Painful Eccrine Spiradenoma Containing Nerve Fibers: A Case Report

Hye Ran Park^a Soo Bin Im^a Hee Kyung Kim^b Dong Seong Shin^a Young Lip Park^c

Departments of ^aNeurosurgery, ^bPathology and ^cDermatology, Soonchunhyang University Hospital, Bucheon, Republic of Korea

Key Words

Eccrine Spiradenoma · Nerve fibres · Pain

Abstract

An eccrine spiradenoma is a rare benign tumor most often seen in the head, neck and upper trunk of young adults. Although spontaneous pain or tenderness is a typical symptom of eccrine spiradenomas, the underlying mechanism has not been fully elucidated. Here, we report the case of a 47-year-old woman who had a spiradenoma in the subcutaneous tissue of her posterior neck accompanied by agonizing pain which was triggered by pressure. Multiple nodular lesions were excised and the typical histopathological findings of spiradenoma were seen. The histopathological architecture of a disorganized nerve fiber encasing the tumor nodules appeared to correlate with the unique clinical symptom of pain.

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Introduction

A spiradenoma is an uncommon benign tumor arising from the eccrine sweat apparatus and is one of nine painful skin tumors, the others being leiomyoma, neuroma, dermatofibroma, angioliipoma, neu-

rilemmoma, endometrioma, glomus tumor and granular cell tumor [1]. The generation of pain is thought to be related to small unmyelinated axons permeating the hyalinized stromal mantle [2]. Some investigators believe that the expansion of cysts in the tumor also gives rise to pain [3]. Although the pain of an eccrine spiradenoma is 'the most frequent and striking symptom', which is seen in 91% of reported patients [4], the mechanism of pain generation has not been elucidated fully. We experienced a patient with spiradenoma who had severe pain triggered by palpation or pressure, which was treated with surgical excision. The unique clinical characteristics of the pain and the surgical and histopathological findings are depicted. The peculiar microscopic architecture of the tumor nodules and nerve fibers in the capsule might explain the pain mechanism of a spiradenoma.

Case Report

History and Examinations

A 47-year-old woman visited the outpatient clinic with a posterior neck mass causing fierce pain that was evoked by pressure. The texture of the skin surface was not different from other areas, except

for a slight elevation. The mobile soft mass was barely palpable over the spinal column near the midline. The agonizing pain was triggered only when the mass was palpated with a certain amount of pressure. No pain was generated by a soft touch or mild pressure. Once pressure triggered the pain, it persisted for approximately 1–2 min in the absence of pressure. The patient described the pain as sharp, similar to an electrical shock, and radiating to the posterior head and both shoulders; it was so severe that she felt like fainting.

The patient had had the lesion for about 20 years. The initial symptom was an intermittent spontaneous pricking sense that occurred several times per day, but was not related to touch or pressure. The pricking sensation changed into pain that was triggered by pressure about 12 years earlier. These pains had caused her to visit a local clinic and undergo magnetic resonance imaging (MRI) 11 years earlier. Although the MRI showed subtle lesions, the doctor did not relate the pain to the lesion.

The patient always asked people to avoid touching her posterior neck. Despite these precautions, she experienced agonizing pain inevitably or unexpectedly, such as when examined by a doctor at another hospital, when scrubbed by a professional

Fig. 1. MRI: T₂-weighted sagittal (a) and axial (b) images showed multiple ovoid masses with discrete margins in the subcutaneous fat tissue of the posterior neck.

scrubber in a public bathhouse, or when someone swatted at a bug on her neck. Whenever a doctor examined her, she experienced fierce pain, which made her evade definitive treatment. Because no visible lesion was detected on her skin surface, we initially suspected some abnormality or tumorous condition in the deep structure and requested cervical spine MRI. On MRI, multiple well-margined ovoid masses were seen in the subcutaneous fat on her posterior neck (fig. 1). She decided to eliminate the source of pain and requested general anesthesia for fear of pain.

Surgical Findings and Procedures

Under general anesthesia, a 4 × 1 cm spindle-shaped vertical skin incision was made over the mass. Eight ovoid or irregularly shaped masses measuring 3–10 mm were removed from the subcutaneous fat (fig. 2). Each yellow-pink mass was encapsulated with an isolated thin fibrous membrane and easily separated from the surrounding fat. Fine vasculature was seen on some of the surfaces. A wedge resection of the subcutaneous tis-

sue around the mass was performed to remove any remaining tiny lesions. Her postoperative course was uneventful and the pain disappeared.

Pathology

Microscopic examination of the histological sections showed sharply delineated solitary strongly basophilic nodules, resembling lymph nodes. The tumor nodules were surrounded by a delicate fibrous capsule, some of which contained blood vessels and prominent thickened nerve fibers (fig. 3). The S-100 protein and neuron-specific enolase revealed positivity in the thickened nerve fibers (fig. 4). The tumor was made up of two cell types, the most frequent being large cells with a large pale nucleus and a nucleolus. The nuclear membrane was thin and distinct, and the chromatin was finely and evenly distributed. The cytoplasm was pale to slightly basophilic. The second cell type was smaller and had a hyperchromatic nucleus and scanty cytoplasm. Neither type of cell showed atypia. This organoid pattern of the epithelial cells was interrupted by dilated vascular channels. Lym-

phocytes were scattered throughout the tumor. The cells were arranged in intertwining bands interspersed with small lumens (fig. 5). Immunohistochemically, the tumor cells expressed pancytokeratin and CK7 (fig. 6).

Discussion

An eccrine spiradenoma is a rare tumor of the eccrine sweat glands and was first described by Kersting and Helwig [4] in 1956. In their study of 134 eccrine spiradenomas, more than 97% of the tumors were solitary blue-red dermal or subcutaneous nodules, ranging from 0.5 to 3 cm in diameter. Eccrine spiradenoma occurs as either solitary lesion or as multiple lesions. In some case, the multiple lesions present in a linear or zosteriform distribution [5–7]. In the current case, multiple tumor nodules were found in subcutaneous tissue. Although it is unclear whether the current case is a single tumor with many lobules or multiple spiradenomas, we favor single tumor with multiple lobules because several nodules were com-

Fig. 2. **a–c** Grossly, the surgical specimen contained 8 ovoid or irregularly shaped masses measuring 3–10 mm in subcutaneous fat. The thinly encapsulated yellow-pink masses were easily separated from the surrounding fat. Fine vasculature was found on some of their surfaces.

Fig. 3. **a** The tumor nodules are surrounded by a delicate fibrous capsule, some of which contain blood vessels and prominent thickened nerve fibers. HE. $\times 40$. **b** A high-power view of a capsule area containing nerve fibers. HE. $\times 200$.

Color version available online

Fig. 4. Immunohistochemically, the nerve fibers in the capsule express S-100 protein (a) and neuron-specific enolase (b). Immunohistochemistry. $\times 100$.

Color version available online

Color version available online

Fig. 5. The tumor cells are arranged in intertwining bands and numerous lumens. HE. $\times 100$.

Fig. 6. The tumor cells are positive for pancytokeratin. Immunohistochemistry. $\times 200$.

pacted in a relatively small dimension. However, the histological finding that each nodule had an isolated capsule and the surgical finding that some nodules were separated by little subcutaneous fat tissue suggest 2 or 3 separate tumors with several daughter nodules.

The most striking clinical feature of the lesions was the presence of pain or tender-

ness in 91% of the patients, which usually occurs in a paroxysm [4]. In contrast, Mambo [8] reported that pain or tenderness was present much less frequently (only 23%) in his clinical and histopathological review of 49 cases of eccrine spiradenoma.

The differential diagnosis should include leiomyoma, neuroma, dermatofi-

broma, angioliipoma, neurilemmoma, endometrioma, glomus tumor and granular cell tumor, described as 'LEND AN EGG' by Naversen [1]. The exact mechanism of pain in most of the painful skin tumors is not clear. In the case of a leiomyoma, which is also among the known painful skin tumors, the pain mechanism was proven to be mediated by the contraction of smooth

muscle fibers and subsequent compression of nerve endings [9, 10]. The pain mechanism of a neuroma is thought to be associated with a swelling at the proximal end of the injured nerve which contains regenerative axon sprouts and commonly exhibits exquisite mechanical sensitivity because of altered membrane properties of both C and A fiber axons [11]. In the case of neuroma, substance P, which is known to be a primary sensory afferent neurotransmitter for mediating nociception and cause a vasodilation in the glomus tumor, is thought to be the cause of pain [12]. The peculiar pain of angiolipoma is thought as mediated by the nerve fibers especially located within the tumor parenchyma, and this theory is supported by positivity for a smooth muscle actin and cytokeratin reactivity [13]. Dermal schwannoma (neurilemmoma) originates from nerve sheaths composed of Schwann cells, which insulate normal nerve fibers and enhance propagation of nerve impulses [14]. Endometrioma is the term given to extrapelvic endometriosis and can be described in almost all body cavities and organs associated with surgical scars [15]. The currently accepted mechanism for the generation of endometriotic pain is divided into two processes, the pain generated by the endometriotic lesion itself and the pain generated by its secondary reactions. Granular cell tumor is in direct continuity with striated muscle and has been thought to have a neurogenic origin associated with the nerves and ultrastructural findings of neurofilaments in the granular tumor cells. This theory was supported by S-100 positivity staining in Schwann cells but not in myofibers [16].

The cause of pain in spiradenoma is also not yet clear. In 1996, Criton and Ara-

vindan [6] stated that pain might be due to the contraction of myoepithelial cells. However, electron microscopy has not proven the presence of myoepithelial cells in the tumor.

Eccrine spiradenoma shows many characteristic histopathological features [4, 8, 17]. Our specimen also displayed these distinctive histological features with two types of cells in the tumor nodule. Several previous studies have reported the expression of the immunohistochemical marker S-100, suggesting a relationship with neural tissue [18–20]. S-100 protein is normally present in cells derived from the neural crest (Schwann cells, melanocytes and glial cells), chondrocytes, adipocytes, myoepithelial cells, macrophages, Langerhans cells, dendritic cells and keratinocytes. The antibodies against S-100 protein have limited diagnostic value for neural tissue because S-100 protein presents various other cell lines and is expressed by Schwann cells not by axons. Ohtsuki et al. [5] examined the fine structure of eccrine spiradenoma and revealed the presence of dispersed Langerhans cells extending fine, irregular processes among the tumor cells in the nodule. The current case showed S-100 positivity at the tumor capsule, not in the tumor nodule, which was the exact position of the prominently thickened and visibly disorganized nerve fiber. To make better confirmation of the neural element, the stain for neuron-specific enolase, which is a nerve axon marker, was also positive (fig. 4).

These histopathological findings could be correlated with the unique clinical symptoms of the patient's pain which is triggered only when the mass was palpated with a certain amount of pressure. The patient complained of a striking pain that

disrupted her daily routine for more than 20 years, but without presenting any external surface lesion. The depth of the lesion contributed not only to the delay of diagnosis, but may also have prolonged the period of interaction with the nerve ending in the subcutaneous tissue and thus exacerbated the pain. As pain mechanism in this eccrine spiradenoma, we can suggest that palpation with pressure may have triggered pain by stretching or mechanically stimulating the hyperexcitable nerve fibers which were disorganized around the tumor nodule for a long period. This case study is somewhat peculiar in that it suggests a relationship between the clinical symptom of agonizing pain with an ancient history and the microarchitecture of the nerve fibers encasing multiple eccrine tumor nodules.

Conclusion

We describe the surgical and histopathological findings of an isolated group of eccrine spiradenomas accompanied by a long-lasting clinical symptom of pain that was remarkable in terms of its severity. The peculiar microscopic architecture of the thickened nerve fibers encasing the nodules of eccrine spiradenoma may explain the pain mechanism.

Disclosure Statement

We certify that there is no conflict of interest with any financial organization regarding the material discussed in this article.

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