Introduction

Retiform hemangioendothelioma (RH) was first described in 1994 as a distinctive form of low grade angiosarcoma, most often occurring on the extremities of young adults. RH often presents as a single cutaneous plaque or subcutaneous nodule that is either asymptomatic or with local discomfort. The characteristic histomorphologic features include proliferation of arborizing blood vessels arranged in a retiform pattern, resembling rete testis. RH differs from angiosarcoma in lacking cytologic atypia and high mitotic rates. This neoplasm grows slowly and frequently recurs but rarely metastasizes. So far, less than 30 cases have been reported in literature, and only two cases being reported with lymph node metastasis.

We report a case of RH in a Chinese woman who presented with aggressive fast growing lesions that led to her ultimate demise in 9 months. The lesions were associated with paroxysmal sharp needle-stabbing like headache. To our knowledge, this is the first report of RH in Chinese patients. Most importantly, the unique clinical features and the aggressiveness of this case would expand the scope of our understanding of RH, a presumptively low grade sarcoma.

Case report

A 61-year-old Chinese woman with complaint of a bleeding, ulcerating, painful skin lesion on the top of her right scalp was admitted to our hospital in November 2008. Three months prior to this visit, the patient firstly noticed several purple-reddish blisters of green bean size on the top of her right scalp. These blister-like lesions quickly enlarged, grew confluent, and developed into a large plaque-like lesion on her right scalp, followed by another lesion behind the right ear. The lesions were associated with paroxysmal sharp needle-stabbing like headache. She underwent wide excision and skin engraftment. Three months post surgery, she experienced tumor recurrence, and died 9 months after the initial diagnosis.

Keywords: Retiform hemangioendothelioma, headache, recurrence
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nodule behind the right ear. She had no fever, vomiting, blurred vision or other complaints. Her past history, family history and social history were unremarkable.

On physical examination, the patient was well-nourished and in no acute stress. Two lymph nodes about 1cm in diameter were palpated in the posterior triangle of the neck. The remaining systemic examination was unremarkable; specifically, there was no bleeding, no ecchymosis, or organomegaly. Skin inspection revealed a large plaque-like lesion on the top of right scalp measuring 6cm × 8cm. The lesion was raised up to 1 cm and had an irregular border. The surface of the lesion was covered by black thick crusts with focal erythematous changes and ulceration (Figure 1A). A second nodular lesion was seen behind the right ear measuring 2cm × 1.5cm that had a smooth surface and was non-mobile (Figure 1B). All routine laboratory tests, including complete blood count, urinalysis, blood glucose level, liver and kidney function and chemistry profile were within normal range. HIV serology test was negative. Bacteria culture from the scalp lesion (scrap of ulcerated areas) reported growth of Staphylococcus aureus and Staphylococcus sciuri. Fungal culture was negative.

Image studies: Chest X-ray radiography, abdominal and pelvis ultrasonography were all unremarkable. Ultrasonography studies of the jaw and facial regions revealed bilateral neck low hypoechoic nodules, likely representing enlarged lymph nodes. Skull bone scan and computed tomographic scan (CT scan) showed intact skull cortex, no evidence of bone lesions. MRI showed no brain lesions. The scalp lesion showed linear density enhancement, and associated soft tissue swelling. This scalp lesion had an irregular undefined border, but there was no evidence of bone invasion. The second lesion (behind the right ear) was oval-shaped with a relatively well demarcated border, measuring 1cm x 2.3cm, with no bone invasion.

Histopathology and immunohistochemistry

Histological examination of tumor tissue from the right scalp showed proliferation of vessels with in a retiform(net-like) pattern involving the superficial and deep dermis (Figure 2A). The vessels were lined by monomorphic cells with scant cytoplasm and rounded, and hobnail-like nuclei (Figure 2B). Nuclear atypia was either absent or mild. Mitotic figures were essentially not identified. In addition, there was a significant lymphocytic infiltrate present. Immunohistochemically, the tumor cells reacted with endothelial markers (CD34, factor-VIII-related antigen), and vimentin, and negative for cytokeratin, S-100, leukocyte common antigen (LCA) and Actin. Ki-67 showed a low proliferation index in tumor cells (10%) (Figure 3A-E).

Treatment and Follow-up Based on the clinical, histological and immunohistochemical features, a diagnosis of RH was made. Subsequently, the patient underwent a wide excision of the tumor.
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Figure 2. A. low power view (Hematoxylin-Eosin, magnification x100) of the scalp biopsy showing epidermal hyperplasia, and dermis infiltrate by a vascular lesion. B. The vascular lesion composed of multiple interconnecting blood vessels arranged in retiform pattern lined by monomorphic hobnail-like endothelial cells, without significant morphological atypia. Many small reactive lymphocytes are present (Hematoxylin-Eosin, magnification x400).

Figure 3. Immunohistochemistry stains. The tumor cells (endothelial cells and pericytes) positive for vimentin(A); and factor VIII-related antigen (B), CD34 (C). Smooth muscle actin highlights the vascular wall, but negative in the tumor cells (D). Ki67 shows a low proliferation fraction of the tumor cells (E).

on the scalp as well as the tumor posterior of the right ear, followed by skin flap transfer and graft from her thigh (Figure 4A-B). Excisional biopsy of neck lymph nodes was also performed. The resection specimen of the scalp tumor showed similar histopathologic features to that described on the pouch biopsy. The lesion from the posterior right ear was essentially identical to the scalp lesion morphologically. Multiple sections were submitted and examined, and no areas of a high grade tumor (angiosarcoma) were identified. The lymph nodes of right neck showed reactive follicular and paracortical hyperplasia, and there was no evidence of metastatic tumor. Because of tumor border of the scalp lesion was unclear grossly, the resection margins of the first excision were positive, confirmed by immunohistochemistry,
and she underwent a second local excision. She received no radiation or chemotherapy post surgery. Three months after the operation, she experienced local recurrence in the scalp area, which was accompanied by concurrence of sharp needle-stabbing like headache. She was seen at local hospital, and the treatment was unclear. She passed away at home 6 months after the surgery.

Discussion

Retiform-hemangioendothelioma (RH) is an extremely rare low-grade malignant angiosarcoma characterized by a net-like growth pattern, a high rate of local recurrence and a low frequency of metastasis [1]. So far, less than 30 cases have been reported in literature [1-3]. In 2008, Tan et al[2] reported one RH case and reviewed previously reported 23 cases of RH patients. Of the 24 cases of RH, 16 tumors occurred in the extremities (12 on lower limbs), 5 in the trunk, and 1 each on the penis, scalp and skull respectively. Most of the patients present with solitary lesions, only one with multiple tumors in the trunk and extremities. Nearly half of the reported 24 patients experienced locally recurrence, but only one patient had regional lymph node metastasis. In 2009, Bhutoria et al [3] reported another case of RH with lymph node metastasis and local tumor recurrence two years after the excision of primary lesion over mons pubis. Up to date, no distant metastasis or tumor-related death has been reported.

Histologically, RH is a vascular tumor characterized by multiple interconnecting, arborizing blood vessels arranged in a retiform pattern, lined by monomorphic hobnail endothelial cells that showed minimal to mild cytologic atypia and no mitotic figures [1, 4, 5]. In addition, many cases show a prominent lymphocytic infiltrate. Immunohistochemically, RH neoplasm endothelial cells react with vascular endothelial markers CD31, CD34, factor VIII-related antigen and bound Ulex europaeus agglutinin [5, 6]. In our case, the tumor cells showed typical morphological and immunophenotypical features of RH. There were minimal to mild cytological atypia no mitosis or necrosis. Ki-67 showed a proliferation rate of approximately of 10%. Multiple sections from the resection specimens were examined, showing no evidence of angiosarcoma. The case fulfilled the criteria for RH.

Our case showed several unusual and unique clinical features: multiple lesions, fast growing, and associated with sharp needle-stabbing like headache. The nature of the headache was atypical for a vascular tumor, and as a result, it was misdiagnosed as herpes zoster infection. The underlying causes of headache was unclear, but likely a result of vasospasm, secondary infection, bleeding, and ulceration of the scalp lesion. Up to now, only one case in the reported RH patients presented with a rapidly growing lesion [7]; one case with multiple lesions located on trunk and extremities; and another case with a single lesion on the scalp reported[2]. In our patient, although it is not clear if
the second lesion behind the ear was another primary tumor or a tumor secondary to soft tissue metastasis of the scalp tumor, the proximity of the lesions as well as sequential occurrence of these two lesions would favor the later. It is noteworthy that there was no evidence of bone or intracranial invasion despite the large size of the scalp lesion, neither metastasis in the local lymph nodes.

The main differential diagnosis of includes cutaneous angiosarcoma, Dabska tumor [8, 9] and angiomatosis. Cutaneous angiosarcoma is a highly aggressive neoplasm with dismal prognosis and a very high incidence of local recurrence and metastasis and a high mortality rate [10, 11]. Histopathologically, angiosarcoma is featured by significant cytologic atypia, presence of conspicuous mitotic figures, tumor infiltrating between individual collagen bundles, and absence of hobnail endothelial cells [10, 11]. RH and Dabska's tumor share some common biologic behavior and histologic features. Some authors have considered that RH might represent the adult counterpart of Dabska’s tumor and coined the term hobnail hemangiendothelioma to encompass both neoplasms [1]. Unlike RH, Dabska’s tumor occurs mostly in children and has slight predilection for the head and neck area. Histologically Dabska’s tumor has well-formed papillary endothelial projections and lack of arborizing rete testis-like architecture. RH can be easily differentiated from cutaneous angiomatosis, which usually occurs in infants or young adults, and often involves a large segment of the body. Histologically, angiomatosis consists of large venous, cavernous as well as capillary-sized vessels that are usually located in the wall or adjacent to a large vein [12].

RH has been considered to be a low grade angiosarcoma with a high incidence of recurrence. A wide surgical excision with histopathologically proven tumor-free margins is the optimal choice of RH treatment. Radiation therapy has also been proven effective in cases with lymph node metastasis [1, 13]. Our patient experienced tumor recurrence at the former scalp surgical field 3 months after surgery. The tumor recurrence was accompanied by similar nature of headache that she suffered before. She received care at local hospital and passed away at home 6 months after surgery. The immediate cause of death was unclear, but likely attributed RH. To our knowledge, this is the first case of RH related death reported.

In summary, our case showed many unusual clinical features, despite the typical histopathologic features of RH. This case illustrates an aggressive example of this tumor, which should prompt an accurate diagnosis and early intervention.

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