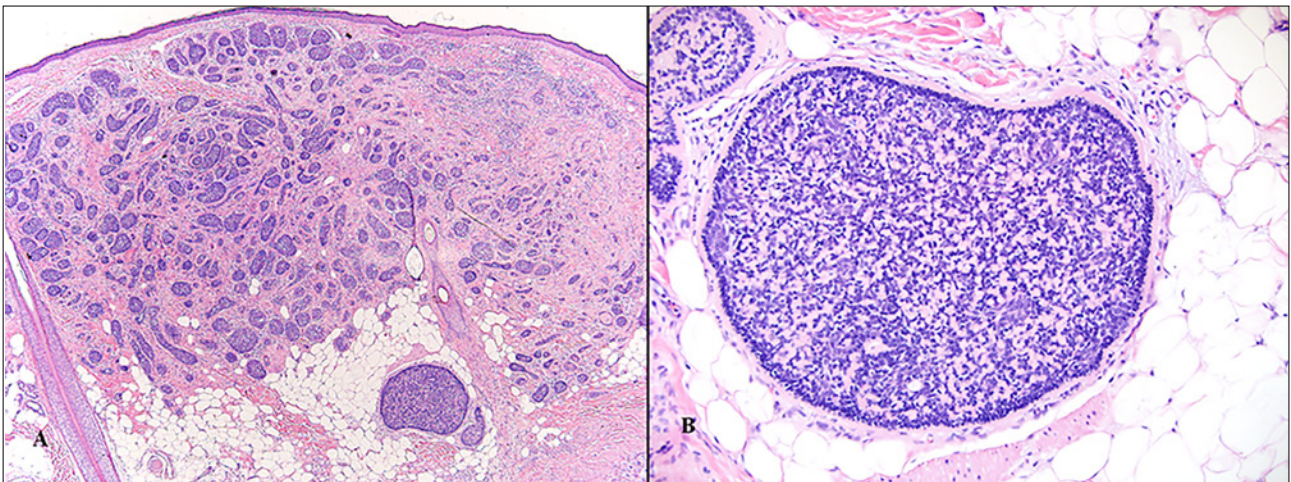


Figure 7. Re-excision of cylindrocarcinoma. (A) One of the sections showing a focus of spiradenoma. H&E stained sections, $\times 40$. (B) High power of spiradenoma seen adjacent to cylindrocarcinoma, H&E stained sections, $\times 200$. [Copyright: ©2015 Kazlouskaya et al.]

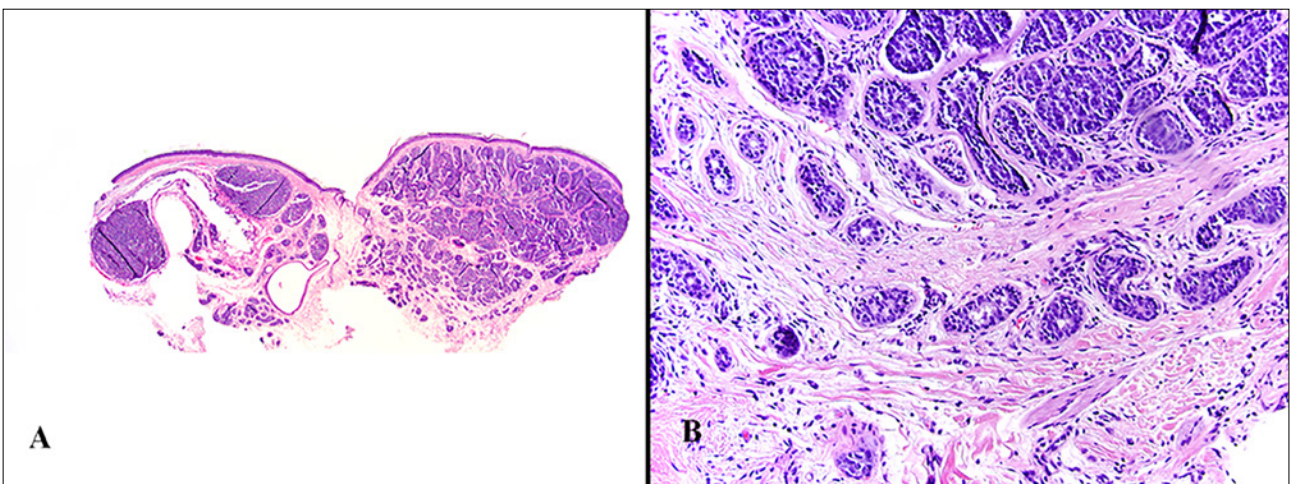


Figure 8. Tumor of the scalp, excised after one year of follow up. (A) Assymmetrical tumor, composed of parts resembling cylindroma and spiradenoma. H&E stained sections, $\times 40$. (B) Infiltrative growth pattern of the tumor nests. H&E stained sections, $\times 200$. [Copyright: ©2015 Kazlouskaya et al.]

and infiltration of subcutaneous tissue with small irregular tumor aggregates. One of the tumors also had areas resembling spiradenoma (Figure 8A and B). The second tumor was curetted and presented with fragments of the tumor, involving subcutaneous fat tissue (Figure 9A and B). Although cytological abnormalities were not striking, both tumors were felt to have malignant differentiation based on their architectural characteristics.

Discussion

Malignant cylindroma (cylindrocarcinoma) is an extremely rare adnexal neoplasm. It was first described by Wiedmann in 1929 on the scalp of a 63-year-old woman [1,2]. After the excision of the lesion, the patient died of visceral and lymph node metastases. So far, less than 50 cases of malignant cylindroma have been reported in literature.

Several authors have reported a greater tendency of malignant cylindroma formation in patients with multiple pre-existing benign lesions. Rare sporadic solitary tumors are also described [3,4]. Brooke-Spiegler syndrome (BSS) is the most frequently associated with malignant cylindromas. The syndrome has autosomal-dominant inheritance. The formation of multiple cylindromas in patients with this syndrome may be due to *CYLD* gene located on 16 chromosome [5].

Clinically, cylindrocarcinomas most commonly are localized on the head and neck. The malignant variant shows rapid enlargement, bleeding, ulceration, color change, fixation and pain.

When the tumor develops from the longstanding benign neoplasm, it is possible to identify gradual or abrupt transition to the malignancy [6]. Histopathologically, malignant cylindroma is characterized by loss of the jigsaw pattern, loss of the delicate hyaline sheaths, loss of peripheral palisading of

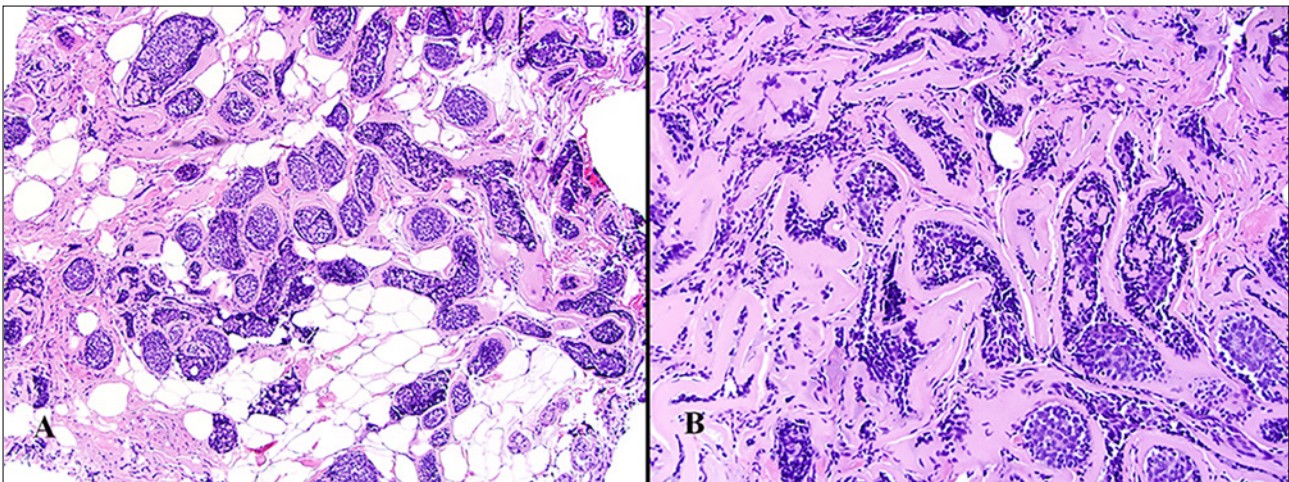


Figure 9. Second tumor, excised after a year of follow up. (A, B) Irregular cylindroma-like nests of tumor, extending into subcutaneous tissue. H&E stained sections, $\times 200$, $\times 400$. [Copyright: ©2015 Kazlouskaya et al.]

the tumor islands at the periphery, and loss of the bimorphic cell composition. It exhibits nuclear pleomorphism, abnormal crowded nuclei, a high mitotic rate, stromal invasion and focal areas of necrosis. Requena et al mentioned that asymmetry, poor circumscription, necrosis en masse may help to make a diagnosis even at low magnification.

As its benign counterpart, malignant cylindroma may be associated with spiradenoma, forming so-called “spiradenocylindrocarcinoma” [8-10]. We have observed a focus of spiradenoma in the subsequent re-excision sections of the presented lesion, and in one of the tumors developed later, but there were no atypical cytological changes seen in the foci, and we concluded that the term “cylindrocarcinoma” is preferable. Features of malignancy, mentioned above, may be scant and seen only in a few histopathological sections. Several cases of well-differentiated malignant cylindromas were reported [3, 11, 12]. Kazakov et al described several histopathological patterns of malignant tumors arising in the setting of pre-existent spiradenomas and cylindromas in patients with BSS [6]. Most frequently, neoplasms resembled salivary gland basal cell adenocarcinomas and had either low grade or high-grade malignant differentiation. Infiltrative and sarcomatoid poorly differentiated pattern was seen in lesser amount of cases. No immunohistochemical markers help to perform a differential diagnosis between benign and malignant cylindromas with certainty. When the neoplasm is undifferentiated, the use of cytokeratins, carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA) may help to define the tumor origin [13]. Expression of S-100, laminin, collagen IV, fibronectin and CD-34 have been reported [14,15]. Presence of estrogen receptors was shown by Apostolou et al [8] Ki-67 may be helpful to highlight a high proliferative rate [9].

Cylindrocarcinoma must be distinguished with the benign cylindroma and spiradenoma. Membranous variant

of basal cell adenoma and its malignant counterpart—basal cell adenocarcinoma of the salivary glands—may be indistinguishable from cutaneous cylindrocarcinomas. As well as cutaneous neoplasms, they may have similar hyaline deposits and share similar genetic abnormalities. Both benign and malignant variants of salivary gland tumors may co-exist with cylindromas/cylindrocarcinomas [16,17]. Several cases of the anal/rectum basaloid tumor with the features of cylindroma/spiradenoma have been reported recently [18,19] Presence of koilocytes, presence of squamous cell carcinoma (SCC) in situ and identification of HPV allow to classify those tumors as HPV-induced SCC in situ.

When malignant cylindroma is diagnosed histopathologically as a solitary lesion, the treatment of choice is wide local excision because of the high recurrence rates and the potential to metastasize. In addition, laser ablation, Mohs’ micrographic surgery, cryotherapy, retinoic acid, trichloroacetic acid, carbon dioxide laser and radiotherapy can be performed [20,21]. In extensive lesions, resurfacing with split skin-grafts is the method of choice for covering the defects [22]. Aggressive behavior with frequent extensive local infiltrative growth and metastases is known for malignant cylindromas. To ensure a better prognosis, early diagnosis and close follow-up is mandatory especially in patients with multiple cylindromas.

The prognosis and prognostic features of malignant cylindromas are not well described due to the low number of reported cases and insufficient follow up on the patients. In the summary of 24 reported cases of malignant cylindroma Gerretsen et al reported that local recurrence was seen in 9 cases, metastases to the lymph nodes or viscera were seen in 11 cases and 11 patients died [23]. Liver and vertebral column are particularly affected. Metastases to thyroid, stomach and bones as well as intracranial invasion and transcranial erosion by cylindromas have been observed [24-26]. Perineural involvement may occur [3].

Our case report represents one more example of this rare entity and widens our horizons of this unique tumor. It may be interpreted as “spiradenocylindrocarinoma.” Some parts of the tumor, including spiradenoma did not show atypia, therefore we prefer the interpretation that the malignant tumor developed from the pre-existing benign tumor composed from cylindroma and spiradenoma.

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