

# Epithelial sheath neuroma: A case series



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## INTRODUCTION

Epithelial sheath neuroma (ESN) is an uncommon cutaneous tumor that was first described in 2000 by Requena et al.<sup>1</sup> This term was coined because of the presence, on microscopic examination, of squamous epithelium surrounding dermal nerve fibers in a sheath. In the literature, 10 cases are reported date, all occurring in patients older than 40 years, predominantly in women. Clinically, it is described as a firm, erythematous papule or nodule located on the upper back. This report describes 3 additional cases of ESN that were identified and successfully treated and reviews previously published cases to further characterize this uncommon lesion.

## CASES

### Case 1

A 61-year-old white woman presented with a 6-week history of a tender 6-mm papule on her left upper back (Fig 1). Apart from a history of breast cancer, she was otherwise in good health. Initial clinical impression of the papule was a basal cell carcinoma. A 3-mm punch biopsy was taken.

Histology found numerous enlarged peripheral nerve bundles closely sheathed by irregular islands of keratinising squamous epithelium, with no overlying epidermal atypia, and mild chronic inflammatory infiltrate within the dermis (Fig 2), consistent with an ESN.

### Case 2

An 82-year-old white woman presented with a 1-month history of an 8-mm tender and pruritic papule on her upper back (Fig 3). Palpation of the papule produced intense localized knife-like pain.

### Abbreviations used:

ESN: epithelial sheath neuroma  
 SCC: squamous cell carcinoma

She was initially prescribed triamcinolone ointment for symptomatic relief, although this was unsuccessful, and punch biopsy was subsequently performed.

An initial diagnosis of moderately differentiated squamous cell carcinoma (SCC) with perineural involvement was made. However, subsequent excisional biopsy of the lesion found a proliferation of nerve bundles with normal squamous epithelium and dense cellular infiltrates composed of lymphocytes and histiocytes (Fig 4). This finding was in keeping with an ESN.

### Case 3

A 59-year-old woman presented with a 6-mm tender erythematous papule on her left upper back that had been present for several months. She reported a tingling sensation upon palpation of the lesion. The clinical impression was that of an SCC.

An initial punch biopsy found small nerve rootlets surrounded by mildly atypical squamous epithelium, with an initial diagnosis of a well-differentiated SCC. However, histologic analysis of the subsequently excised lesion showed neuronal hyperplasia with no overlying epidermal changes. This finding led to a diagnosis of ESN, for the initial biopsy.

## DISCUSSION

A review of all reported cases (Table I) suggests that the clinical appearance of ESN is rather nonspecific,

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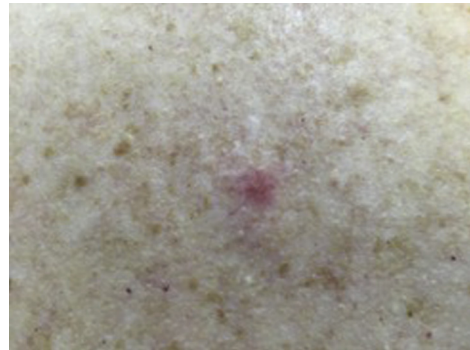
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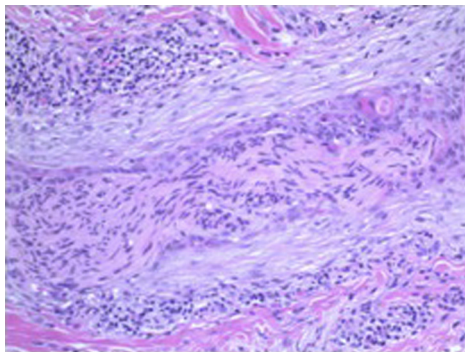
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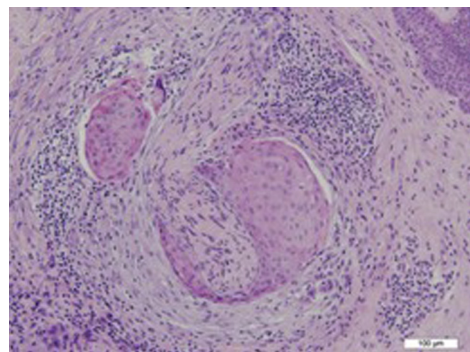
**Fig 1.** A 6-mm ESN on the left upper back.



**Fig 3.** An 8-mm ESN on the upper back.



**Fig 2.** Histology of papule biopsied. Enlarged peripheral nerve bundles with surrounding squamous epithelium.



**Fig 4.** Histology of papule biopsied. Proliferation of nerve bundles with normal squamous epithelium.

and may often be mistaken for basal cell carcinoma, SCC, inflamed or irritated nevus, or an inflamed cyst. Patients may present asymptotically or with localized pruritus, and palpation of the lesion may lead to neuropathic-like pain, as seen in 2 of our cases.

### Histology

Histologically, ESN is characterized by multiple enlarged peripheral nerve fibers that are sheathed in a mature squamous epithelium. The bundle of nerves consists of axons, Schwann cells, and perineural cells, and the squamous sheaths may have a concentration of keratinized and dyskeratotic cells. The lesion can be surrounded by mildly myxoid stroma, which contain lymphocytic infiltrates.

### Differential diagnosis

The differential diagnosis of ESN includes reactive neuroepithelial aggregates<sup>6</sup> and re-excision perineural invasion (RPI).<sup>7</sup> Reactive neuroepithelial aggregates show similar neuroepithelial bundles as ESN but only have 1 or 2 aggregates that contain no enlarged nerves and have been reported on the face only. RPI is another condition that needs to be considered, as it also shows squamous epithelium adjacent to normal cutaneous nerves. The specific diagnostic criteria of RPI proposed

include: the lesion is limited to the immediate previous biopsy site, absence of residual neoplastic cells, and benign morphology of perineural epithelial cells.<sup>7</sup> In other words, ESN can be distinguished from RPI by absence of previous excision history or histologic evidence of trauma or scar tissue at the site.

### Pathogenesis

Although a definite pathogenesis of ESN has not been established, several possible mechanisms have been postulated in the literature. ESN may represent an unusual reactive hyperplasia of peripheral nerves and epithelium in response to external stimuli, such as rubbing, and the entrapment of infundibular or epidermal squamous epithelium within the perineurium.<sup>8</sup> Another suggested mechanism is the squamous metaplasia of the perineurium that surrounds the enlarged nerve bundles as a response to some form of localized inflammation.<sup>9</sup> Dunn et al<sup>10</sup> also proposed in their report that the lesion may arise from neural crest remnants after embryonal development that differentiate into neural and squamous epithelial elements. Wang et al<sup>11</sup> suggested that ESN may arise from localized inflammation or minor trauma that induces the production of interleukin-6-mediated hyperplasia.

**Table I.** Demographic and clinical features of ESN in reported cases

|                              | Age | Sex    | Site             | Size      | Symptoms            |
|------------------------------|-----|--------|------------------|-----------|---------------------|
| Patient 1                    | 61  | Female | Left upper back  | 6 mm      | Tender              |
| Patient 2                    | 82  | Female | Mid upper back   | 8 mm      | Tender and pruritic |
| Patient 3                    | 59  | Female | Left upper back  | 6 mm      | Paraesthesia        |
| Requena et al <sup>1</sup>   | 62  | Female | Mid upper back   | Coin size | Unknown             |
| Requena et al <sup>1</sup>   | 73  | Male   | Mid upper back   | Unknown   | Pruritus            |
| Requena et al <sup>1</sup>   | 68  | Female | Right upper back | 6 mm      | None                |
| Requena et al <sup>1</sup>   | 73  | Male   | Mid upper back   | Unknown   | Pruritus            |
| Hirano et al <sup>2</sup>    | 69  | Female | Mid upper back   | Unknown   | Pruritus            |
| Lin et al <sup>3</sup>       | 49  | Female | Right upper back | 5 mm      | Pruritus            |
| Husain et al <sup>4</sup>    | 43  | Male   | Back             | 20 mm     | No                  |
| Noparstak et al <sup>5</sup> | 82  | Female | Right mid back   | 12 mm     | Tender              |

### Conclusion

Given the variety of possible differential diagnoses of ESN, an adequate clinical and pathologic correlation is often required to reach a diagnosis of ESN. In all cases of ESN, excision was the treatment choice, with no report of recurrence during follow-up.

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