Malignant Cylindroma of the Scalp Arising in a Setting of Multiple Cylindromatosis: A Case Report

Riya M. Kuklani · Frederick L. Glavin ·
Indraneel Bhattacharyya

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Abstract An unusual case of malignant cylindroma of the scalp arising in a 79-year-old white female with multiple cylindromatosis is presented. The tumor apparently arose from a cylindroma and had features of spiradenoma. Multiple cylindromatosis is an uncommon hereditary autosomal dominant disease, which is characterized by multiple skin adnexal tumors like cylindromas and trichoepitheliomas and occasional spiradenomas. Cylindroma is an uncommon benign tumor, which originates from skin appendages and is most commonly found on the scalp and face with a strong predilection for middle-aged and elderly females. Although cylindromas are usually benign neoplasms, carcinoma arising in such neoplasms is rare with only sporadic reports in literature. Her family history was negative for a similar disease. The patient's main concern was painful lesions over her right ear that interfered with wearing of her glasses. The clinical, histological immunohistochemical features, and treatment are presented along with a review of the literature.

Keywords Multiple cylindromatosis · Brooke–Speigler syndrome · Malignant cylindroma · Cylindroma · Spiradenoma

Introduction

Multiple cylindromatosis is a rare hereditary autosomal dominant condition typically characterized by multiple cylindromas and trichoepitheliomas and occasional spiradenomas [1]. Cylindromas are benign skin appendage tumors with two distinct clinical presentations, namely, solitary and multiple [2, 3]. Solitary cylindromas occur most commonly on the skin of the head and neck and occur sporadically and typically are not inherited [3, 4]. Multiple cylindromas are inherited in an autosomal dominant pattern and occur on the scalp and rarely on the trunk and the extremities [3, 5]. Multiple lesions can cover the entire scalp giving an appearance of a disfiguring turban-like appearance hence the eponym “turban tumor” [5]. Multiple cylindromas are more common in females and occur over a wide age range, with majority of patients in second or third decades of life [3, 6]. Malignant transformation of a solitary cylindroma is extremely rare and is somewhat more common, but unusual (33 cases reported) in patients with multiple lesions [2]. Characteristic clinical features indicating malignant change include rapid enlargement, increased tenderness, and change in color of a long-standing ulcerative lesion or bleeding [2, 5, 7–11]. The malignant cylindroma is locally aggressive, often metastasizes, and requires careful long-term follow-up [2, 4].

We report a rare case of malignant cylindroma arising in a patient with multiple cylindromatosis on the temporal region and discuss the histological and immunohistochemical

R. M. Kuklani · I. Bhattacharyya (✉)
Oral and Maxillofacial Pathology, Department of Oral and
Maxillofacial Diagnostic Sciences, University of Florida College
of Dentistry, P.O. Box 100414, Gainesville, FL 32610, USA
e-mail: ibhattacharyya@dental.ufl.edu

R. M. Kuklani
e-mail: rkuklani@dental.ufl.edu

F. L. Glavin
Division of Dermatopathology, Department of Pathology,
Immunology and Laboratory Medicine, University of Florida
College of Medicine, P.O. Box 100414, Gainesville,
FL 32610, USA
e-mail: fglavin@pathology.ufl.edu

features of this lesion. In addition, we summarize the cases reported in the literature.

Case Report

A 79-year-old Caucasian female presented with a chief complaint of a large painful growth over the right ear (Fig. 1a), which interfered with her wearing glasses. She reported a 20-year history of multiple growths on her scalp, back, forehead, face, and neck (Fig. 1b). She indicated that a diagnosis of Brooke–Spiegler syndrome (BSS) had been rendered by her dermatologist. She had a similar but smaller well-circumscribed exophytic lesion on her right shoulder removed and diagnosed as cylindroma, a few years back. She also reported lesions involving her ear canals and the skin of the nose as well as perioral region bilaterally. All lesions were skin colored and exhibited telangiectatic surface blood vessels. The lesions appeared sessile, firm to palpation, and were essentially non-tender except for the lesion behind the right ear. Her parents and her daughter are unaffected and did not have similar lesions. The patient's medical history was non-contributory and all laboratory investigations were within normal parameters. The lesion on her shoulder had recurred once before. Surgical excision of large right temporoparietal lesion was done and tissue submitted for microscopic examination.

Microscopic Examination

Multiple sections of the tissue were obtained and revealed a large neoplastic growth largely exhibiting a circumscribed-basaloid epithelial neoplasm divided in to discrete nodules with abundant basement membrane material within and around the nodules, in a cylindroma-like pattern (Fig. 2a). Focally a spiradenoma pattern was noted (Fig. 2b) where the nodules were not as prominently surrounded by the eosinophilic basement membrane material. In this focus, the two cell types: small dark basaloid cells with hyper-

chromatic nuclei, and a more frequent larger cell with a pale nucleus, which tends to be near the center of the clusters with an infiltrate of lymphocytes and plasma cells were seen. However, in several sections, a malignant component was noted. The malignant component was extensive and exhibited irregular asymmetrical proliferation of multiple nodules and strands of hyperchromatic cells (Fig. 3a). In these areas, a solid and glandular or pseudo-glandular appearance with tightly packed cells and a vascular stroma was noted (Fig. 3b). The glandular spaces displayed a pale eosinophilic mucoid material intermixed with inflammatory cells and erythrocytes (Fig. 4a). The cellular component exhibited prominent cytologic atypia with individual cell necrosis and numerous mitotic figures (Fig. 4a). In addition, areas of cellular and nuclear pleomorphism with prominent nucleoli were noted (Fig. 4b). The malignant component varied in architectural pattern ranging from a poorly differentiated cylindromatous/spiradenomatous pattern to that of a obvious adenocarcinoma that extended into the subcutis. Immunohistochemical stains were diffusely positive for low molecular weight keratin (CAM 5.2) throughout the specimen and focally reactive for S-100 protein in the malignant portion of the lesion. Stains for epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA) were negative. A diagnosis of malignant cylindroma arising in association with multiple cylindromatosis was rendered. No genetic counseling was done. To date (one year post-operatively), the patient is alive and well with no recurrence or complications.

Discussion

Malignant cylindroma was first recognized by Ancell [12] in 1842 in a family, the members of which presented with multiple scalp tumors; the term cylindroma has subsequently been used to describe these lesions. Clinically, the lesions are nodular, smooth, pink, and skin colored; maybe solitary or multiple and may vary in size. The lesions are usually painless but it is not unusual to have pain [4].

Fig. 1 **a** Large painful growth over the right ear, which interfered with her wearing glasses. **b** Multiple variably sized, skin colored, confluent lesions are seen on scalp, forehead, face, and neck

Fig. 2 **a** Cylindroma-like pattern was predominant with cellular islands resembling jigsaw puzzle with scant stroma and no hyaline sheets (H & E stain; magnification $\times 10$). **b** The section revealed a small nodule of spiradenoma (arrows) (H & E stain; magnification $\times 20$)

Fig. 3 **a** Malignant portion of tumor with continuity with both epidermis and eccrine and apocrine ducts (H & E stain; magnification $\times 10$). **b** Higher power image of malignant cylindroma (H & E stain; magnification $\times 20$)

Fig. 4 **a, b** Photomicrographs of the tumor exhibiting atypical cells with high nuclear/cytoplasmic ratios and increased mitoses. Cellular and nuclear pleomorphism and prominent nucleoli are seen throughout the neoplastic process (H & E staining; magnification $\times 40$)

Solitary cylindromas typically occur on scalp with no positive familial history [5]. Multiple cylindromas are associated with BSS with positive family history [13]. Malignant transformation of cylindroma is very rare and even more so with the solitary type than with the multiple variant [4, 9, 11]. In 1929, Wiedemann first described malignant cylindroma [14]. The prevalence of this condition is not well established since the literature largely consists of case reports, according to a previous review 24 cases of malignant cylindroma has been published from 1987 to 1993 [2]. We identified a total of 33 well-documented cases of malignant cylindroma in the literature using a Pubmed database search. The number of cases still remains variable since not all cases are well documented. We present the demographics, family history, age of onset, metastasis,

therapy, local recurrence, follow-up for a total of 34 cases including the present case (Table 1) [2, 5, 7, 15–19].

Multiple cylindromas appear shortly after puberty and present as numerous, rounded nodules of various sizes, which gradually increase in size and number throughout adult life. Ulceration with rapid growth and pain is one of the principal reasons for patients seeking care, but our patient presented with lesions, which were essentially asymptomatic. Her chief complaint was that the lesion interfered with her wearing glasses.

According to current understanding of malignant cylindroma, a positive family history is almost always reported, however, our patient did not present any family history. Despite variable phenotypic expressions of a predominant tumor in BSS, a unique gene *CYLD* has been

Table 1 Clinical features of 34 patients with malignant cutaneous cylindroma [3, 5, 10, 17–21]

Patient no.	Age (year)	Sex	Family history	Solitary/multiple	Location	Treatment	Follow-up	Remarks
1	79	M	Unk	M	S	X	Nod	
2	63	F	Unk	S	S	X	Dod	Local recurrence with lymph node and visceral metastasis
3	96	F	Unk	S	E	X	Nod	
4	90	M	–	S	S	X,R	Nod	Local recurrence with visceral metastasis
5	74	F	Unk	S	T	X	Dod	Local recurrence
6	68	F	Unk	S	S	X	Nod	Local recurrence
7	66	M	Unk	S	S	X	Unk	
8	78	F	Unk	S	S	X,R	Nod	
9	71	F	Unk	S	S	X	Nod	Local recurrence
10	50	F	+	M	S	–	Dod	Lymph node and visceral metastasis
11	60	M	Unk	M	FT	X,R	Nod	Lymph node metastasis
12	63	F	+	M	S	X,R	Dod	Visceral metastasis
13	60	M	–	S	S	X	Dod	Local recurrence
14	59	M	–	S	S	X,R	Dod	Local recurrence
15	72	F	+	S	F	X	Dod	Visceral metastasis
16	64	F	–	M	S	X	Dod	Local recurrence with lymph node metastasis
17	81	F	+	S	S	X	Nod	
18	78	F	+	M	S	X	Nod	
19	76	F	Unk	S	S	X	Nod	Lymph node metastasis
20	76	M	Unk	S	S	X	Dod	
21	60	M	+	M	S	X	Nod	Lymph node metastasis
22	69	F	+	S	S	X	Dod	Local recurrence with lymph node and visceral metastasis
23	77	F	+	S	T	X	Nod	
24	72	M	+	S	T	X	Dod	Local recurrence with lymph node metastasis
25	39	M	–	M	S	X	Nod	Local recurrence
26	68	F	+	M	ST	X	Dod	Local recurrence
27	63	F	–	S	T	X,R	Nod	Local recurrence with lymph node metastasis
28	68	F	–	M	S	X,R	Nod	
29	55	F	+	M	SF	X	Dod	Lymph node metastasis
30	73	F	–	S	S	X	Nod	
31	62	M	–	S	S	X	Nod	
32	72	F	–	S	S	X	Dod	Visceral metastasis
33	75	F	+	M	TS	–	Nod	
Present case	79	F	–	M	SFT	X	Nod	Disease free 12½ month post-operatively

E extremity, *F* face, *S* scalp, *T* trunk, *X* excision, *R* radiation therapy, + present or positive, – not present or negative, *nk* no data available, *Dod* died of disease, *Nod* no evidence of disease

identified, which is considered to be responsible for multiple cylindromas [20].

The characteristic histologic features of malignant cylindroma are (a) loss of jigsaw pattern, (b) loss of hyaline sheaths, (c) loss of peripheral palisading at the tumor island periphery, (d) loss of bimorphic cell composition, (e) marked nuclear anaplasia, (f) stromal invasion, (g) focal

areas of necrosis, (h) pleomorphism of nuclei, and (i) increased and abnormal mitoses. Tumor islands are composed of two cells types. The peripheral cells are small and highly basophilic with palisading of nuclei. The larger central cells are more pale staining cells. Malignant tumors can spread along draining lymphatic vessels to the related viscera [8]. There may be metastases to regional lymph

nodes, stomach, thyroid, liver, lung, and bones [8]. Transcranial erosion and intracranial invasion by cylindromas has also been reported [21].

The histogenesis of cylindroma has remained a subject of intense and controversial debate. Numerous theories have been suggested as to the question of whether they are apocrine or eccrine origin [2, 6]. Meybehm and Fischer [22] performed an immunohistochemical analysis of nine spiradenomas and seven cylindromas. They report that the two lesions present histomorphological similarities to adnexal structures and which can be evidenced by the immunohistochemical expression of S-100, lysozyme, alpha-smooth muscle actin, and cytokeratin staining patterns including keratins 7, 8, and 18 [22]. Other markers indicating derivation from both eccrine and apocrine glands include positive reactivity to EMA, CEA, mucin-like carcinoma-associated antigen (b12), laminin, collagen IV, fibronectin, and CD34. Immunohistochemical analysis in our case revealed diffuse positivity for low molecular weight keratin (CAM 5.2) and focal reactivity to S-100 protein only in the malignant portion of the lesion. EMA and CEA were negative.

The preferred method of treatment for solitary lesions is wide local excision because of undesirable recurrence rates and the risk of malignant transformation of these tumors. Other treatments include scalping, Mohs' micrographic surgery, laser ablation, electrodesiccation/curettage, cryotherapy, trichloroacetic acid, retinoic acid, carbon dioxide laser, and radiotherapy [23]. Multiple cylindromas usually require extensive plastic surgery that may be obviated by progressively excising a group of nodules in multiple procedures [23]. Malignant cylindromas are locally aggressive and usually metastasizes. Gerretsen et al. [2] reported metastases in 16 patients (67%), local recurrences in 9 patients (41%), death as a result of their tumor in 7 patients (29%). Our patient remains disease free to date, 12 months post-surgery.

Conclusions

Malignant cylindroma arising in multiple cylindromatosis is a rare condition. Malignant transformation of cylindroma is uncommon, but should be considered in clinically altered tumors, especially in patients with multiple cylindromas of the head or trunk. Malignant cylindroma is an aggressive tumor with tendency of local destructive growth and potential to metastasize. Therefore, early diagnosis offers the patient the best options for management. Since malignant transformation of benign cylindromas occurs more often in the multiple forms, close clinical follow-up of patients with multiple cylindromas is mandatory.

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