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Case Report

Restless legs syndrome: an unusual cause for a perplexing syndrome

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Restless legs syndrome (RLS) is a well-defined symptom complex, occurring either as idiopathic RLS or in association with many other disorders. Although no definite etiology is known for this condition, several pathophysiological mechanisms have been proposed. There is supportive evidence that RLS is a central nervous system (CNS) dysfunction, suggesting involvement of the descending dopaminergic (DA) pathways, but it can also occur with spinal disorders. We present a patient suffering from RLS who eventually was diagnosed with a foramen magnum tumor. Based on the available evidence, we attempt to correlate the location of the tumor with the patient's symptoms of RLS.

Keywords: foramen magnum meningioma; RLS; DA agents; neurotransmitters

Case history

This 40 year-old woman presented to a neurologist in September 1994, with a 7 year history of insidious onset of burning dysesthesia in both legs. The dysesthesia extended from the knees down and was associated with pain to light touch. She also reported restlessness during the night and difficulty sleeping. She was previously treated with Diazepam, which became ineffective. She was placed on Carbidopa-levadopa 10/100 tid and later changed to sustained release Carpidopa-levadopa bid.

Her past medical history was non-contributary and the only surgical procedure was a bilateral breast augmentation. In her family history, her maternal grandmother complained of restless legs. Her neurological examination revealed a normal mental status and intact sensation to all modalities. On motor examination there was no weakness or spasticity and her gait was normal. Deep tendon reflexes were 2^+ and equal in the upper extremities but 4^+ in the lower extremities with an unsustained ankle clonus and an extensor plantar on the right.

Since her symptoms persisted, Imipramine 25 mg hs, increasing to 50 mg after 1 week, was added to her Carbidopa-levadopa CR. Her symptoms and her sleep improved considerably so that she now was able to sit and watch television comfortably. Clonazepam was added to her regimen. She continued to have bouts of discomfort with restless legs. Therefore, further evaluation was recommended, especially to rule out multiple sclerosis (MS).

Radiological investigations in June 1995 revealed calcifications below the foramen magnum on a single lateral cervical spine film. A CT scan of the cervical spine confirmed a variable calcified mass, with slightly lobulated margins in the area of the right foramen magnum. The tumor extended cranially into the posterior fossa and caudally along the right anterior cervical canal down to the C2 vertebral body (Figure 1). An MRI demonstrated an extra-axial mass in the right foramen magnum displacing the medulla and spinal cord to the left, confirming its superior and inferior extensions. There was variable enhancement with gadolinium. These findings were consistent with a foramen magnum meningioma (Figure 2).

At the time of neurological referral, she reported that without her medications she would not be able to sit down for even 1 min. Her neurological examination was unchanged with continued presence of the right pyramidal symptoms and absence of any weakness or sensory changes. Prior to surgery a vertebral angiogram demonstrated a tumor blush in the area of the foramen magnum with its blood supply originating from an enlarged posterior meningeal artery.

A suboccipital craniectomy and cervical laminectomy of C1 and C2 were performed in August 1995. The tumor, located intradurally on the right, extended from the superior portion of C3 vertebra into the posterior fossa; it was quite calcific and incredibly fibrous and markedly displaced the spinal cord from right to left (Figure 3). A total removal of the tumor

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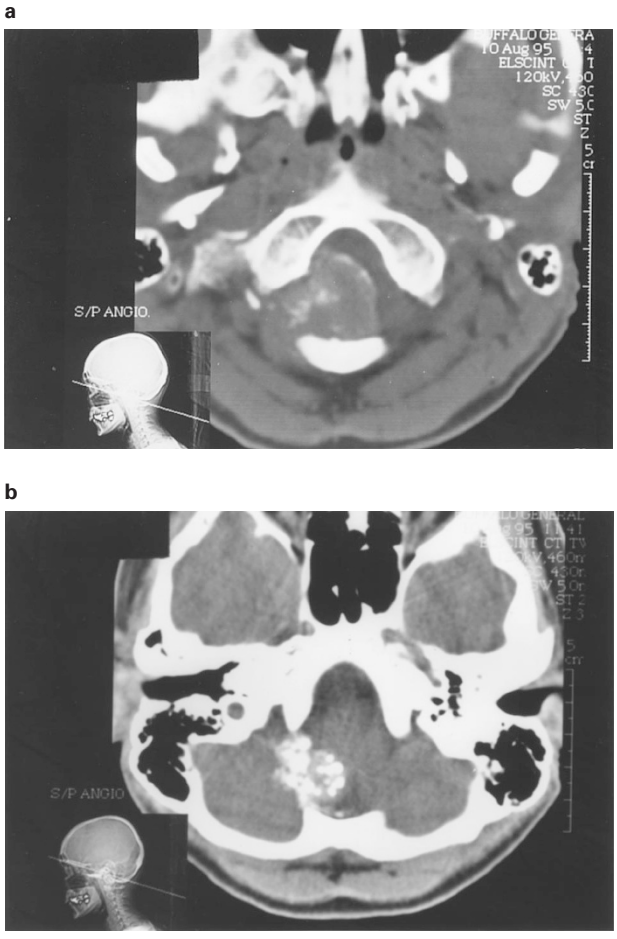

Figure 1 (**A**) CT scan at foramen magnum with enhancement: Large calcified tumor occupying greater part of foramen, primarily right side. (**B**) CT scan above foramen magnum: primarily calcified portion of tumor extending into right posterior fossa

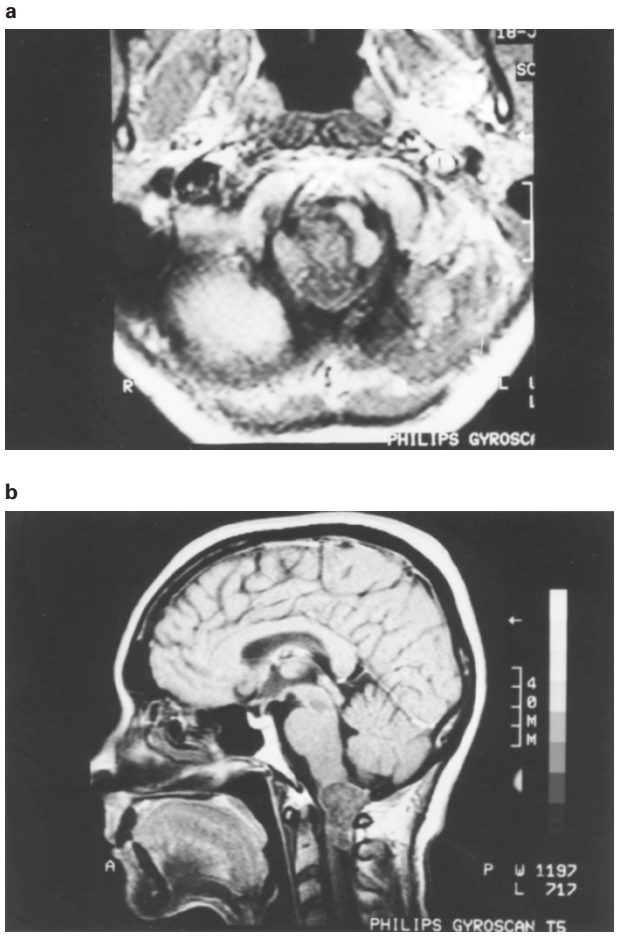

Figure 2 (**A**) MRI T_1 weighted: Axial view reveals tumor filling right side of foramen and markedly compressing and deforming brainstem to the left. (**B**) MRI T_1 sagittal view: Extension of tumor from body of C2 into posterior fossa

was accomplished. The pathology confirmed the tumor to be a meningioma.

Her postoperative course was uneventful and the majority of her RLS had been alleviated. There was no weakness in either extremity, however, her reflexes remained brisk in the lower extremities. Two years after surgery she was referred to a Sleep Disorder Clinic because of continued insomnia. She had minimal symptoms and was on small doses of Pergolide mesylate, 0.25 mg at 20.00 h and hs and Clonazepam 0.5 mg hs.

Discussion

Lesions at the craniocervical junction (foramen magnum) are divided into the intradural, the extramedullary and the intramedullary compartments.[1] Intradural lesions are more frequent and include meningiomas and schwannomas. Foramen magnum meningiomas, usually located anteriorly and lateral to the medulla and spinal cord, are known for their atypical presentation with a variety of confusing symptoms, sometimes mimicking MS. The meningioma reported here exemplifies this unusual presentation in which an extensive, large tumor in a critical location astonishingly produces only minor neurological symptoms.

RLS is a fairly common condition afflicting 1% to 10% of the population and is equally distributed between men and women, but more commonly in older subjects.[2] Although its onset is at any age, it can occur in infancy and early childhood.[3] RLS is the fourth leading cause of insomnia and is present in 11% to 27% of pregnancies, particularly during the second half of gestation.[4]

The main symptoms of RLS are unusual paresthesias, particularly in the calves, and motor restlessness. These symptoms vary and frequently exacerbate with rest or relaxation and are worse in the evening and early night.[2,5] Associated features include sleep

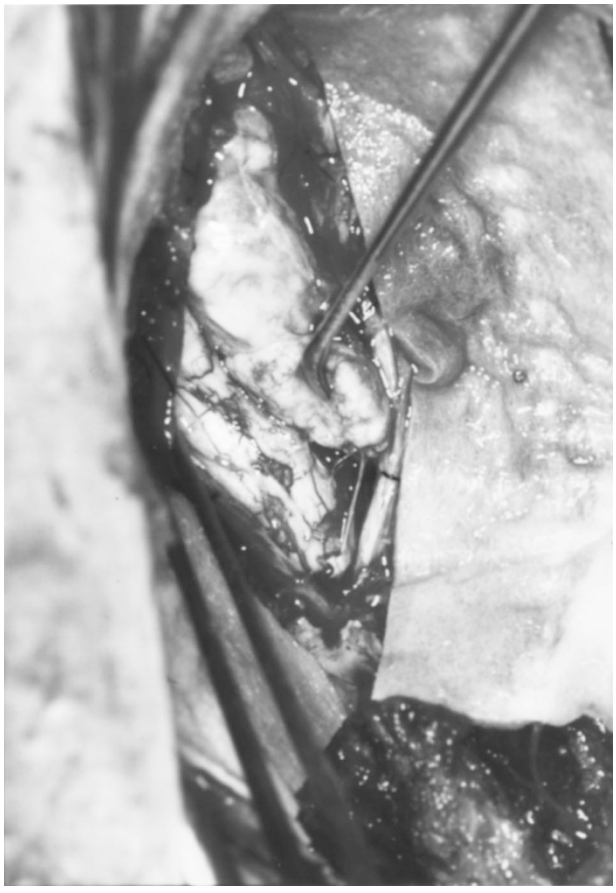

Figure 3 Operative view exposes greater part of meningioma below foramen magnum and shows displacement and distortion of cervical cord.

disturbance due to periodic limb movements in sleep (PLMS); dyskinesias, and a family history suggesting autosomal dominant inheritance.[6]

RLS is associated with a variety of medical conditions, neurological disorders, and vascular problems and insufficiency.[5,7,8] Among the more frequent conditions are anemias, blood dyscrasias, uremia, myelopathies and neuropathies.[4,7] RLS can be exacerbated by caffeine, alcohol, lithium and neuroleptics.[3,9] The neurologic examination in patients with idiopathic RLS is usually normal. EMG, and other electrophysiological studies, electron microscopy and MRI studies all fail to demonstrate any abnormalities.[10,11] Polysomnography supports the diagnosis and worsening of symptoms of RLS by documenting the sleep disturbances and PLMS.[9] There is supportive evidence that RLS is a CNS dysfunction with likely more than one mechanism involved. The most popular hypothesis has been that it is a disorder of the central sensory – motor integration with an imbalance between the serotogenic and DA pathways involving the descending DA system. The latter are inhibitory influences on pyramidal tract function.[12,13] Others suggest a disturbance of the inhibitory reticulospinal pathways.[3] The locus of involuntary motor activity is likely to be subcortical, possibly at the level of the peri-aqueductal gray matter of the midbrain/diencephalon region, or the pons.[3,9]

Another hypothesis is that the region of the motor activity is at the level of the spinal cord.[14] This is supported by several observations: (1) Dopamine containing neurons have been demonstrated in the spinal cord,[7,15,16] (2) RLS occurring after myelitis,[17] (3) by the effective treatment with DA drugs,[12] and (4) by the appearance of abnormal movements in spinal cord injured patients.[4,18] Finally, the association of RLS with pregnancy, venous insufficiency, peripheral embolism, and relief of symptoms with vasodilators point to a vascular mechanism in some patients.[4,8]

The treatment of idiopathic RLS include: *dopaminergic agents*; these improve all features of RLS including subjective discomfort and dyskinesias.[3,7,9,19] However, the side-effects of L-dopa include augmentation or rebound;[20] *Benzodiazepines*,[9] *narcotics* and more recently *gabapentin*.[3,21] Other useful agents mentioned are beta-blockers, serotonin precursors, tricyclic antidepressants, acetaminophen and red wine.[2,22] When RLS is associated with an underlying medical disorder or deficiency state, treatment of the underlying condition may alleviate the symptoms. Avoidance of smoking, alcohol, caffeine, and exacerbating medications are important. A moderate degree of exercise tends to suppress symptoms, whereas either sustained activity or bursts of heightened exercise may worsen the condition.[2]

Conclusion

RLS is a fairly common condition with a well-defined symptom complex and occurs in association with many medical disorders. Several hypotheses have been proposed to explain the pathophysiological mechanisms of RLS. There is supportive evidence of a CNS dysfunction, suggesting involvement of the DA pathways. In addition, there is documentation that RLS occurs with spinal disorders and a vascular mechanism may be responsible in some patients.

We report an additional cause for the etiology of RLS, namely, a meningioma of the foramen magnum. We correlate the location of the tumor to the symptoms of RLS and suggest two responsible factors: (1) Pressure on the pyramidal tract, especially on the anterior leg fibers, may trigger a spinal generator. (2) Severe compression and rotation of the brainstem, may affect the modulating center in the peri-aqueductal gray matter and thus involve the descending DA pathways. The distortion of the brainstem by the tumor may be the more likely of the two factors, but both mechanisms may be evoked.

The question of an unrelated co-existence of the tumor with manifestations of RLS could be raised. However, the symptoms of RLS reported by the patient did not represent spasticity of her lower limbs and her RLS subsided postoperatively. Her pyramidal

tract signs can easily be explained by the location of the meningioma since idiopathic RLS is known not to be associated with any neurological abnormalities.

Note added in proof

This case report was presented at the 43rd Annual Conference of the American Paraplegia Society in Las Vegas, September 2–4, 1997.

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