Multifocal glomus tumours of the fingers in two patients with neurofibromatosis type 1

L De Smet, R Sciot, E Legius

CASE REPORTS

Case 1

A 53 year old female presented with extreme pain in the pulpa of the right ring finger and the left middle finger. The pain had been present for more than one year. She had been diagnosed with neurofibromatosis type 1 (NF1) based on clinical features (more than six cutaneous café au lait spots, iris Lisch nodules, axillary freckling, cutaneous neurofibromas, and first degree relatives with NF1). Several soft tissue tumours in the face had been removed and diagnosed histologically as neurofibromas. Despite numerous cutaneous soft tissue nodules spread all over her body, there were no nodules found at the specific painful region of the affected fingers. Love's test was positive. Transillumination and radiographs were negative.

Under local anaesthesia both pulpae were explored and a small nodule was found in each one. Histological examination of the excised nodules showed a typical glomus tumour in each (fig 1).

Postoperative follow up was uneventful and all symptoms disappeared immediately postoperatively. At 18 months follow up, there was no evidence of recurrence. A cytogenetic study with fluorescence in situ hybridisation with NFI gene specific probes excluded a total NFI gene deletion in peripheral blood lymphocytes in this patient.

Case 2

The diagnosis of NF1 in this 35 year old man was based on the presence of multiple (more than six) café au lait spots, cutaneous neurofibromas, axillary freckling, the presence of iris Lisch nodules, and a first degree relative with NF1. He complained of extreme pain in the third and fourth finger of his right hand, dorsally at the base of the nail. A slight reddish spot was present at this location. Love's test was positive. The pain could be provoked by exposure to cold. In fact the patient worked as a grocery store clerk and working in a cold storage room triggered severe pain attacks in the third and fourth finger of his right hand.

Both pulpae were explored under local anaesthesia. A 1.5 mm diameter tumour was found in both nail roots. Histological examination confirmed the diagnosis of glomus tumour. The symptoms disappeared immediately. No genetic studies have been performed yet in this patient.

DISCUSSION

In this letter, we describe two patients with NF1 and multiple phalangeal glomus tumours. Phalangeal glomus tumours are usually solitary and the association with NF1 has only rarely been reported. The occurrence of multiple glomus tumours in the nail beds is extremely rare in the general population. However, several published cases of NF1 patients (at least five) and the two patients reported here had multiple glomus tumours. The occurrence of multiple phalangeal glomus tumours in several patients with NF1 suggests that...
this is not an incidental association but that NF1 patients have an increased, albeit low, incidence of glomus tumours. Moreover, it is possible that glomus tumours of the pulpa are not always diagnosed in NF1 patients because the symptoms might be attributed to the presence of cutaneous neurofibromas in the same region and resection of the superficial nodules (cutaneous neurofibromas) is insufficient to diagnose and resolve the problem. Therefore, it is important to be aware of the possibility of glomus tumours in NF1 patients with pain in the fingers because surgical intervention to remove the glomus tumour cures the pain.

Neurofibromas in NF1 patients are composed of fibroblasts, mast cells, perineural cells, axons, and Schwann cells. It has been shown that the Schwann cells are the tumoral cells in neurofibromas and it is known that Schwann cells are of neural crest origin. We hypothesise that glomus cells are of neural crest origin too. Neural crest stem cells (NCSC) can be isolated from mammalian fetal peripheral nerves, and form three different cell types in culture, neurones, Schwann cells, and smooth muscle-like myofibroblasts. These myofibroblasts are positive for alpha-smooth muscle actin (SMA) and might be the precursors of the SMA positive glomus cells that a second hit in the glomus organ of the nailbed. Therefore, it is possible that a second hit in the NF1 gene in a SMA positive glomus cell results in a glomus tumour in NF1 patients in a similar way as a second hit in a Schwann cell is responsible for a neurofibroma. Further molecular work on these SMA positive cells is needed to substantiate this hypothesis. However, these glomus tumours are very small and it will be necessary to develop selective culture conditions to grow and expand these SMA positive tumoral cells as has been done for neurofibroma derived Schwann cells.

Authors’ affiliations
L De Smet, Department of Orthopaedic Surgery, University Hospital Pellenberg, Katholieke Universiteit Leuven, Leuven, Belgium
R Sciot, Department of Pathology, University Hospital Gasthuisberg, Katholieke Universiteit Leuven, Leuven, Belgium
E Legius, Centre for Human Genetics, University Hospital Gasthuisberg, Katholieke Universiteit Leuven, Leuven, Belgium
Correspondence to: Professor E Legius, Centre for Human Genetics, University Hospital Gasthuisberg, Herestraat 49; B-3000 Leuven, Belgium; Eric.Legius@med.kuleuven.ac.be

REFERENCES
Multifocal glomus tumours of the fingers in two patients with neurofibromatosis type 1

L De Smet, R Sciot and E Legius

*J Med Genet* 2002 39: e45
doi: 10.1136/jmg.39.8.e45

Updated information and services can be found at:
http://jmg.bmj.com/content/39/8/e45

These include:

**References**
This article cites 12 articles, 2 of which you can access for free at:
http://jmg.bmj.com/content/39/8/e45#BIBL

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections
- Neuromuscular disease (254)
- Neurooncology (77)
- Peripheral nerve disease (95)
- Screening (oncology) (230)
- Clinical diagnostic tests (353)
- Reproductive medicine (516)

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/