Intractable Localized Pruritus as the Sole Manifestation of Intramedullary Tumor in a Child

Case Report and Review of the Literature

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Importance: Persistent localized pruritus is a rare manifestation of central nervous system tumors. Delayed diagnosis can lead to devastating complications.

Observations: We report an otherwise healthy 19-month-old girl who presented with signs of localized intractable pruritus of 6 months’ duration on the left side of the neck, shoulder, and arm, resistant to systemic antihistamines and topical corticosteroids. Findings from skin biopsy, viral culture for varicella-zoster virus, and skin prick test to common food and animal allergens were nondiagnostic. Neurologic examination results were unremarkable. After several months of localized intractable pruritus, magnetic resonance imaging of the cervical spine with and without contrast was performed, which revealed an intramedullary spinal cord tumor extending from just above the foramen magnum to C6. The tumor was surgically resected and found to be a ganglioglioma. Within a week after the surgery her pruritus completely resolved.

Conclusions and Relevance: We recommend a detailed neurologic examination in any case of persistent localized pruritus, in the absence of primary dermatologic causes. Given the challenges of performing a reliable neurologic examination in children, neuroimaging might be considered in children with intractable localized pruritus of unknown etiology of the head and neck or upper extremity, even in the absence of focal neurologic deficits.

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REPORT OF A CASE

A 19-month-old previously healthy girl presented with localized intractable scratching of 6 months’ duration. This started as a 5-cm area on the left upper chest and gradually spread to her left shoulder, left side of the nape of the neck, and down to the left arm, left elbow, and left lateral forearm. As a result of scratching, she had developed excoriated papules localized to the aforementioned areas. Treatment with low-potency topical corticosteroids, cetirizine, and diphenhydramine had been unsuccessful. Her medical history was only notable for chronic ear infections, for which she had bilateral tympanostomy tubes placed. Her growth and development were normal. She had no other systemic symptoms. She had a family history of atopic dermatitis in both parents.

On physical examination, she had excoriated erythematous papules and postinflammatory hypopigmentation and hyperpigmentation on the left posterior shoulder extending medially on her back to the posterior aspect of the neck on the left side, as well as on the left anterior shoulder and volar aspect of the left forearm (C2 though C6 dermatomes, not crossing the midline) (Figure 1).

Findings from bacterial culture and viral culture for herpes simplex and varicella-zoster virus performed on the excoriated papules were negative. A punch biopsy specimen of one of the excoriated papules showed mild spongiosis, hyperkeratosis, and superficial keratinocyte necro-
sis consistent with excoriated dermatitis. Because there was a notable family history of food allergies, seasonal allergies, and atopic disease, a skin prick test to common food allergens and animals was performed, but results were negative. An effort to increase the potency of topical corticosteroids and maximize non-sedating as well as sedating antihistamines did not improve the pruritus.

Four months after her original presentation to dermatology clinic, she still had intractable pruritus and scratching localized to the left C2 through C6 dermatomes. At that time, the patient was referred for pediatric neurologic evaluation for possible neuropathic pruritus. Findings from neurologic examination including cognition, cranial nerves, cerebellar function, muscle tone and strength in all 4 extremities, gait, and sensation to light touch were within normal limits.

Given the difficulty and at times unreliability of an accurate neurologic examination in young children, imaging of the corresponding areas of the central nervous system (CNS) innervating the affected pruritic areas was performed, which included magnetic resonance imaging (MRI) of the cervical spine before and after intravenous administration of gadopentetate dimeglumine. This revealed fusiform expansion of the upper cervical spinal cord and lower brainstem from just above the foramen magnum to C6, consistent with an intramedullary spinal cord tumor (Figure 2). Subsequent MRI of the brain and thoracolumbar spine did not reveal further abnormalities. She underwent resection of the cervical spinal tumor. Findings from pathologic examination of the excised tumor were consistent with ganglioglioma. Her pruritus resolved completely after surgery. Her postoperative course was complicated by surgical wound infection and pseudomeningocele, for which she underwent surgical repair and needed an extended course of antibiotics and pseudomeningocele. For which she underwent surgical repair and needed an extended course of antibiotics. Postoperatively, she developed neurogenic bladder weakness in the left upper extremity. Her pruritus completely resolved after surgical resection of the tumor.

Neural pathways for itch include a “labeled-line” specific to itch with nonmediated, mechanoinsensitive C fibers, and finely medullated polymodal C fibers. The primary peripheral afferent neurons ascend to the dorsal horn of spinal cord, where they synapse with the second-order neurons. The axons of the second-order neurons cross the midline and eventually course through the spinal tract to thalamus. For the activation of several brain areas, including the primary somatosensory cortex (S1), accessory somatosensory cortex, and insula seems to be involved in itch perception. Thus, lesions anywhere in the peripheral nervous system or CNS that damage itch-transducing, conducting, or processing neurons appear to be capable of causing neuropathic itch.

COMMENT

Dermatologists tend to look for the cause of pruritus in the symptomatic area, but the causative lesion may be half a meter away in a nerve, nerve root, spinal cord, or the brain.4

Although rare, pruritus can be the presenting feature of intracranial tumors. In a 4-year follow-up of 77 patients with brain tumors, 13 patients (17%) complained of pruritus. The most characteristic finding was pruritus of the nostrils, which was observed in 6 patients, mainly caused by brain tumors extending to the base of the fourth ventricle.3 The mechanism of pruritus in brain tumors is thought to be damage to or activation of prefrontal cortex or premotor areas by the tumor. Coactivation of ipsilateral premotor areas might reflect the desire to scratch.1

Intramedullary neoplasms are another group of CNS tumors that can present with pruritus. The cell bodies of second order, itch neurons are in lamina I of the dorsal horn. Intramedullary neoplasms can cause irritation and excessive firing of these lamina I neurons causing intractable pruritus.4 In adults, cervical intramedullary ependymoma has been reported as the cause of unilateral upper extremity pruritus.5,6

In pediatric populations, we found 6 reported cases of persistent localized pruritus in the head and neck or upper extremities due to brainstem or spinal cord tumors.7-10 Of these children, 5 (83%) had café-au-lait macules, which were diagnosed as neurofibromatosis. Pruritus was unilateral in 4 cases (66%). Remarkably, in most cases (66%), findings from the initial neurologic examination were normal. In 5 cases, neurologic signs and symptoms developed later during their course, which included headache, nausea, drooling, neck pain, gait imbalances, cranial nerve signs, and paraparesis. Lack of neurologic findings in the initial examination reflects the unreliability and challenges of accurate neurologic examination in young children and highlights the importance of additional diagnostic modalities including imaging. Diagnosis was confirmed in all cases by means of MRI. Two cases had prior computerized tomographic scans, which failed to show the tumor.7
Treating neuropathic itch is difficult; antihistamines, corticosteroids, and most pain medications are largely ineffective. Current treatment recommendations include local or systemic administration of inhibitors of neuronal excitability (especially local anesthetics) and physical barriers to reduce scratching. In the reported cases of neuropathic pain due to CNS tumors in children, surgical excision of the tumor resulted in complete resolution of pruritus in 50% of cases, and in 1 case, pruritus improved but did not completely resolve. However, 2 cases had persistent neurologic deficits and pruritus after surgical resection of the tumor. This might reflect incomplete resection of the tumor, damage to the itch transmitting neurons during surgery, or long-term changes in the neuronal microenvironment causing persistent neuronal firing.

On the basis of our literature review, the most common intramedullary neoplasms associated with pruritus in the pediatric population include astrocytoma (66%), followed by glioma (34%). To our knowledge, this is the first reported case of ganglioglioma presenting as intractable scratching. Ganglioglioma is a very rare, benign, slow-growing CNS tumor that mainly affects children. It occurs predominantly in the supratentorial area and presents with chronic seizures. Spinal cord ganglioglioma constitutes 1% of all intramedullary tumors and can present with limb weakness. Malignant transformation of ganglioglioma has been reported. Thus, early complete surgical resection is the treatment of choice. The role of adjuvant chemotherapy or radiotherapy remains controversial. Because of the risk of tumor recurrence, close clinical follow-up after surgery is recommended.

In conclusion, as our case represents, localized pruritus may be a clue to the presence of a spinal cord tumor in a child without any focal neurologic findings. Considering the morbidity associated with undiagnosed CNS lesions, detailed neurologic examination and neuroimaging should be considered in children with persistent localized pruritus in the absence of any other causes for pruritus.

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REFERENCES

Top-Accessed Article: Combination Gel of 1% Amitriptyline and 0.5% Ketamine to Treat Refractory Erythromelalgia Pain

Sandroni P, Davis MP. Combination gel of 1% amitriptyline and 0.5% ketamine to treat refractory erythromelalgia pain: a new treatment option? Arch Dermatol. 2006;142(3):283-286.

Erythromelalgia is a rare skin disorder characterized by severe burning pain, warmth, and erythema that is aggravated by heat and exercise. It is considered to be a neurovascular disorder associated with a small nerve fiber neuropathy and altered voltage-gated sodium channels. In recent years, neuromodulating agents, such as gabapentin and pregabalin, as well as topical lidocaine, were found to be useful therapies. However, there are cases of erythromelalgia that remain resistant to these conventional therapies and cause extreme suffering. Sandroni and Davis report using a novel treatment featuring combination gel of 1% amitryptiline hydrochloride and 0.5% ketamine hydrochloride in lecithin pluronic organogel applied 4 to 5 times a day in 5 patients with intractable erythromelalgia. In 4 of these patients, a significant response was noted, with the improvement rate ranging from 50% to 95%.

The rationale for this combination can be explained by specific pathways that are targeted. Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist and a modulator of glutamatergic receptors. This is important since NMDA and glutamate are known to play a key role in neuropathic pain. Amitriptyline is a tricyclic antidepressant, which helps reduces pain in various disorders owing to its ability to block voltage-gated sodium ion channels. While topical application in limited body areas in this study did not lead to systemic absorption, the safety profile of this preparation has not been fully assessed. Nonetheless, this anecdotal report holds promise as a potential treatment for other forms of neuropathic pain and possibly neuropathic itch.

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