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Hypervascular neurofibromas in a case of neurofibromatosis type 1 - a case report

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Abstract

Neurofibromatosis type 1 is one of the most frequently inherited diseases affecting 1:3500 newborn. The diagnosis of Neurofibromatosis type 1 is not dilemmatic because of typical clinical features. The key feature of Neurofibromatosis type 1, neurofibromas, are complex tumours arising from peripheral nerve sheaths. Neurofibromas may be focal growths or can extend along the length of a nerve, involving several fascicles and including nerve branches. Neurofibromas sometimes exhibit hypervascular characteristics. Few reports suggest the bleeding tendency observed in neurofibroma, although not common, occasionally causes a large amount of bleeding during surgical intervention. Hypervascular characteristics of these tumors may be a confusing factor for the diagnostician. This report describes the case of Neurofibromatosis type 1 presented with neurofibroma exhibiting hypervascular characteristics and emphasizes the importance of necessary investigations prior to surgical procedures.

Key words: Hypervascularity, Neurofibroma, Neurofibromatosis, Schwann cells.

Introduction

Neurofibromatosis type 1 (NF-1) also known as Von Recklinghausen's neurofibromatosis, is one of the most frequently inherited disease affecting 1:3500 newborn. NF-1 was described by Smith in 1849 and Von Recklinghausen in 1882. It has an autosomal dominant inheritance with complete penetrance, variable expression and a high rate of new mutation, of about 50%. The NF-1 gene is a tumour suppressor gene mapping to chromosome 17q11.2. The diagnosis of NF-1 is not dilemmatic because of typical clinical features and is based on criteria developed by National Institutes of Health Consensus Conference in 1987(1).

The key feature of NF1, neurofibromas, are complex tumours arising from peripheral nerve sheaths. Neurofibromas consist primarily of Schwann cells, fibroblasts and a large amount of extracellular matrix with collagen surrounding an axon, but they may also contain many other cell types including perineural cells, mast cells, pericytes, and endothelial cells. Neurofibromas are hypervascular tumors. We present a case of NF-1 with neurofibroma exhibiting hypervascular characteristics.

Case Report

A 22years-old male patient reported with the complaint of a swelling on left middle one third of face present since birth. The swelling had gradually progressed to the present size. It was associated with intermittent pricking type of pain and the feeling of heaviness over the swelling on lying down to left side. Also had noted multiple nodules on hands, back and chest since childhood. He gave no history of paresthesia, difficulty in breathing or swallowing. Past medical & dental histories were non-contributory. There was no history of familial, contagious or hereditary diseases.

General examination revealed multiple nodules present on the chest, back & both the arms; measuring about 0.5cm-1.5cm in size, well defined, smooth & non pigmented. On palpation, they were non tender, soft & compressible. Generalized irregularly shaped macules were noted over the chest, axilla and back; measuring about 1cm x1cm in size. Head and neck examination revealed gross facial asymmetry on left side. Bridge of nose was widened. On left side, ala of nose appeared to be enlarged measuring about 2x2 cm in size with ill defined borders. Surface appeared to be normal with no secondary changes. Another nodule measuring about 1 x 0.5cm in size, noted distal to enlarged ala on left side with similar features.(Fig.1) Lip on left side appeared to be pulled down. The left malar region appeared to be enlarged extending anteriorly to ala of nose, posteriorly to tragus of ear, superiorly to infraorbital rim and inferiorly to the lower border of mandible. Excess hair growth was noted on lower half of swelling. No other surface changes were noted. On palpation, the swelling lateral to left ala



Fig.1. Gross facial asymmetry due to enlarged ala nose on left side. Multiple nodules are also seen.

of nose was soft, tender, ill defined and compressible. No pulsation or paresthesia was noted on palpation. Intra oral examination did not reveal any abnormalities. The case was provisionally diagnosed as Neurofibromatosis type 1.

Routine radiographic examinations were carried out. Panoramic radiograph revealed normal condyle and coronoid process on both the sides. All the four first molars exhibited pulpal calcifications. Mandibular canal and mental foramen appeared to be normal. Haziness was observed in relation to left maxillary sinus. Ophthalmological examination revealed multiple Lisch nodules in



Fig.2. Doppler ultrasonography showing hypervascularity.

relation to both the eyes. Before the tumour was excised, ultrasonography was carried out which revealed heterogeneous echogenic area with internal hypoechoic area and echogenic areas in subcutaneous tissues in the swelling present lateral to left ala of nose. Multiple vascular channels were seen coming through it with low resistance arterial flow pattern. Few bright echogenic specks were also seen within the lesion suggestive of calcification. Hypoechoic non vascular areas were seen suggestive of old hematoma. (Fig.2) Ultrasonographic diagnosis was given as hemangioma.

In order to rule out possibility of co existing hemangioma, cranial angiogram was carried out. It showed no vascular malformations in both the carotid arteries. (Fig.3) Hypervascularity observed in the ultrasonography was not due to the vascular malformation but due to the inherent hypervascular characteristics of the tumor. Debulking procedure was done for lesion over the left nose. Moderate amount of bleeding was encountered during the procedure. Histopathologic analysis of tissue specimen showed interlacing bundles of spindle shaped cells with long wavy nuclei and some areas showing plump nuclei in the connective tissue. Neural bundles were seen in many areas. The connective tissue was fibrous with brownish pigmented areas scattered throughout the sections. Numerous endothelial lined spaces were seen. The pigmented areas showed the presence of macrophages. Mast cells were also seen. The fibrous tissue showed invasion into the adjacent structures like adipose tissue and muscles. All of the features were su-



Fig.3. Cranial angiogram showed no vascular malformations in both the carotid arteries suggestive of NF-1.

Discussion

NF-1 is the most commonly inherited disorder with an autosomal dominance inheritance. There are many types of neurofibromatosis of which type 1 is the most

common one (2). NF1 gene produces an mRNA that is expressed in almost all tissues but most highly in brain, spinal cord, and the peripheral nervous system(3). Recent advances in molecular genetics via gene mapping by restriction fragment length polymorphism and positional cloning have localized the defective NF1 gene to the pericentromeric region of the proximal long arm of chromosome 17 (chromosome band 17q11.2) making genetic diagnosis possible(4).

Currently, the diagnosis of NF1 is made in an individual with any two of the following clinical features(5):

1. Cafe'-au-lait spots
2. Intertriginous freckling
3. Lisch nodules
4. Neurofibromas
5. Optic pathway gliomas
6. Distinctive bony lesions
7. A first-degree family relative with NF1

Cafe'-au-lait macules usually develop between the early months of life and 2 years of age and may be the first feature to manifest. The colour varies from yellowish to chocolate brown. The size and number of these macules is important in the diagnosis of NF-1. The presence of more than or equal to six cafe'-au-lait macules, measuring more than 0.5 cm in diameter before puberty or 1.5 cm in diameter after puberty are diagnostic. Axillary and inguinal freckling (Crowe's sign) is detected most frequently between 3 and 5 years of age. These freckles are typically small (less than 93mm in diameter). Lisch nodules are melanocytic iris hamartomas and are pathognomonic of NF1. The most distinctive and common neoplasm seen in NF-1 is neurofibroma. Neurofibromas are benign Schwann cell tumours that arise from the fibrous tissue surrounding peripheral nerve sheaths and are composed of Schwann cells, fibroblasts, perineural cells, and mast cells. Neurofibromas may be subdivided according to their appearance and location into 4 groups: focal or diffuse cutaneous; subcutaneous; nodular or diffuse plexiform; or spinal(5).

Neurofibroma is a typical hypervascular tumor. Few reports suggest the bleeding tendency observed in neurofibroma, although not common, occasionally causes a large amount of bleeding during surgical intervention. Intra-tumoural bleeding in large diffuse plexiform-type neurofibromas is a life-threatening problem (6). Schwann cells have angiogenic potential. Blood vessel formation can be stimulated by a number of polypeptides, including angiogenin, transforming growth factors α and β , epidermal growth factor, and the fibroblast growth factors, acidic and basic Fibroblast Growth Factors; additional, less well characterized angiogenic factors have also been described (7). Immunohistochemical staining and the reverse transcribed polymerase chain reaction method demonstrated vascular endothelial growth factor and basic fibroblast growth factor to

be highly expressed in neurofibroma cells at both protein and mRNA level. These findings suggest that the vascular endothelial growth factor and basic fibroblast growth factor contribute to both the angiogenesis and hypervascularity of neurofibroma (8).

Moreover, haemorrhage in neurofibroma has been thought to be a result of friable vasculature secondary to arterial dysplasia or vascular invasion by the tumour. The neurofibromatous tissue itself also has an abnormal vascular structure with thin-walled blood vessels lying in loose neural stroma that replaces the normal adipose tissue (9). Therefore, any attempt to remove a neurofibroma must be taken with great care and planning, including the preparation and anticipation of major blood volume replacement, especially in the head and neck region.

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