CASE REPORT

Facial plexiform neurofibroma: is it truly just skin deep?

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SUMMARY

A middle-aged Chinese woman presented with a slowly enlarging mass over the right side of her face that was later proven histologically to be a plexiform neurofibroma. This was associated with a localised depression over her right temple. There were no other features of neurofibromatosis-1. The presentation and biological behaviour of plexiform neurofibromas are reviewed in this manuscript. Particular attention is paid to the interaction of plexiform neurofibromas with their surrounding structures, as well as the postulated mechanisms by which this occurs.

BACKGROUND

An isolated plexiform neurofibroma, regardless of being a localised mosaic neurofibromatosis-1 (NF-1) variant or a de novo lesion, is uncommon and may present a diagnostic challenge for clinicians who may not have encountered one.

Furthermore, there have been multiple case reports of plexiform neurofibromas affecting their surrounding structures, especially that of the bony architecture.

This appears to be the case for this manuscript and how exactly this interaction occurred was interesting.

A

B

C

Figure 1 (A) Right supraorbital soft tissue mass; (B) depressed right temple and (C) right postauricular soft tissue mass.

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Although, a plexiform neurofibroma is a subcutaneous lesion, its clinical effects may not be limited to being skin deep.

CASE PRESENTATION

A middle-aged Chinese woman presented with swelling of the right side of her face for the past 10 years. Apart from cosmetic disfigurement, she was otherwise asymptomatic. On examination, there was an extensive, subcutaneous soft tissue swelling that extended inferiorly from the right supraorbital region (figure 1A) to the right periauricular region (figure 1C). There was also a localised depression over her right temple (figure 1B). The mass was non-tender and had an ill-defined border. She did not have a family history of NF-1.

She eventually sought medical advice as this mass has reached a size sufficient enough to cause cosmetic impairment and that she was curious as to the exact nature of the mass.

INVESTIGATIONS

CT scan of the face was performed. It shows an extensive soft tissue mass most prominent over the right periauricular region

(figure 2A,B). It also demonstrated some degree of periosteal reaction of the underlying right zygomatic bone (figure 2C,D).

A biopsy of the subcutaneous mass at the postauricular region confirmed the histological diagnosis of a plexiform neurofibroma (figure 3A,B).

DIFFERENTIAL DIAGNOSIS

Apart from the diagnosis of a neurofibroma, possibilities included Kimura's disease and lipodystrophy over the right temple.

TREATMENT

The patient opted for conservative treatment as the mass was benign in nature and surgery may have resulted in a poor cosmetic outcome.

OUTCOME AND FOLLOW-UP

The patient was given an open date follow-up subsequently.

Figure 2 (A) Right supraorbital soft tissue mass on CT scan; (B) right periauricular soft tissue mass on CT scan; (C) periosteal reaction of the underlying right zygomatic bone and (D) absence of periosteal reaction on the contralateral side.

Figure 3 (A) Ill-defined spindle cell tumour in the dermis (H&E section $\times 20$). (B) The tumour is composed of spindle cells with wavy nuclei in a fibrillar stroma (H&E section $\times 200$).

DISCUSSION

Plexiform neurofibromas are benign peripheral nerve sheath tumours composed of a variable mixture of Schwann cells, perineurial elements, fibroblasts and haematopoietic cells bathed in a collagenous or myxoid.¹ At the cellular level, specific interactions between these cells are thought to engender tumour initiation and progression. It is hypothesised that tumourigenic Schwann cells secrete high concentrations of stem cell factors which recruits c-kit expressing mast cells. In turn, activated mast cells release inflammatory cytokines stimulating the tumourigenic Schwann cells and their surrounding fibroblasts and blood vessels.^{2 3}

Plexiform neurofibromas usually present as ill-defined, subcutaneous or dermal masses. Their occurrence has been described in various anatomical sites, most commonly in the head and neck region.⁴ Cartellieri and Swoboda⁵ reported a similar presentation in a patient with an auriculotemporal nerve neurofibroma.

Plexiform neurofibromas are not considered to be pathognomonic of NF-1, but are highly suggestive. When proven to exist in a patient not known to have NF-1, a concerted effort should be made to look for other features of NF-1 since it has a complete penetrance but variable expression.

In the absence of other systemic features of NF-1, a solitary plexiform neurofibroma can represent a sporadic, isolated lesion or a case of mosaic localised NF-1. Mosaicism is a

well-recognised phenomenon in genetic diseases—it denotes the presence of two or more populations of cells with different genotypes in an individual. Mosaicism in NF-1 may manifest itself as a mild generalised disease, or a localised/segmental disease. Ruggieri and Huson commented that neurofibroma as the sole manifestation in mosaic localised NF-1 is the form most frequently reported in the literature. In their own reported case series, 20 of 124 patients with mosaic localised NF-1 had neurofibromas only, of which 8 were further subcategorised as plexiform neurofibromas.⁶

The plexiform neurofibroma in our patient may represent a sporadic, isolated lesion or herald a limited mosaic NF-1 pattern. There have been many case reports pertaining to either in the medical literature. The only definitive way of distinguishing between the two is to perform a genetic analysis of the cells comprising the lesion. This was not performed in our patient as it may have not altered management.

An important clinical question is whether a plexiform neurofibroma is capable of influencing its surrounding bone, and if so, through what mechanisms.^{7 8}

One article reported a NF-1 patient with diffuse plexiform neurofibroma and occipital bone dysplasia.⁷ The authors asserted that NF-1 gene plays an important role in the regulation of osteoprogenitors and emphasised the importance of looking out for associated bone dysplasia when considering surgical excision of a scalp plexiform neurofibroma. Another retrospective study reported that majority of skull defects in patients with NF-1, either in the form of sphenoid dysplasia and/or calvarial defect, are associated with the presence of an adjacent plexiform neurofibroma.⁸ Of 21 patients with skull defects, 18 patients had a documented plexiform neurofibroma. In 16 patients, the plexiform neurofibroma was found overlying the sphenoid dysplasia and/or calvarial defect. The authors postulated the theory of a dynamic skull defect pathophysiology, which integrates the finding of adjacent lesions applying an exogenous force with intrinsic bone tissue abnormality related to neurofibromin deficiency. An unknown variable in this equation was thought to be how the local microenvironment of the plexiform neurofibroma may interact with the surrounding bony environment and vice versa.⁸

If our patient is similarly thought to have mosaic localised NF-1, then it naturally follows that at least some of the cells may be neurofibromin deficient.

CT scan of our patient's face did not include the cuts covering the temple regions. This would have been helpful in terms of demonstrating any bony depression underlying the right temple which was clinically sunken in. The other possibility would have been wasting of the right temporalis muscle but the CT face demonstrated good muscle bulk without any significant adipose tissue replacement.

Interestingly, however, CT scan of our patient's face indicated presence of periosteal reaction of the underlying right zygomatic bone. This is absent over the contralateral side, suggesting the presence of the overlying plexiform neurofibroma is responsible for its occurrence. What this further entails is that bony changes may assume an osteoclastic nature rather than the osteoblastic nature which is more frequently reported in the medical literature.

Then there is the issue of the local environment. Although the histology of plexiform neurofibroma in a patient with NF-1 is indistinguishable from that of a patient without NF-1, it does not necessarily imply that the microenvironment of both plexiform fibromas is exactly the same. Several studies have suggested that an isolated plexiform neurofibroma is associated with a

more benign course.¹ If true, the discrepancy in oncogenic potential may be due to differences in their respective micro-environment, perhaps in terms of cell signalling.

Learning points

- ▶ The possibility of a neurofibroma should be considered in an ill-defined subcutaneous mass located in the head and neck region.
- ▶ Associated changes in the surrounding structures, especially of the bony architecture, should be sought.
- ▶ The possible mechanisms by which a neurofibroma influences its surrounding structures include, but are not limited to, exogenous compression, intrinsic bone tissue abnormality and effect of the neurofibroma microenvironment.

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