Case Report

Neurofibromatosis 1 with invasive spinal cord compression (case report)

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Neurofibromatosis, being found as one incident in 2500-3000 births, is a genetic disease that involves either skin system, nervous system or both systems simultaneously and that leads to important cosmetic and functional disorders. Although, cervical cord compression is not frequently found in nervous system compression, nevertheless, it takes a very important place since it may lead to severe neurological deficits and it may be treated by combination of surgical intervention with physical medicine and rehabilitation in early stage. There are not many treatment options in the advanced cases. In our study, we aimed to discuss treatment approaches by evaluating a patient with complex case of neurofibromatosis in whom whole spinal cord is full of neurofibromas accompanied by cervical cord compression.

Key words: Neurofibromatosis 1, spinal cord compression, physical medicine and rehabilitation.

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a genetically transmitted autosomal dominant disease with incidence of one in 2500-3000 births (Huson et al., 1989; Kluwe et al., 2003). It is a kind of neurocutaneous disease type and a defect of NF1 gene located on chromosome 17q11.2 is responsible for this disease (Leroy et al., 2001).

NF1 is diagnosed by the presence of two or more diagnostic criteria. Diagnostic criteria include six or more café-au-lait spots (greater than 5 mm in diameter before puberty and greater than 15 mm in diameter after puberty), two or more neurofibromas or a plexiform neurofibroma, axillary or inguinal freckles, optical glioma, two or more Lisch nodules, various bone lesions (sphenoid dysplasia, pseudoarthrosis, scoliosis) and first-degree relative diagnosed with neurofibromatosis (Apaydin et al., 1997; Washington et al., 2010). The cervical cord compression due to cervical root neurofibroma is an important clinical consideration in patients with NF type I. However, this case has been rarely reported (Leonard et al., 2007). In this study, we aimed to present a complex case of neurofibroma that filled bilateral cervical neural foramina at all levels of cervical position and caused cervical cord compression.

CASE

A 46-year-aged male patient diagnosed with neurofibromatosis type 1 appealed to our clinic due to complaints of progressive fatigue in his right arm and leg, neck and right arm pain and frequent falling. His medical history revealed that he was diagnosed of NF1 depending via tests performed for fibromas observed on his skin at 18 years old. The complaints of pain and fatigue started suddenly 7 years ago in the patient. This fatigue and pain have increased by time and affected his professional and social life. Feeling fatigue on his right leg started without pain in the recent 1 year.

Walking disturbances and falling became frequently due to this fatigue. The family history of the patient included diagnosis of NF1 in his 1st and 2nd degree relatives. His 12-year-old son was diagnosed with optic...
glioma. The patient had no additional disease. He had no use of medication and alcohol. He had smoking history of 80 pockets/year.

The physical examination of the patient revealed invasive neurofibromas in his body. The range of motion (ROM) in the cervical region which had multidirectionally active limited motion, lateral flexions and rotations were painful. The ROM of his right shoulder showed active and passive limited motion and was multidirectionally painful, his left shoulder was open and painless. The ROM of right elbow and right wrist were passive open, active limited and painful, ROM of left elbow and left wrist were open painless. Muscle strengths of upper extremities were 2/5 on right while it was normal on the left. The sensation was bilaterally normal. The deep tendon reflexes (DTR) of the upper extremities were brisk (4+). Hoffmann reflex was bilateral positive. The ROM of lumbar region was multidirectionally open and painless. The ROM of right hip was limited and painless while left hip was open painless. The knee was bilaterally open and painless. The ROM of right ankle was active limited and passive open painless. Left ankle was normal. The straight leg raising test and Trendelenburg test were negative. The muscle strength hip flexion of right lower extremity was 3/5, while knee extension was 5/5, the ankle dorsiflexion, toe dorsiflexion and foot plantar flexion were 2/5. The muscle strength was normal on the left side. The sensation of lower extremity was normal. His DTRs were bilateral corresponding (4+), Babinski was bilateral positive. The patient had clonus. The patient did not have urinary and fecal incontinence.

The laboratory evaluation revealed normal values for whole blood count, sedimentation, C-reactive protein, alkaline phosphatase, parathormone, calcium, hepatic and renal function tests and whole urine test. The performed magnetic resonance imaging (MRI) for spinal cord revealed neurofibromas that filled bilateral neural foramina at all levels of cervical region and increased T2 signaling compatible with myelomalacia causing a thinning of spinal cord at the level of cervicomedullar region and C3-C4 (Figure 1). The massive formations accompanied by neural foraminal widenings at all dorsal levels were found compatible with neurofibroma by performed MRI. The massive formations with subcentimetric dimensions in lumbar and sacral foramina and massive formations of sacral plexus compatible with extraforaminal nerve root process were found compatible with neurofibroma via Lomber MRI.

A remarkable thickening of cutaneous-subcutaneous tissue and contour lobulation were monitored in cranial MRI. The findings were found compatible with neurofibroma. No compression was encountered in the parenchyma. The patient was consulted with Neurosurgery Clinic. No surgical intervention was considered because the patient had high muscle strength loss, compression level may lead to several complications during and after operation and that recurrence probability is high.

The patient's neck, shoulder and ankle ROM were performed 2 times a day, and each set of exercises in 20 replicates. Stretching exercises were performed 2 times a day in the form of stress and rest for 10 s. And strengthening exercises, 10 repetitions were given 2 times a day. Transcutaneous electrical stimulation (TENS) applied to the shoulder and neck and neuromuscular electrical stimulation (Compex) was applied to the ankle for 30 min a day. Plastic high-intensity walking mold (PAFO) was given to prevent frequent fallings. As medication, pregabalin was initiated two times a day totally 50 mg while baclofen was initiated daily 10 mg and increased up to 30 mg.

The patient underwent 8 sessions of physical medicine
and rehabilitation programme because the patient wanted to go out of hospital. The patient reported decreased falling frequency and reduced fatigue in his right leg. However, there was no significant change in his muscle strength. The patient was discharged due to his request. The patient applied 20 sessions of radiotherapy to his cervical region 2 months later (In the Department of Radiation Oncology, Kocaeli University, Uganda). After treatment, the patient had increased muscle fatigue on his left arm and left leg and impaired walking problems during particularly when descending and climbing stairs.

DISCUSSION

NF1 has been first described by Freidrich von Recklinghausen in 1882. Neurofibromatosis (NF1, NF2, Schwannomatosis) in the United States affects more than 100,000 people. It also affects more than 2 million people worldwide (Huson et al., 2010). The majority of the cases (71%) such as our patient- had a family history. NF1 gene is found on 17th chromosome and a tumour-suppressor gene which codes the protein neurofibromine (Leroy et al., 2001; Gutmann, 2001).

Neurofibroma is one of the major characteristic features. Single or multiple cutaneous neurofibromas were observed in above 95% cases. The plexiform neurofibroma (PN) is found in 30% cases (Saltik et al., 2005). The symptoms of PN depend on localization site of the lesions and compression of neighbour structures. Intestinal/airway obstruction, findings of brain and cranial systems such as hydrocephalia, mental retardation, dementia, epilepsy, osseous changes such as lordosis, kyphoscoliosis, pseudoarthrosis and spina bifida, and endocrine disorders such as acromegaly, creatinism, hypoparathyroidism, myxedema and pheochromacytoma may be observed due to plexiform neurofibromas (Huson et al., 2010; Bayramgürler et al., 2003 ; Ragge 1993). (It has been reported that majority of the adult patients with cervical plexiform neurofibroma are asymptomatic cases however cervical plexiform neurofibroma may also lead to massive formations, pain and neurological deficits in the neck (Ward et al., 1994). Our case had a plexiform neurofibroma which involved whole spinal cord accompanied by multiple skin neurofibroma and caused spinal cord compression at the cervical level.

In patients with NF1, the cervical cord compression occur due to compression of neurofibromas to the cervical nerve root in the patients diagnosed NF1. However, they have not been frequently reported (Leonard et al., 2007; Créange et al., 1999). Physical therapy is useful in mild cases. The duration of physical therapy programme which is effective may be changed for patients. Severe cases may require surgery which is the pressure of the spinal cord (Taleb et al., 2011; Craig and Govender, 1992; Tonogai et al., 2008).

Leonard et al. (2007) have reviewed approximately 1500 patients with NF1 followed-up by two major centers between the years 1996 to 2006 in their retrospective study. The cervical cord compression was detected in 13 patients aged between 9 and 61 years. The cervical cord compression was at the levels of C2 and C3 in majority of the patients. The 7 patients had progressive quadripareisis while totally 3 patients had parapareisis, found at lower extremity in 2 patients and at upper extremity in 1 patient, also incontinence was detected in 1 patient while 3 patients without kyphotic deformity had complaints of cervical pain. The 11 of 13 patients were had undergone a single and multiple-level cervical laminectomy and a subtotal resection for neurofibromas. A secondary operation was required in 2 patients by the advancing time (Leonard et al., 2007).

Créange et al. (1999) have reviewed approximately 158 patients with NF1 and they found spinal cord compression or cauda equina syndrome in five patients. Despite the surgery, two patients with cervical cord compression developed quadriplegia and one of them died. Quadriplegia and neurological sphincter dysfunction were developed in two patients because of cauda equina syndrome. Intraspinal neurofibromatosis did not show any progression in 1 patient for 7-year follow-up (Créange et al., 1999). Sarica et al. (2008) have present-ed a 32-year-old case diagnosed NF1 with quadripareisis who had neurofibromas along whole spinal cord and cord compression at the level of C4-C5 and who had undergone a partial resection at the level of C3 and a total resection at the levels of C4,C5, C6. Postoperatively, clinical course of the patient significantly improved by application of physical rehabilitation and myorelaxant medication (Sarica et al., 2008).

In the present study, the patient had hemiparesis differently from the cases reported above. An operation was not decided in this patient considering the level of cervical cord compression, advanced clinical condition and postoperative recurrence probability. Duong et al. (2011) have made a retrospective study between 1980-2006 and examined 1895 patients with NF1. Death rate due to NF1 was investigated and found that 56 patients died due to complications of NF1. Spinal cord compressions was found in 3% as part of the complications (Duong et al., 2011). Helmers and Irwin (2009) have reported a 17-year-old case with NF1 with complaints of cervical pain and headache who had 4/5 extremity muscle strength and was treated with 20 sessions of cervical stabilization, posture exercises, stretching, interferential current and US during 13 weeks. The muscle strength of the patient increased up to 4+/5 and his complaints significantly decreased (Helmers and Irwin 2009). Although, the case in the present study could not continue physical medicine for more than 8 sessions because of social reasons, nevertheless, he expressed that frequency of fallings and fatigue of lower extremity decreased at the end of this process. We conclude that non-significant change in muscle strength resulted from high loss of muscle strength, inability to eliminate the compression causing this clinical condition and necessity...
of earlier onset and longer duration of physical medicine.

**Conclusion**

Conclusively, surgical intervention should be decided on the patients with NF1 accompanied with spinal cord compression considering compression level, invasion grade and clinical condition of the patient if a neurological deficit is present. The best outcomes are obtained when the patient has minimal preoperative neurological deficit. Also preoperative and postoperative treatment modalities are the important instruments in reversing muscle strength loss, reducing pain and improvement of the normal daily activities of the patient depending on the clinical condition.

**ABBREVIATIONS**

NF1, Neurofibromatosis type 1; ROM, range of motion; DTR, deep tendon reflexes; MRI, magnetic resonance imaging; TENS, transcutaneous electrical stimulation; PN, plexiform neurofibroma.

**REFERENCES**


