British Society for Clinical Neurophysiology Medical Student Essay Prize 2018

'How Clinical Neurophysiology helped in the diagnosis/management of a patient'

Delayed radiation-induced bulbar palsy mimicking amyotrophic lateral sclerosis

Sarah Nichol, University of Glasgow

Summary

This case report follows a 58 year old gentleman presenting with a one year progression of bulbar palsy signs and symptoms. His main complaint was difficulty in swallowing and slurring of his speech. He reported no upper or lower limb weakness. On neurological examination, there was visible atrophy of the tongue muscles as well as slight weakness of the tongue against resistance. Fasciculations of the tongue were present on visual examination. In any case of adult onset bulbar symptoms, amyotrophic lateral sclerosis (ALS) is a suggested diagnosis. This case shows how collation of clinical history, medical history and electrodiagnostic studies leads to the diagnosis of a known, but rare, mimic of bulbar-onset ALS.

Background

Amyotrophic lateral sclerosis (ALS) is a subtype of motor neurone disease (MND) characterised by progressive degeneration of motor neurons. It usually presents with both upper and lower motor neuron signs arising from one segment of the neuroaxis, typically beginning with either motor neuron degeneration in a cortical, bulbar or ventral cord location, to then spread to contiguous areas as the disease progresses [1]. Classic presenting signs and symptoms include weakness in lower limb or upper limb, muscle cramps and fasciculations. Other presenting symptoms are difficulty with speech and swallowing or even rarer, respiratory muscle problems and breathing difficulties. As the disease progresses muscles become weaker and more are affected, eventually leading to inability to chew or swallow, talk or walk [2]. The most frequent cause of death in patients with ALS is respiratory failure due to weakness of the respiratory muscles, with a recent study reporting it to be the cause of 61% of patient deaths, with pneumonia following, resulting in 9% of deaths [3].

The incidence of ALS is between 1.5 to 2 per 100000 people with males being more commonly affected than females in the ratio 1.4:1. The mean age of disease onset is 63 years and as a disease of poor prognosis 50% of patients die within 3 years of the first presenting symptoms, leading to 90% after 5 years [2]. Around 30% of amyotrophic lateral sclerosis cases present with isolated bulbar symptoms, also referred to as bulbar-onset ALS [2], which in itself is an adverse prognostic indicator [1]. A recent study showed that the median interval between the onset of dysarthria and dysphagia to anarthria and loss of ambulation was 18 and 22 months respectively, with survival only remaining a few months after that [4].

The diagnosis of all motor neuron disorders relies on both clinical evaluation and electrodiagnostic testing. Neurophysiology is an important tool in patients presenting with signs and symptoms of motor neuron disease. Previously, the diagnosis of motor neuron diseases such as ALS was largely clinical and

heavily weighted on the progressive presentation of the specific clinical signs and symptoms[5]. Now, neurophysiologic evidence is considered equivalent to clinical signs and symptoms and in reaching a diagnostic certainty of ALS there must be clear evidence of widespread denervation without conduction block [6]. Electrodiagnostic tests such as nerve conduction studies and electromyography are not only used to support a diagnosis of ALS but more importantly to exclude other treatable diseases that mimic ALS [7].

With Riluzole being the only licensed drug in the UK for people suffering with MND, offering a modest improvement on survival but no cure, the foundation in the management of these patients is the use of the multidisciplinary team focusing on symptomatic management, and as the disease progresses, palliative care. Physiotherapists will provide exercises and techniques to try and improve mobility, occupational therapists will assist in aspects of daily living, including communication and mobility aids, and speech and language therapists will help with problems regarding dysarthria and dysphagia. This is all on top of a background of neurologists, specialised nurses, social workers and the palliative care team [1].

ALS is a devastating diagnosis to receive, with a prognosis much poorer than other disorders affecting motor neurons. Understanding the rapid progression of the disease along with the realisation that there is no cure has a substantial impact on both the patient's life and their family's. Relaying the diagnosis to the patient must be performed with the utmost sensitivity and is a challenge for all clinicians involved.

'The best test of a physician's suitability for the specialized practice of neurology is not his ability to memorize improbable syndromes but whether he can continue to support a case of motor neurone disease, and keep the patient, his relatives and himself in a reasonably cheerful frame of mind'- **W Bryan Matthews** [8].

Case Presentation

A 58-year-old gentleman presented to the clinical neurophysiology department after referral from his GP with a one year history of bulbar palsy signs and symptoms. He noted a progression in difficulty to swallow and complained of occasionally choking on his meals. His speech had become slightly more slurred over the past year but he did not feel this was affecting him greatly. There was a period where he noticed intermittent twitching of his leg muscles but this had now resolved. He did not feel as though he had any weakness in his limbs or that he has become weaker and did not report any sensory, visual or autonomic changes.

His only medical history included treatment for tonsillar cancer 16 years previously to the onset of these symptoms. This treatment included radiotherapy, chemotherapy and surgery. He reported that he had no difficulties with his speech or swallowing immediately after the treatment and that these have only surfaced in the past year. He is currently on no medication and family history was also insignificant.

On examination, mental status and higher mental function were intact. Speech was slightly dysarthric but understandable. Fasciculations and atrophy were noted in the tongue along with slow, weak tongue

movements. However, there was no evidence of neck or facial weakness and jaw jerk was negative. In the limbs there was no visible evidence of wasting or fasciculations. Using the medical resource council grading [9] , strength tests in all movements of upper and lower limbs were 5/5. All reflexes were of normal quality and babinski response was negative bilaterally. Sensory and coordination examination were completely intact and accompanied by a normal gait.

Investigations

All initial laboratory investigations were normal, including a negative result for anti-acetylcholine receptor autoantibodies as well as normal results for other relevant autoantibody tests. A normal creatine kinase level was found on a background of normal routine blood tests. The magnetic resonance imaging (MRI) scan was reported normal. Examination of cerebrospinal fluid (CSF) to rule out an infective or inflammatory cause was not necessary at this stage.

Electromyography (EMG) and nerve conduction studies were performed in a clinical neurophysiology laboratory. Both sensory and motor nerve conduction studies were essentially within normal limits in both the upper and lower limbs, demonstrating normal amplitudes and nerve conduction velocities (figures 1, 2). In addition, the f wave latency studies were normal (figure 3) and the repetitive nerve stimulation of the right abductor digiti minimi also stood within the normal limits (figure 4) . On EMG, responses were generally normal in the limbs and neck with no denervation findings associated with ALS (figure 5), as well as stimulated single fibre of the left orbicularis oculi revealing satisfactory jitter with no blocks (figure 6). However, on performing EMG on the left tongue, the patient appeared to have frequent bursts of myokymia (figure 7). Overall, the electrodiagnostic testing shows no changes to support a diagnosis of ALS and therefore using the revised el Escorial criteria was not necessary to establish a diagnosis [10].

NERVE Stimulation Sies	**Recording Site**	**Peak**	**Amplitude**	**Latency**	**Distance**	**Nerve conduction velocity**
		ms	**µV**	**ms**	**cm**	**m/s**
Right MEDIAN						
Wrist	Dig II	2.65	35.7	2.20	10.5	47.7
Right RADIAL						
Forearm	Snuff	1.75	30.7	1.75		
Right SURAL						
Calf	Lateral Malleolus	2.65	14.9	1.75		
Left SUPERFICIAL PERONEAL						
Lat Leg	Ankle	4.35	9.8	3.75		

Figure 1. Sensory nerve conduction studies

NERVE Stimulation Site	**Recording Site**	**Latency**	**Amplitude**	**Distance**	**Nerve conduction Velocity**
		ms	**mV**	**cm**	**m/s**
Right MEDIAN					
Wrist	APB	2.95	7.4		
Right ULNAR					
Wrist	ADM	2.65	12.4		
.Elbow	ADM	7.30	11.8	30	64.5
Left COMMON PERONEAL					

Ankle	EDB	5.60	6.1		
Fibular Head	EDB	15.60	4.1	43	43.0
Right TIBIAL (KNEE)					
Ankle	AH	6.65	4.6		
Left TIBIAL (KNEE)					
Ankle	AH	7.25	5.4		

APB (Abductor Policis Brevis), ADM (Abductor Digiti Minimi), EDB (Extensor Digitorum Brevis), AH (abductor hallucis)

Figure 2. Motor nerve conduction studies

Nerve	Minimum F- wave latency (ms)
Right ULNAR	32.25
Right MEDIAN	25.75
Right TIBIAL (KNEE)	60.05
Left TIBIAL (KNEE)	63.45

Figure 3. F-wave study

Muscle / Train	Time	Rate	Amp	4-1	10-1	Fac Ampl	Area	4-1	10-1	Fac Area
		pps	mV	%	%	%	mVms	%	%	%
Right ABD DIG MIN (UL)										
Baseline	0:00:00	3	5.1	12.7	12.3	100	13.7	-0.4	1.4	100

Figure 4. Repetitive nerve stimulation of right abductor digiti minimi

Differential diagnosis

There are diseases other than bulbar-onset ALS that manifest as bulbar palsy and there can be many different underlying aetiologies. Myasthenia gravis is an autoimmune condition affecting the neuromuscular junction. It causes skeletal muscle weakness and commonly presents with ocular and bulbar symptoms. This provides the incentive to test for the anti-acetylcholine receptor autoantibody [11]. A genetic condition worth mentioning is Kennedy disease which is also known as X-linked spinobulbar muscular atrophy [10]. It is a neurodegenerative disorder mainly manifesting with lower motor neuron involvement and has a collection of symptoms similar to other neuromuscular disorders [12]. MRI is used to rule out possible structural lesions such as brainstem gliomas and brainstem vascular infarcts and investigation of the CSF to rule out infective or inflammatory causes [1]. It is possible that metabolic conditions such as thyrotoxicosis can present with aggressive muscle wasting and weakness similar to ALS [1].

This patient's clinical picture of progressive motor only weakness accompanied by bilateral tongue atrophy and fasciculations has a high positive predictive value for a diagnosis of ALS [11]. However on investigation, the only abnormality found was myokymia in the EMG studies. The presence of myokymia in the tongue and no evidence of denervation on EMG studies on top of a history of previous radiation

therapy suggests the rare condition of delayed radiation-induced bulbar palsy, which is known mimic of bulbar-onset ALS [10].

Muscle	Spontaneous Activity					MUAP			Recruitment
	IA	Fib	PSW	Fasc	H.F.	Amp	Dur.	PPP	Pattern
Right. TIBIALIS ANTERIOR	N	None	None	None	None	N	N	N	N
Left. TIBIALIS ANTERIOR	N	None	None	None	None	N	N	N	N
Right. GASTROCNEMIUS (MED)	N	None	None	None	None	N	N	N	N
Left. GASTROCNEMIUS (MED)	N	None	None	None	None	N	N	N	N
Left. VASTUS MEDIALIS	N	None	None	None	None	N	N	N	N
Right. VASTUS MEDIALIS	N	None	None	None	None	N	N	N	N
Right. BICEPS	N	None	None	None	None	N	N	N	N
Right. FIRST DORSAL INTEROSSEOUS	N	None	None	None	None	N	N	N	N
Left. FIRST DORSAL INTEROSSEOUS	N	None	None	None	None	N	N	N	N
Right. STERNOCLEIDOMASTOID	N	None	None	None	None	N	N	N	N
Right. ORBICULARIS OCULI	N	None	None	None	None	N	N	N	N
Left. TONGUE	N	None	None	None	2+*	N	N	N	N
*myokymia									

IA(Insertion activity), Fib (fibrillations), PSW (Positive Sharp Waves), Fasc (Fasciculations), H.F. (high frequency)

Figure 5. Electromyography

Muscle		N	Jitter	Block	MIPI	MCD	MSD	FR
			µs		µs	µs	µs	pps
Left ORBICULARIS OCULI	1.1	99	5.41	-	3352.9	5.41	5.41	10
	1.2	99	13.00	-	4193.7	13.00	13.00	10
	1.3	100	9.32	-	5859.6	9.32	9.32	10
	1.4	98	8.48	-	8994.8	8.48	8.48	10
	1.5	98	13.97	-	10476	13.97	13.97	10
	1.6	99	21.95	-	11940	21.95	21.95	10
	1.7	68	17.08	-	13172	17.08	17.08	10
	1.8	98	25.38	-	14342	25.38	25.38	10
	2.1	89	17.42	-	3442.8	17.42	17.42	10
	2.2	100	22.87	-	5836.5	22.87	22.87	10
	2.3	98	11.73	-	8987.5	11.73	11.73	10
	2.4	99	27.99	-	10733	27.99	27.99	10
	Mean		16.22	-	8444.2	16.22	16.22	10
	% Blocked			0				

Figure 6. Stimulated single fibre EMG

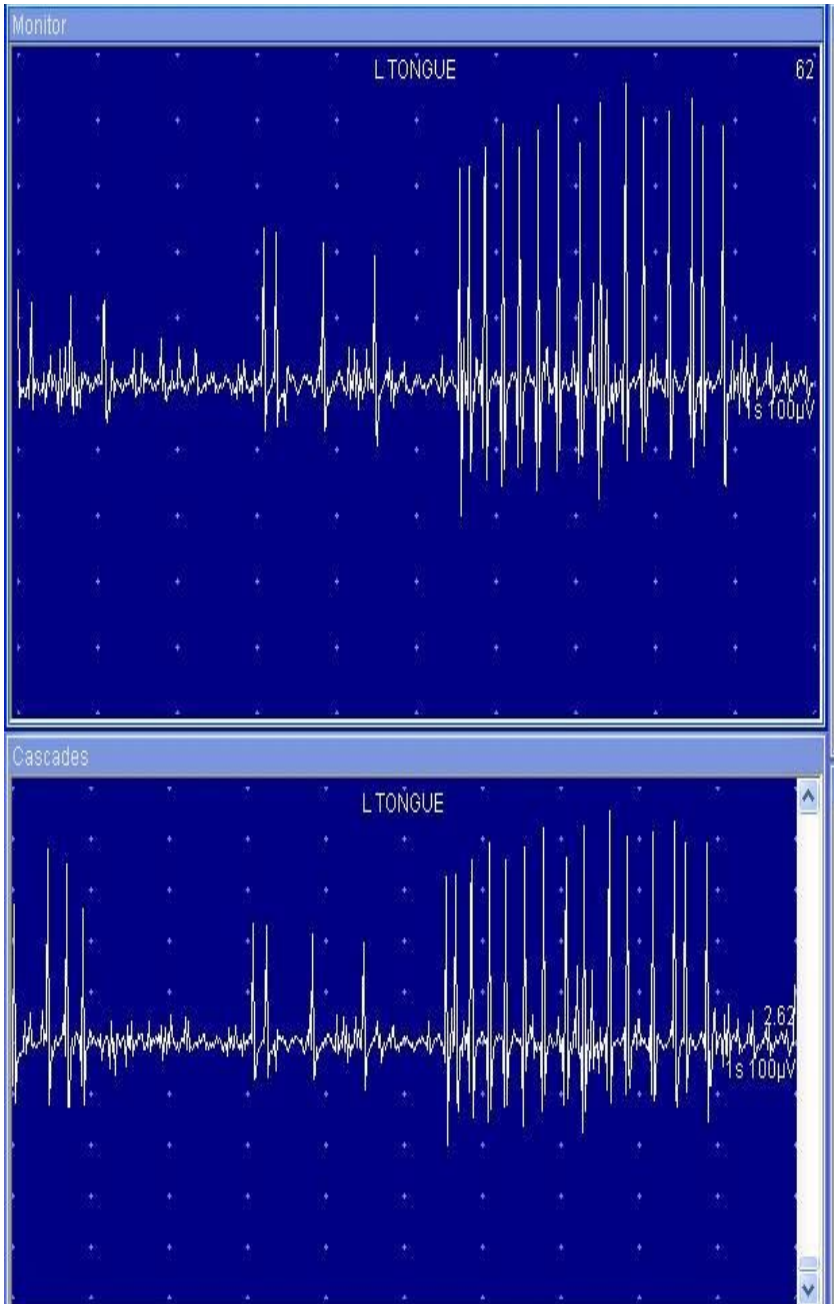

Figure 7. Visual representation of myokymia on EMG

Treatment

Delayed radiation-induced bulbar palsy has a much slower progression and a substantially better prognosis than that of ALS. However it can still lead to significant disability. While there is no cure, management of the disease is possible. Pharmacological treatment is offered in conjunction with speech and language therapy to address and manage problems relating to dysarthria and dysphagia. Spontaneous movements such a myokymia can be controlled with the use of antiepileptic drugs such as

phenytoin and carbamazepine [12]. Supporting the theory that vasculopathy is the underlying aetiology for radiation induced nervous system injuries, there is evidence that use of anticoagulants can offer some clinical improvement [13].

Discussion

To be able to evaluate the findings present in electrodiagnostic testing such as nerve conduction studies (NCS) and electromyography (EMG) when investigating a possible case of ALS, one must understand the underlying pathophysiology. The neurodegenerative disorder is characterised by progressive motor neuron death. After cell death, retrograde axonal degeneration occurs, subsequently followed by denervation and reinnervation in the corresponding muscles [2].

As a disease characterised by motor neuron death, sensory NCS should remain normal. Evidence of demyelination, conduction block and other abnormalities in sensory nerve conduction should not be observed on NCS and would suggest a different underlying pathology [14]. Regarding motor NCS there are a few possible variations in findings. In patients with ALS, the compound muscle action potentials (CMAPs) can either appear normal, or have reduced amplitude, prolonged distal latencies and increased nerve conduction velocities. The aforementioned changes in CMAPs tend to progress as severity of muscle weakness increases [5].

Needle EMG studies are fundamental for diagnosis and are used to provide evidence of denervation and chronic reinnervation over multiple nerve roots [14]. Importantly they can identify lower motor neuron involvement subclinically. Clinically unaffected muscles in ALS will still commonly show signs of fasciculations and partial denervation. This is a feature specific to ALS and helps eliminate conditions that mimic it from the differential diagnosis. This is essential in the steps towards an earlier diagnosis and management [6] . In order for features of EMG to be consistent with a diagnosis of ALS, both evidence of acute denervation and chronic reinnervation must be present and these are represented by their respective EMG findings. A combination of fibrillations, positive sharp waves and fasciculations are all signs of acute denervation. However it is important to note that these findings are not specific to ALS [14]. Morphologic changes in motor units potentials (MUPs) such as increased duration, increased polyphasicity and increased amplitude provide evidence of chronic denervation, reflect the underlying pathophysiology of the reinnervation process of collateral axon sprouting. Decreased recruitment of motor units is also seen and is a sensitive marker of lower motor neuron abnormality [14]. The balance between signs of acute denervation and chronic reinnervation on EMG are influenced by the underlying progression of the disease and can be used as a prognostic indicator [6].

A specialised EMG study called single fibre EMG can also be used in reaching a diagnosis of ALS. While it is a diagnostic technique primarily used in neuromuscular junction disorders, collateral axon sprouting in ALS creates instability of neurological transmission. This can be visualised as an abnormality of jitter, blocking and fibre density on single fibre EMG and this positively correlates with increasing muscle weakness in ALS patients [15].

Myokymic discharges are scarcely ever reported on EMG in patients with axonal disorders such as ALS [16]. They are more often associated with demyelinating disorders, with facial muscle myokymia most

commonly being reported in relation to multiple sclerosis [17]. Myokymic discharges are spontaneously generated bursts of individual motor units that occur rhythmically, firing at a uniform rate of around 5-150 Hz. They normally last for a few seconds and are interrupted by periods of silence [18]. Clinically they are often mistaken for fasciculations as they have the same appearance; rippling and undulating movements under the skin and EMG is necessary to differentiate between the two [19]. Disorders involving myokymia are classified anatomically, either as facial or limb myokymia [17].

Myokymic discharges may be as a result of radiation-induced neuropathy and can appear decades after the original radiotherapy. A similar case report in 2016 reported a 68-year-old women presenting with difficulty in speaking and evidence of myokymic discharges in her tongue approximately 12 years after radiation therapy to head and neck [20]. Radiation induced myokymia usually presents as brachial or lumbosacral plexopathy [20]. Even though facial myokymia following cranial radiation is much less common and has been reported fewer times than limb myokymia following peripheral radiation, it is still a relatively specific finding [19]. Other possible causes of facial myokymia that must be ruled out include brainstem tumours, demyelinating lesions within the brainstem and metastatic recurrence of the cancer previously treated with radiotherapy [17].

While the underlying pathophysiology of myokymic discharges is relatively unknown it is thought to be related to motor axon membrane hyperexcitability [18]. Alteration of the axon membrane microenvironment is what leads to the hyperexcitability of the axon membrane and is affected by multiple mechanisms such as demyelination, radiation, direct neurotoxic effects, ischemia, hypoxia and oedema [21]. Possible theories explaining the pathophysiology behind delayed radiation-induced myokymia include that of radiation exposure causing direct damage to the axon, leading to local demyelination and membrane instability, or radiation damaging the vascular endothelium resulting in secondary damage to the neural tissue [19]. Ultimately, this is still a poorly understood condition and more research is required to characterise it fully.

The patient in the present report manifested only tongue myokymic discharges on EMG and no other abnormalities suggesting muscle fibre denervation. The presence of dysphagia and dysarthria, alongside atrophy, weakness and involuntary movements of the tongue suggest involvement of all the nerves supplying the bulbar muscles (cranial nerves IX, X, XII) and is therefore diagnostic of a bulbar palsy [22]. The patient's history of previous radiation therapy, and no other evidence of a different pathology, meant that delayed radiation-induced bulbar palsy was the most likely diagnosis.

Delayed radiation-induced bulbar palsy is a rare complication of therapeutic radiation. It is one of many rare nervous system disorders associated with therapeutic radiation. These include radiation necrosis, cerebrovascular disease, cognitive deficits, endocrinopathies, encephalopathy, myelopathy, plexopathy, radiculopathy, neuropathy, and secondary tumors [23]. Regarding cranial radiotherapy, a study showed that roughly 10% of people receiving high dose cranial radiotherapy for nasopharyngeal cancer (NPC) developed neurological complications, with a median latency of 5 years [24]. Specifically relating to cranial nerve palsies, fewer than 40 patients who developed conventional radiation therapy-induced cranial nerve palsy after treatment for NPC have been reported in the English literature since 1966 [25]. Noting this, there is even less literature available on delayed radiation-induced cranial nerve palsy

following therapy for tonsillar cancer. The small number of such cases is likely due to the fact that cranial nerves are relatively radioresistant. Of the cases that have been reported, there is a propensity for the lower cranial nerves to be more susceptible to radiation-induced damage than upper cranial nerves [26], with the most frequently affected nerves being the hypoglossal nerve followed by the vagus nerve and spinal accessory nerve [25]. This could be due to the course these nerves run through the neck and provides a possible explanation as to why a bulbar palsy presentation could be more common than other cranial nerve palsies after cranial radiotherapy [25] .

While delayed radiation-induced bulbar palsy does not have the same rapid progression of deterioration to eventual loss of life as ALS, we must be mindful of the important role that the bulbar nerves play in our activities of daily living including articulation, phonation and deglutition. Damage to them can have an immense impact on a patient's quality of life. Although the patient in our case report presented with mild bulbar palsy symptoms and claimed that it had little impact on him, it is likely his signs and symptoms will very slowly worsen. As a disease equally irreversible as ALS, loss of these functions must be handled with close symptomatic treatment and management [27].

Conclusion

As the prognosis of ALS is excessively poor compared with other motor neuron disorders and is a disease with a huge impact on patient quality of life, it is essential that the correct diagnosis be reached. Misdiagnosis surrounding such an undesirable diagnosis can cause severe patient distress and diminish patient confidence in onward management. Clinical neurophysiology and its accompanying electrodiagnostic tests increase diagnostic accuracy and are essential in the diagnosis or exclusion of diagnosis of ALS. As a result of ALS being such a devastating diagnosis, neurologists and neurophysiologists alike seek to find a mimic to be the underlying pathological cause. Because ALS and its mimics all present very similarly, patient history, laboratory and radiological investigations, electrodiagnosis and the principles of neurophysiology are key in establishing a confident diagnosis. Even though mimics are often as equally irreversible as ALS itself, it is still highly important to distinguish the two so that the correct information is provided to the patient and appropriate counselling and management offered as soon as possible. In this case history, neurophysiology was vital to patient care and management, and without such investigations, the diagnosis of delayed radiation-induced bulbar palsy could not have been determined.

References

1. Howard R. Management of motor neurone disease. Postgraduate Medical Journal. 2002;78(926):736-741.
2. Amyotrophic lateral sclerosis - Symptoms, diagnosis and treatment | BMJ Best Practice [Internet]. Bestpractice.bmj.com. 2018 [cited 23 July 2018]. Available from: https://bestpractice.bmj.com/topics/en-gb/330/aetiology
3. Wolf J, Safer A, Wöhrle J, Palm F, Nix W, Maschke M et al. Causes of death in amyotrophic lateral sclerosis. Der Nervenarzt. 2017;88(8):911-918.
4. Turner M, Scaber J, Goodfellow J, Lord M, Marsden R, Talbot K. The diagnostic pathway and prognosis in bulbar-onset amyotrophic lateral sclerosis. Journal of the Neurological Sciences. 2010;294(1-2):81-85.
5. Joyce N, Carter G. Electrodiagnosis in Persons With Amyotrophic Lateral Sclerosis. PM&R. 2013;5(5):S89-S95.

6. Mills K. The basics of electromyography. Journal of Neurology, Neurosurgery & Psychiatry. 2005;76(suppl_2):ii32-ii35.
7. Preston D, Shapiro B. Electromyography and neuromuscular disorders. London: Elsevier Saunders; 2013.
8. Matthews WB. Practical neurology. 2nd edn. Philadelphia: F.A. Davis Company; 1970.
9. Aids to the examination of the peripheral nervous system. Postgraduate Medical Journal. 1977;53(621):419-419.
10. Bertorini T. Neuromuscular disorders. Philadelphia: Elsevier Saunders; 2011.
11. Turner M, Talbot K. Mimics and chameleons in motor neurone disease. Practical Neurology. 2013;13(3):153-164.
12. Shapiro B, Rordorf G, Schwamm L, Preston D. Delayed radiation-induced bulbar palsy. Neurology. 1996;46(6):1604-1606.
13. Glantz M, Burger P, Friedman A, Radtke R, Massey E, Schold S. Treatment of radiation-induced nervous system injury with heparin and warfarin. Neurology. 1994;44(11):2020-2020.
14. Duleep A, Shefner J. Electrodiagnosis of Motor Neuron Disease. Physical Medicine and Rehabilitation Clinics of North America. 2013;24(1):139-151.
15. Liu M, Cui L, Guan Y, Li B, Du H. Single-fiber electromyography in amyotrophic lateral sclerosis and cervical spondylosis. Muscle & Nerve. 2013;48(1):137-139.
16. Whaley N, Rubin D. Myokymic discharges in amyotrophic lateral sclerosis (ALS): A rare electrophysiologic finding?. Muscle & Nerve. 2010;41(1):107-109.
17. Rauf J, Akhtar J, Khealani B, Ali L. Peripheral (limb) myokymic discharges in motor neuron disease. Case Reports. 2012;2012(jul30 1):bcr2012006399-bcr2012006399.
18. Kelkar P, Kimura J. Myokymia in Axonal Disorders. Journal of Clinical Neuromuscular Disease. 2005;7(2):55-58
19. Glenn S, Ross M. Delayed radiation-induced bulbar palsy mimicking ALS. Muscle & Nerve. 2000;23(5):814
20. Tiftikcioglu B, Bulbul I, Ozcelik M, Piskin-Demir G, Zorlu Y. Tongue myokymia presenting twelve years after radiation therapy. Clinical Neurophysiology Practice. 2016;1:41-42.
21. Gutmann L. AAEM minimonograph #37: Facial and limb myokymia. Muscle & Nerve. 1991;14(11):1043-1049.
22. Rea P. Hindbrain (Rhombencephalon). Essential Clinical Anatomy of the Nervous System. 2015;:91-98.
23. Cross N, Glantz M. Neurologic complications of radiation therapy. Neurologic Clinics. 2003;21(1):249-277.
24. Lee A, Law S, Foo W, Pooh Y, Cheung F, Chan D et al. Retrospective analysis of patients with nasopharyngeal carcinoma treated during 1976–1985: Survival after local recurrence. International Journal of Radiation Oncology*Biology*Physics. 1993;26(5):773-782.
25. Lin Y, Jen Y, Lin J. Radiation-related cranial nerve palsy in patients with nasopharyngeal carcinoma. Cancer. 2002;95(2):404-409.
26. JANSSEN S, GLANZMANN C, YOUSEFI B, LOEWENICH K, HUBER G, SCHMID S et al. Radiation-induced lower cranial nerve palsy in patients with head and neck carcinoma. Molecular and Clinical Oncology. 2015;3(4):811-816.
27. Huang A, Song S, Dominguez L, Nguyen J, Goldman R, Reiter E. Delayed lower cranial neuropathies following primary radiotherapy for oropharyngeal squamous cell carcinoma. The Laryngoscope. 2013;123(5):1207-1209.