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Multiple Sclerosis and Neurofibromatosis Type 1

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Abstract: Neurofibromatosis is a widespread mesodermal dysplasia with protean clinical and radiographic manifestations. This study presented five rare cases of this disorder. Each case was presented in details including radiological examinations. Therapeutic options were investigated and the appropriate choices were administered to patients. These cases are not likely to be highly encountered in routine practice and their reporting helps clinicians not to miss their diagnosis. The present study showed five cases with neurofibromatosis. Some cases showed therapeutic responses while others did not. More studies are encouraged to look for more approaches with therapeutic responses for neurofibromatosis.

Key words: Neurofibromatosis, dysplasia, radiology, disorder, clinical, therapeutic

INTRODUCTION

Neurofibromatosis is a widespread mesodermal dysplasia with protean clinical and radiographic manifestations. It is inherited as autosomal dominant but mutation plays an important role (Antonio *et al*., 2013). The frequency in Britain is 0.3/1000 live births (including symptomatic and asymptomatic) (Barnard and Geddes, 1987; Hinrichs *et al*., 1987; Ferner *et al*., 2007). As it can be seen in Table 1, neurofibromatosis has been categorized into two types: NF-1(Von-Recklinghausen) disease) and NF-2 (Bilateral acoustic neurofibromatosis NF type 1 is associated with neoplasms of astrocytes and neurons (gliomas and hamartomas). While NF-2 is associated with tumours of Schwann cells (Schwannomas) and the tumours of meninges (Hughes, 1994; Ferner, 2011). The gene of disorder of this disease is located in 17q11.2 (Antonio *et al*., 2013).

Table 1: Clinical features of NF1

Variables	Clinical features
Nervous system	Plexiform neurofibromas
	Intellectual handicap
	Coordination problems
	Spinal neurofibromas
	Peripheral nerve malignancy
	Gliomas (particularly optic nerve)
	Aqueduct stenosis
	Epilepsy Hypsarrhythmia
Skeletal	Scoliosis
	Vertebral scalloping
	Lateral thoracic meningocele
	Lambdoid suture'defects
	Pseudoarthrosis of distal long bones
Genitourinary	Neurofibromas
	Pelvic rhabdomyosarcoma
Endocrine	Duodenal carcinoid
	Cardiovascular
	Hypertension
	Renal artery stenosis
	Intracranial artery stenosis
Respiratory	Neurofibromas of oral cavity, larynx and mediastinum
Gastrointestinal	Visceral neurofibromas
Haematopoietic	Atypical forms of childhood leukaemia
Skin	Juvenile xanthogranuloma

Multiple sclerosis prevalence in England is around 60/100000 but is higher in Scotland. There is strong association between NF-type 1 and other congenital anomalies but the association with multiple sclerosis has been confirmed recently but only a few cases have been reported. Table 1 shows the clinical features of neurofibromatosis type 1 (Thompson *et al*., 1990; Ferner *et al*., 1993; Mackenzie *et al*., 2014).

MATERIALS AND METHODS

In a large series of cases diagnosed in South West England, Bristol Region, South Wales and Jordan as multiple sclerosis, only five patients with neurofibromatosis have been confirmed with stigmata of NF-type 1 and the coincident finding is presumed to be related to mutation in genetic factors.

Case histories

Case 1: A 33 years old male patient presented with 1 month history of deterioration in power of the legs and numbness. The patient had congenital dysmorphic features and was educationally subnormal. There was also left lower moter neuron facial weakness, right 7th cranial

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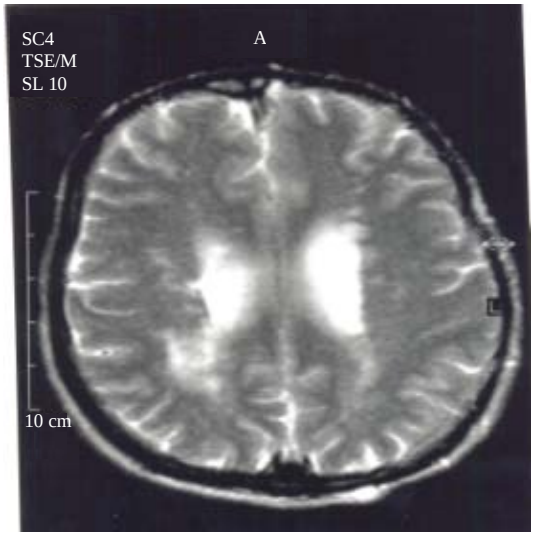

Fig. 1: Axial MRI T2WI: bilateral periventeicular MS plaques

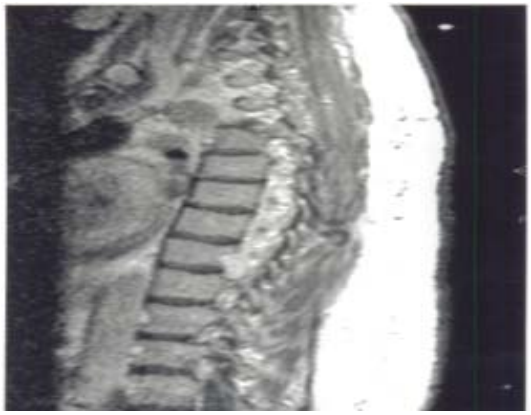

Fig. 2: Sagittal MRI T1WI's post Gad-DTPA: Neurofibroma at T9 vertebra

nerve palsy, profound weakness of all muscle groups in the lower limbs and bilateral sensory loss in lower limbs. Investigations including CT and MRI showed neurofibromata at T6 and T9. MRI also showed hydrocephalus and Arnold-Chiari-malformation. Ventilation/Perfusion scan showed multiple pulmonary emboli. An IVC filter was installed. The patient also underwent D6 laminectomy for total removal of intradural schwannoma. The patient was referred to the neurofibromatosis clinic with long standing hemi hypertrophy, arrested hydrocephalus, cutaneous haemangiomata on the left arm and hand. Later, CSF showed an oligomonoclonal bands. MRI showed features of multiple sclerosis (Fig. 1 and 2).

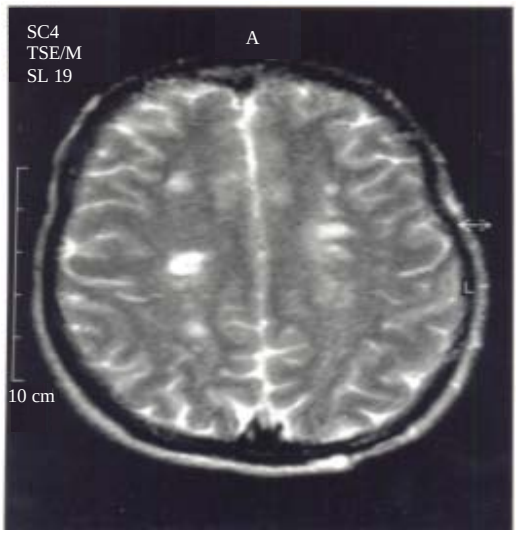

Fig. 3: Axial MRI T1WI post Gad-DTPA: Large enhancing neurofibromas, schwannoma arising at Lt neural foramina of T4

Case 2: A female patient was born on 6-April-1951 and presented with severe neurofibromatosis and 4 months history of parasthesia in hands and feet withsome difficulty in walking long distances. No fixed deficit or sphincteric disturbances were reported. The patient had surgery 20 years ago for debulking of neuro fibroma but no other problems.

On examination: GCS 15/15, normal power in all four limbs, hyper-reflexic with upgoing plantars but no clonus. The sphincter tone and limb sensation were normal. There was no ataxia. The diagnosis was initially neurofibromatosis with possible cord compression. Investigations showed possible CSF oilgoclonal bands.

Lumbar puncture: Clear and colourless CSF, WCC: 2 and protein: 0.34 G/L. Later, MRI showed high signalin the brain and spinal cord on T2-W SE. The patient's final diagnosis was neurofibromatosis and multiple sclerosis. The patient was under follow-up with no regular medications (Fig. 3 and 4).

Case 3: A 40 years old female, presented to neurologyclinic with tremor, weakness of the Rt upper arm, visual cloudiness and painful tingling in hands and compression. Investigations showed possible CSF oligoclonal bandseet of 8 months history.

On examination: She has multiple Cafe-au-Lait spots over her abdomen and axilla and multiple cutaneous

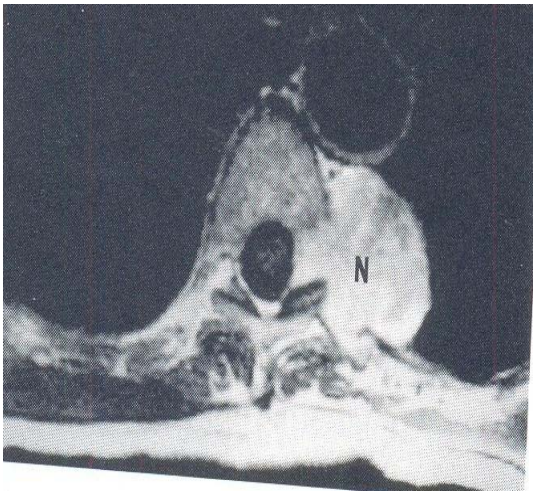

Fig. 4: Axial MRI T1WI post Gad-DTPA: large enhancing neurofibromas, schwannoma arising at Lt neural foramina of T4

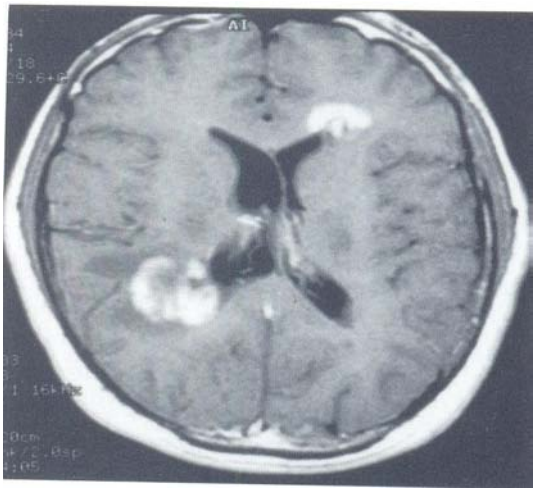

Fig. 6: Axial CT scan with 4 contrast: bilateral optic nerve gliomas-pathognomonic for neurofibrimatosis

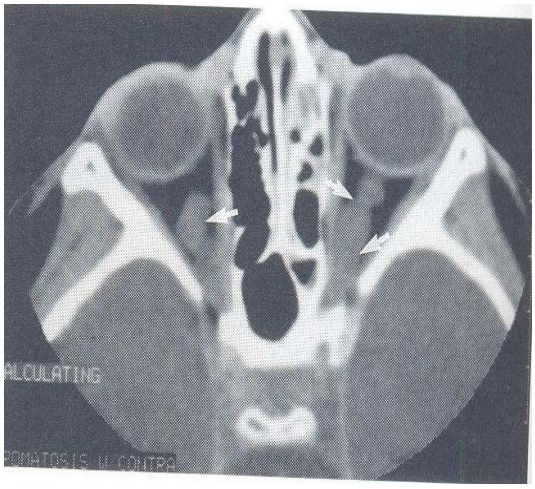

Fig. 5: Axial MRI T1WI post Gad-DTPA: at least two enhancing MS plaques

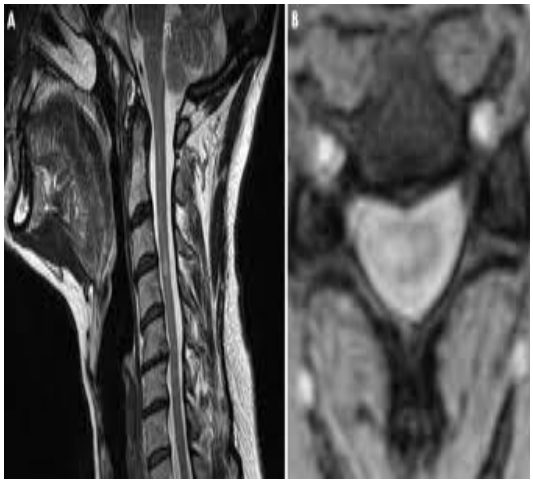

Fig. 7: Sagittal and axial T2W MRI: high signal intensity lesion in cervical spinal cord due to MS plaque

neurofibromas (Fig. 5 and 6). Ophthalmology examination showed pale disc and corrected visual acuity was 8/18 on the right side and 5/6 on the left. Neurological examination showed mild increase in the tone of the left arm and left hemiparesis in the periventricular regions with hyperreflexia. CSF showed oligoclonal bands. She had other stigmata of neurofibromatosis. The patient was treated with oral methyprednisolone without significant improvement.

Case 4: A 30 year old male patient with no family history of neurofibromatosis 1, presented with Cafe-au-Lait spots and other stigmata of neurofibromatosis type 1 and progressive weakness and stiffness of his legs.

On examination: He has multiple cutaneous neurofibromas and axillary freckling, IQ of 50, right sided optic atrophy, spastic ataxia and hyperreflexia. CSF electrophoresis showed oligoclonal bands. He was treated with intravenous methyprednisolone with minimal benefit. His cervical MR showed high signal lesion due to MS plaque (Fig. 7). Researcher brain MRI showed multiple hamartomas (Fig. 8).

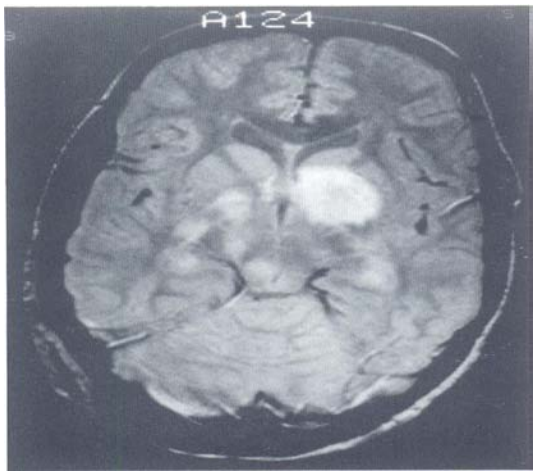

Fig. 8: Axial MRI Proton density: multiple hamartomas in neurofibromatosis type 1

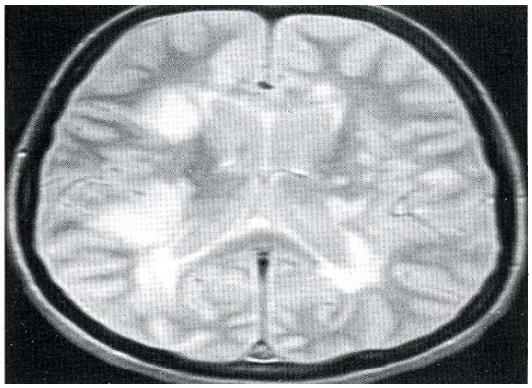

Fig. 9: Axial proton density MRI: multiple bilateral deep white matter MS plaques

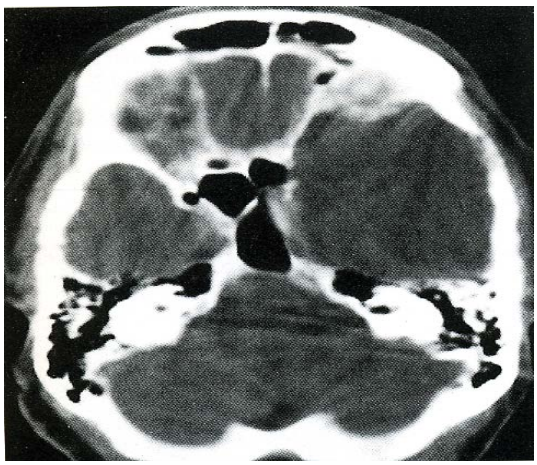

Fig. 10: Axial brain CT scan: absent left sphenoid wing

Case 5: A 52 years old female patient developed Café-au-Lait spots on her abdomen and axillary freckling when she was teenage. At the age of 30, she started to have progressive slowness of her walking, attack of loss of vision and upper limb weakness.

On examination: She had several Cafe-au Lait spots and multiple neurofibromas, hyperreflexia with the power of upper limbs was 3/5. EMG showed hypotonia and some degree of urinary urgency but the sphincters were intact. Visual evoked response was delayed on the left side.

Proton density MRI showed high signal lesions in the periventricular deep white matter; consistent with MS plaques. Brain CT scan showed absent Lt greater wing of sphenoid (Fig. 9 and 10). The patient was treated with oral prednisolone but her condition deteriorated and remained handicapped in her home with a nurse looking after her.

RESULTS AND DISCUSSION

Neurofibromatosis is one of the most common autosomal dominant disorders affecting approximately 1 of every 3000-5000 people in general population.

Neurofibromatosis is a genetic disorder that primarily affects cell growth of neural tissues. The genetic locus of NF-1 is mapped to the long arm of chromosome 17 and NF-2 is linked to an abnormality of chromosome 22.

Neurofibromatosis type 1 accounts for over 90% of all cases of neurofibromatosis (Stumpf, 1987; Hughes, 1994; Ferner, 2011).

Neurofibromatosis is not an uncommon disease in the South West of England but the prevalence of isolated multiple sclerosis is at least 1 in 1000 in the same area. The association of neurofibromatosis type-1 and other systems is well recognized but the recently proven association with multiple sclerosis has also been recognized (Weinshenker *et al*., 1989; Osborn *et al*., 1990). We presented five cases of neurofibromatosis type-1 with clinical and radiological features of multiple sclerosis.

CONCLUSION

The present study showed five cases with neurofibromatosis associated with multiple sclerosis. Some cases showed therapeutic responses while others did not. More studies are encouraged to look for more approaches with therapeutic responses for neurofibromatosis and multiple sclerosis.

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