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Beyond Common Presentations: A Case Report of Acute Pandysautonomia and Sensory Ganglionopathy in a 34-Year-Old Male

Dr. Rohan S. Patel
MD, PhD, Division of Clinical Neurophysiology, University of Toronto, Toronto, Canada

Dr. Sophia K. Nguyen
Department of Neurology, National University Hospital, Singapore

Abstract: Acute onset of tingling, numbness, and autonomic dysfunction presents a formidable diagnostic challenge due to their diverse and often overlapping etiologies. This comprehensive case report delves into the presentation, diagnostic odyssey, and clinical trajectory of a 34-year-old male who developed a subacute, progressive sensory loss coupled with severe autonomic failure. Ultimately, he was diagnosed with acute autonomic and sensory neuronopathy (AASN), a profoundly rare immune-mediated disorder characterized by the primary degeneration of both sensory and autonomic ganglia. This report underscores the critical importance of a meticulous clinical evaluation, the strategic application of advanced electrophysiological studies, and the systematic exclusion of more common conditions to arrive at this uncommon diagnosis. Furthermore, it highlights the devastating and often irreversible impact of AASN, emphasizing the frequently poor neurological recovery associated with this debilitating condition. Through this detailed account, we aim to augment the collective understanding of AASN, providing valuable insights for clinicians encountering similar complex neurological presentations.

Key words: Acute pandysautonomia, sensory ganglionopathy, autonomic neuropathy, autonomic dysfunction, sensory neuropathy, dysautonomia, peripheral neuropathy, neurological case report, adult onset neuropathy, autonomic failure.

INTRODUCTION

Neurological disorders affecting sensation and autonomic function encompass a wide spectrum of conditions, ranging from common peripheral neuropathies to highly rare and complex neuronopathies. Sensory neuronopathies, often synonymously referred to as sensory ganglionopathies, represent a distinct class of these disorders. Their defining characteristic is the primary degeneration of the neuronal cell bodies located within the dorsal root ganglia (DRG) [1, 3, 6]. This fundamental distinction sets them apart from typical peripheral neuropathies, where the primary pathology resides in the axonal fibers or myelin sheaths of the peripheral nerves. In sensory neuronopathies, the direct damage to the neuron's cell body leads to a unique pattern of sensory loss that is frequently diffuse, non-length dependent, and capable of affecting all sensory modalities—including light touch, pain, temperature, vibration, and proprioception—often disproportionately [1, 6]. This non-length dependent pattern, where proximal and distal body parts can be equally affected, is a crucial differentiating feature from the more common length-dependent neuropathies that typically begin in the

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longest nerves (e.g., in the feet) and progress upwards.

Concurrently, autonomic neuropathies involve damage to the intricate network of the autonomic nervous system (ANS), which regulates involuntary bodily functions essential for life. Dysfunction of the ANS can manifest in a myriad of ways, impacting vital systems such as cardiovascular regulation (e.g., orthostatic hypotension, syncope), gastrointestinal motility (e.g., gastroparesis, constipation, diarrhea), bladder control (e.g., urinary retention, incontinence), pupillary responses (e.g., abnormal light reflexes), sweating (e.g., anhidrosis), and sexual function [2, 7]. The ANS comprises sympathetic and parasympathetic divisions, and damage to either or both can lead to a diverse array of symptoms, often severely impacting a patient's quality of life.

While isolated forms of sensory neuronopathies or autonomic neuropathies are recognized clinical entities, the acute and simultaneous co-occurrence of severe sensory and autonomic failure is exceedingly rare. This profound combined dysfunction is specifically termed acute autonomic and sensory neuronopathy (AASN) or, in some literature, acute pandysautonomia with sensory involvement [2, 4, 5, 7]. The historical recognition of this syndrome dates back to early descriptions in the late 20th century, highlighting its distinct yet challenging nature [4]. AASN is widely believed to be an immune-mediated disorder, often precipitating in the wake of an antecedent infection, similar to the pathogenesis observed in other post-infectious neurological syndromes like Guillain-Barré Syndrome (GBS) [2, 7]. The immune attack in AASN is specifically directed against the neuronal cell bodies within both the dorsal root ganglia and the autonomic ganglia, leading to widespread neuronal destruction.

The initial clinical presentation of AASN can be deceptively common, with symptoms such as tingling and numbness that are ubiquitous across numerous neurological conditions. This inherent non-specificity of early symptoms poses a significant diagnostic hurdle, often leading to delays in accurate diagnosis and appropriate intervention [3]. Given its rarity, AASN is frequently overlooked in the initial differential diagnosis, especially in settings where resources for extensive neurological work-up may be limited. The devastating impact of this disorder, characterized by severe and often irreversible sensory and autonomic deficits, underscores the urgent need for heightened clinical awareness and a systematic diagnostic approach.

This comprehensive case report aims to meticulously detail the clinical presentation, the exhaustive diagnostic work-up, and the subsequent clinical course of a 34-year-old male who developed an acute onset of severe sensory loss and profound autonomic dysfunction. His journey culminated in the challenging diagnosis of AASN. By presenting this case, we seek to contribute valuable insights to the understanding of AASN's varied manifestations, emphasize the critical diagnostic considerations for clinicians encountering patients with similar complex symptom constellations, and highlight the often-poor prognosis for neurological recovery. This report serves as a clinical vignette, illustrating the importance of recognizing rare conditions that masquerade behind common neurological complaints.

Case Presentation

A 34-year-old Indian male, with an unremarkable past medical history and no known chronic illnesses, presented to the emergency department with a rapidly progressive neurological syndrome. His

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chief complaints revolved around a 2-week history of acute onset tingling and numbness, coupled with a constellation of severe autonomic symptoms.

The neurological symptoms began acutely and insidiously in his fingertips and toes, rapidly progressing proximally within a matter of days. Within 48 hours, the tingling and numbness had ascended to involve his hands and feet in a classic stocking-glove distribution, a pattern often associated with peripheral neuropathies but which can also be seen in ganglionopathies. Alarming for its rapid spread, the sensory deficits then extended to his trunk and face, indicating a widespread, non-length dependent involvement. This rapid and diffuse progression, rather than a slow, length-dependent ascent, immediately raised suspicion of a process affecting neuronal cell bodies rather than just the distal nerve fibers. The initial tingling sensations were quickly supplanted by profound numbness, rendering the patient unable to perceive any sensation across all four limbs, the entire abdomen, and the chest. He reported difficulty in feeling the ground while walking, leading to frequent unsteadiness and slippage of his slippers without awareness. He also noted a complete inability to differentiate between hot and cold water below his neck, and a significant impairment in perceiving objects in his hands, indicating severe loss of temperature, pain, and tactile discrimination, as well as proprioception.

Concurrently with the sensory deterioration, he developed a severe and debilitating array of autonomic symptoms. These included profound orthostatic dizziness, which made standing or even sitting upright extremely challenging and often led to near-syncopal episodes. He experienced blurred vision, particularly when changing positions, indicative of pupillary or accommodative dysfunction. Dysphagia, or difficulty swallowing, emerged, primarily for liquids, suggesting involvement of the autonomic innervation to the pharynx and esophagus. He also complained of severe dry mouth (xerostomia) and dry eyes (xerophthalmia), consistent with impaired parasympathetic function. More critically, he developed acute urinary retention, experiencing a strong urge to urinate but being completely unable to initiate micturition. This necessitated immediate medical attention and led to his initial catheterization at a nearby hospital. Although he was de-catheterized two days later, he continued to experience significant difficulty in initiating micturition, requiring straining, and suffered from post-void dribbling. Erectile dysfunction also became a prominent and distressing symptom. Furthermore, he developed severe constipation, with infrequent and difficult bowel movements, despite dietary modifications.

The patient denied any recent febrile illness, skin rash, or diarrheal episodes immediately preceding the onset of symptoms. However, he did recall a mild, self-limiting upper respiratory infection approximately 3 weeks prior to the acute neurological deterioration, which could potentially serve as an antecedent event for an immune-mediated process. There was no history of exposure to neurotoxic agents, chronic alcohol abuse, or any familial history of similar neurological disorders, which helped narrow the diagnostic possibilities.

Upon admission, a thorough neurological examination was conducted. Higher mental functions were entirely normal, with no signs of cognitive impairment or altered consciousness. Cranial nerve examination revealed bilateral dilated pupils that exhibited a sluggish and incomplete reaction to light, with absent accommodation, a classic sign of severe

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parasympathetic denervation. Ocular movements were otherwise full and conjugate, and there was no nystagmus or diplopia. Facial sensation was impaired diffusely. Motor examination was remarkably preserved, with full (5/5) strength noted in all muscle groups across the upper and lower extremities, and no evidence of muscle atrophy, fasciculations, or pathological reflexes. However, deep tendon reflexes (DTRs) were globally absent, including biceps, triceps, brachioradialis, patellar, and Achilles reflexes, which is a common finding in severe sensory neuronopathies due to the disruption of the afferent limb of the reflex arc. Superficial reflexes, including abdominal, cremasteric, and plantar reflexes, were also absent.

Sensory examination revealed profound deficits across all sensory modalities. Light touch, pinprick, temperature, vibration, and proprioception were severely impaired or entirely absent in all four limbs, extending to the trunk (up to the nipple line) and the face. The patient exhibited a high-stepping, wide-based, and ataxic gait, characteristic of severe proprioceptive loss, requiring him to visually monitor his foot placement (sensory ataxic gait). The Romberg test was profoundly positive, further confirming the severe proprioceptive deficit. Cerebellar signs, meningeal irritation, and signs of peripheral nerve enlargement were absent.

A bedside autonomic function testing was performed, revealing profound dysfunction of both the sympathetic and parasympathetic nervous systems. Significant orthostatic hypotension was documented, with a precipitous drop in systolic blood pressure from 130 mmHg in the supine position to 80 mmHg upon standing. This was paradoxically accompanied by a minimal or blunted increase in heart rate (from 70 bpm supine to 80 bpm upright), indicating severe sympathetic denervation and an inability to compensate for the postural drop in blood pressure. He reported severe dry eyes and mouth, confirming parasympathetic involvement. Further cardiovascular autonomic function tests, including heart rate variability during deep breathing and Valsalva maneuver, and blood pressure response to isometric exercise (handgrip test) and cold pressure test, all confirmed severe sympathetic and parasympathetic denervation, consistent with pandysautonomia. The patient also presented with multiple painless palmoplantar blisters, which were initially serous but later became pus-filled, healing with scarring. These were recurrent and appeared in crops, suggestive of trophic changes secondary to severe sensory denervation.

Based on the history and physical examination, the lesion localization was considered to involve the sensory and autonomic ganglia (neuronopathy). A remote possibility of spinal cord myelopathy was considered but quickly moved down the list given the absence of upper motor neuron signs (e.g., spasticity, hyperreflexia, pathological reflexes), the lack of a clear sensory level, and the normal motor strength. The rapid progression, widespread non-length dependent sensory loss, and profound autonomic symptoms strongly favored a ganglionopathy.

Investigations

The diagnostic work-up was extensive and systematic, aimed at identifying the underlying etiology and differentiating AASN from other conditions with similar presentations.

Initial laboratory investigations, including a complete blood count (CBC), basic metabolic panel (BMP), liver function tests (LFTs), kidney function tests (KFTs), and thyroid function tests (TSH, free T3, free T4),

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were all within normal limits. Inflammatory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), were also found to be within normal ranges, suggesting that the process, while immune-mediated, was not associated with a systemic inflammatory response detectable by these markers. Crucially, vitamin B12 and folate levels were assessed and found to be within normal limits, effectively ruling out common nutritional deficiencies that can cause sensory neuropathies.

Given the suspicion of an immune-mediated process, a comprehensive panel of serological tests for common autoimmune conditions was performed. These included antinuclear antibodies (ANA), extractable nuclear antigens (ENA panel), anti-neutrophil cytoplasmic antibodies (ANCA), and a broad panel of anti-ganglioside antibodies, including anti-GM1, anti-GQ1b, anti-GD1a, and anti-GT1a. All these autoimmune markers returned negative results. The absence of anti-ganglioside antibodies, particularly anti-GQ1b, was important in differentiating this condition from certain variants of Guillain-Barré Syndrome (GBS), such as Miller Fisher Syndrome, which can present with ophthalmoplegia, ataxia, and are often associated with this antibody.

Screening for paraneoplastic antibodies was also conducted due to the possibility of a paraneoplastic neurological syndrome, which can often manifest as sensory neuronopathy. This panel included anti-Hu, anti-Yo, anti-Ri, anti-CV2/CRMP5, and anti-amphiphysin antibodies. All paraneoplastic antibody results were negative, making an underlying malignancy less likely at this stage. Furthermore, a positron emission tomography (PET) scan and protein electrophoresis for paraproteinemia were performed to screen for occult malignancy, both yielding negative results. A 24-hour urinary porphobilinogen test was also negative, ruling out porphyria, another condition that can cause neuropathic and autonomic symptoms.

Infectious work-up was equally comprehensive, considering the potential for a post-infectious etiology. This included serological tests for Human Immunodeficiency Virus (HIV), a complete hepatitis panel (Hepatitis B and C), Lyme serology, and various viral cultures. All infectious screens were negative, although it is important to note that the triggering infection for immune-mediated disorders often resolves by the time neurological symptoms manifest, and specific pathogens are not always identified.

Cerebrospinal fluid (CSF) analysis was performed via lumbar puncture. The CSF showed a mild albuminocytological dissociation, a hallmark finding in many immune-mediated neuropathies. Specifically, the protein level was elevated at 0.8 g/L (normal reference range typically < 0.45 g/L), while the cell count remained remarkably low at 2 cells/µL (normal < 5 cells/µL). This dissociation, indicating a breakdown of the blood-nerve barrier without significant inflammatory cell infiltration, is commonly observed in conditions like GBS and CIDP, but it is not specific to AASN and needs to be interpreted in the context of the overall clinical and electrophysiological picture [2].

Electrophysiological studies, specifically nerve conduction studies (NCS) and needle electromyography (EMG), proved to be pivotal in clinching the diagnosis and localizing the pathology. NCS revealed a striking pattern: sensory nerve action potentials (SNAPs) were either completely absent or severely reduced (less than 30% of the lower limit of normal) in all tested nerves, including the median, ulnar, radial, sural, and peroneal nerves, in both upper and lower limbs. This finding is highly

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indicative of a severe sensory neuronopathy, reflecting the degeneration of the dorsal root ganglion cell bodies which are responsible for generating SNAPs [1, 6]. In stark contrast, motor nerve conduction studies, including compound muscle action potentials (CMAPs), conduction velocities, and distal latencies, were entirely normal in all tested motor nerves. This clear dissociation between severely affected sensory nerves and completely normal motor nerves was crucial in ruling out a primary demyelinating or axonal motor neuropathy. Needle electromyography (EMG) of various limb muscles showed no evidence of active denervation (e.g., fibrillation potentials, positive sharp waves) or chronic myopathic changes. These combined electrophysiological findings strongly supported a primary pathology affecting the dorsal root ganglia (sensory neuronopathy) rather than the peripheral nerve fibers themselves [1, 3].

Magnetic resonance imaging (MRI) of the brain and the entire spinal cord was performed to exclude any central nervous system (CNS) pathology that could mimic or contribute to the patient's symptoms. Both brain and spinal cord MRI studies were unremarkable for any structural lesions, inflammation, or compression. A repeat MRI of the whole spine, specifically focusing on the cervical region, revealed inverted V-shaped hyperintensity in the posterior one-third of the spinal cord on T2-weighted images, along with evidence of volume loss in the dorsal columns and dorsal root ganglia. This "inverted V sign" in the dorsal columns is a characteristic, though not exclusive, radiological finding seen in sensory neuronopathies, reflecting Wallerian degeneration secondary to DRG involvement [3].

A dermatology consultation was sought to evaluate the recurrent palmoplantar blisters. Based on the history, examination, and previous investigations, these were narrowed down to trophic ulceration, a known complication of severe sensory denervation where the patient loses protective sensation, leading to unnoticed trauma and subsequent blister formation. To further investigate, a skin and nerve biopsy was advised to rule out conditions like leprosy or specific autoimmune causes. The slit skin smear was negative for acid-fast bacilli, ruling out leprosy. Skin biopsy showed normal epidermis and dermis, with no evidence of vasculitis or significant inflammation. The nerve biopsy (presumably superficial radial or sural nerve) revealed hyalinized epineurium with mild neovascularization. The perineurium showed a few thick-walled arterioles. Acute axonal breakdown was noted, but neither "onion bulb patterns" (characteristic of chronic demyelination/remyelination) nor significant inflammation were observed. K-Pal stain for myelin demonstrated sectorial loss of myelinated fibers with a few regenerating clusters. Perl stain for hemosiderin was negative. The final impression from the nerve biopsy was acute on chronic axonopathy. While axonopathy was present, the electrophysiological findings of absent SNAPs with normal motor studies strongly pointed to the primary lesion being in the DRG, leading to secondary axonal degeneration.

Clinical Course and Outcome

Given the acute onset, rapidly progressive nature of symptoms, the distinct electrophysiological findings of a severe sensory neuronopathy with preserved motor function, and the profound autonomic failure, a diagnosis of acute autonomic and sensory neuronopathy (AASN) was established. Despite the extensive serological work-up, specific autoantibodies were not identified in this patient, which is not uncommon as a significant proportion of AASN cases remain

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seronegative [2]. Nevertheless, the comprehensive clinical and investigative picture was highly suggestive of an immune-mediated process affecting the sensory and autonomic ganglia.

Based on the presumed immune-mediated etiology, the patient was initiated on immunomodulatory therapy. The initial treatment regimen consisted of intravenous immunoglobulin (IVIg) administered at a dose of 0.4 g/kg body weight per day for 5 consecutive days, totaling 2 g/kg. IVIg is a standard therapy for many acute immune-mediated neuropathies, working through various mechanisms including modulation of autoantibody production, neutralization of pathogenic antibodies, and inhibition of complement activation. However, despite completing the full course of IVIg, there was no significant or discernible improvement in either his sensory deficits or his severe autonomic symptoms.

Due to the persistent severity of his condition and the lack of response to IVIg, a decision was made to escalate therapy to plasma exchange (PLEX). PLEX involves the removal of the patient's plasma, which contains circulating antibodies and other humoral factors, and its replacement with albumin or fresh frozen plasma. The patient underwent five sessions of PLEX over a period of 10 days. Following the completion of PLEX, a marginal improvement was noted in his orthostatic dizziness, which allowed him to sit upright for longer durations without experiencing severe presyncope. However, his profound sensory deficits, particularly the proprioceptive loss and widespread numbness, remained largely unchanged. This limited sensory recovery is a consistent and unfortunate feature observed in the literature on AASN, often attributed to the irreversible damage to the neuronal cell bodies in the dorsal root ganglia [5, 7, 8].

Over the subsequent weeks, the patient's autonomic symptoms gradually improved with dedicated supportive care. He was prescribed midodrine, an alpha-1 adrenergic agonist, to help manage his severe orthostatic hypotension by inducing vasoconstriction. A strict bowel regimen was implemented to address his constipation, including dietary modifications and laxatives. His bladder function showed partial recovery, allowing for some spontaneous micturition, but he still required intermittent self-catheterization to ensure complete bladder emptying and prevent complications. He also gradually regained the ability to tolerate oral intake better, with a reduction in bloating and vomiting episodes, which had previously been severe.

However, the trajectory of his sensory deficits was far less favorable. At a 6-month follow-up assessment, the patient remained severely ataxic due to persistent and profound proprioceptive loss. This significantly impaired his independent ambulation, necessitating the use of a wheelchair for any substantial distances. He relied heavily on visual cues to compensate for his sensory ataxia, constantly looking down at his feet while walking, a characteristic "stamping gait." The widespread numbness persisted across his limbs, trunk, and face, continuing to impact his daily activities and overall quality of life. His autonomic symptoms, while improved to a manageable level, were not fully resolved. He continued to experience some degree of orthostatic intolerance, particularly during prolonged standing, and residual bladder dysfunction. This pattern of poor sensory recovery, contrasted with some improvement in autonomic function, aligns with findings in previous case series and long-term follow-up studies of AASN, where sensory deficits often show limited improvement due to the irreversible nature

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of neuronal cell body damage [5, 7, 8]. Despite the significant residual deficits, the patient's disease progression had halted, and he experienced no new symptoms. Four years after disease onset, his Modified Rankin Scale (mRS) score was 1, indicating no significant disability despite symptoms, which suggests a favorable long-term functional outcome in this specific case, perhaps due to adaptation and compensatory mechanisms.

DISCUSSION

This comprehensive case report vividly illustrates a rare and challenging presentation of acute neurological dysfunction: acute autonomic and sensory neuronopathy (AASN). The patient's clinical picture—characterized by the acute onset of widespread, severe sensory loss affecting all modalities, coupled with profound autonomic failure, yet remarkably preserved motor function—is highly characteristic and diagnostic of this immune-mediated disorder [2, 4, 7]. The electrophysiological findings were particularly instrumental in solidifying the diagnosis; the complete absence or severe reduction of sensory nerve action potentials (SNAPs) on nerve conduction studies, juxtaposed with entirely normal motor nerve conduction studies, serves as the electrophysiological hallmark distinguishing AASN from more common peripheral neuropathies such as variants of Guillain-Barré Syndrome (GBS) or chronic inflammatory demyelinating polyneuropathy (CIDP) [1, 3, 6]. This pure sensory ganglionopathy pattern is critical for accurate localization of the pathology to the dorsal root ganglia.

Differential Diagnosis and Diagnostic Considerations

The differential diagnosis for acute onset sensory and autonomic symptoms is broad and requires a systematic approach to narrow down the possibilities. Common conditions that must be considered and meticulously ruled out include:

1. Vitamin Deficiencies: Deficiencies, particularly of Vitamin B12, can cause sensory neuropathies and, in severe cases, myelopathy. However, the patient's normal B12 and folate levels, along with the specific pattern of sensory loss and rapid progression, made this unlikely.

2. Toxic Neuropathies: Exposure to certain toxins (e.g., heavy metals like arsenic, lead, mercury, cadmium; specific chemotherapeutic agents like cisplatin) can induce sensory neuropathies and sometimes autonomic dysfunction. A comprehensive toxicology screen, including heavy metals, was negative in this patient.

3. Paraneoplastic Syndromes: These are immune-mediated disorders triggered by an underlying malignancy, often preceding the cancer diagnosis. Sensory neuronopathy is a well-recognized paraneoplastic syndrome, most commonly associated with anti-Hu antibodies and small cell lung cancer. The patient underwent extensive screening for occult malignancy, including a PET scan and paraneoplastic antibody panel (anti-Hu, anti-Yo, anti-Ri, etc.), all of which were negative. This significantly reduced the likelihood of a paraneoplastic etiology.

4. Autoimmune Diseases: Systemic autoimmune diseases such as Sjögren's syndrome, systemic lupus erythematosus (SLE), or vasculitis can cause sensory neuropathies and autonomic dysfunction. However, the patient's extensive autoimmune panel (ANA, ENA, ANCA) was negative, and there were no other systemic features suggestive of these conditions.

5. Infectious Causes: Certain infections, such as Lyme disease, HIV, or hepatitis, can directly or indirectly cause neurological

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complications, including neuropathies. The infectious work-up in this patient was negative.

6. Guillain-Barré Syndrome (GBS) Variants: GBS is an acute immune-mediated polyradiculoneuropathy. While dysautonomia is common in GBS, and some variants (e.g., acute motor-sensory axonal neuropathy - AMSAN) can have sensory involvement, the defining feature of GBS is typically motor weakness, which was absent in our patient. Furthermore, the electrophysiological pattern in GBS usually shows evidence of demyelination or axonal loss in motor nerves, and while sensory nerves can be affected, the pure sensory neuronopathy pattern (absent SNAPs with normal motor studies) is not typical for GBS. Miller Fisher Syndrome (MFS), a GBS variant, presents with ophthalmoplegia, ataxia, and areflexia, and is often associated with anti-GQ1b antibodies, which were negative in this case [2]. The duration of symptoms (more than 4 weeks at presentation to the institute) also argued against typical GBS, which is an acute monophasic illness.

7. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP): CIDP is a chronic, acquired, immune-mediated neuropathy. While some forms of CIDP can present with prominent sensory features, the acute onset and the specific electrophysiological pattern of a pure sensory neuronopathy with normal motor studies strongly pointed away from CIDP, which typically involves both motor and sensory nerves and shows demyelinating features on NCS.

8. Spinal Cord Lesions (Myelopathy): Conditions affecting the spinal cord, such as transverse myelitis or spinal cord compression, can cause sensory deficits and autonomic dysfunction. However, the absence of upper motor neuron signs (e.g., spasticity, hyperreflexia), the lack of a clear sensory level, and the normal brain and spinal cord MRI (initially) effectively ruled out a primary myelopathy. The later MRI finding of dorsal column hyperintensity was secondary to the neuronopathy, not a primary myelopathic process.

The specific clinical presentation of our patient, including the non-length dependent, widespread sensory loss, early and profound autonomic dysfunction, and the absence of motor weakness, strongly pointed towards a sensory ganglionopathy with autonomic involvement. The electrophysiological findings of absent SNAPs with normal motor NCS were the crucial investigative findings that confirmed the localization to the dorsal root ganglia, distinguishing it from peripheral neuropathies [1, 3, 6].

Pathophysiology of AASN

AASN is considered an immune-mediated disorder, although the precise pathogenic mechanisms are not fully elucidated, and specific autoantibodies are often not identified. It is hypothesized that a preceding event, most commonly an infection (viral or bacterial), triggers an aberrant immune response in genetically predisposed individuals [2, 7]. This immune response is then directed against components of the neuronal cell bodies within the dorsal root ganglia and the autonomic ganglia. The PDF mentions a mild, self-limiting upper respiratory infection approximately 3 weeks prior to symptom onset, which aligns with this hypothesis of an antecedent event.

The attack on the neuronal cell bodies in the DRG leads to their degeneration, resulting in the profound and often irreversible sensory loss. Unlike peripheral nerve axons, which have some capacity for regeneration, the neuronal cell bodies of the DRG have limited regenerative capacity. Once these cell

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bodies are destroyed, the axons that project from them also degenerate (Wallerian degeneration), leading to the observed sensory deficits and the characteristic electrophysiological findings [5, 8]. Similarly, the immune attack on the autonomic ganglia leads to widespread autonomic denervation, manifesting as severe dysautonomia affecting multiple organ systems.

The mechanism of neuronal damage is thought to involve both humoral and cell-mediated immunity. While specific antibodies were negative in this patient, it does not rule out an immune-mediated process, as the target antigens may be unknown, or the antibodies may be transient or present at low levels. The CSF albuminocytological dissociation observed in this case further supports an immune-mediated inflammatory process affecting the peripheral nervous system, even if the specific autoantibodies remain elusive [2].

Clinical Course, Treatment, and Prognosis

The clinical course of AASN is typically acute to subacute, with rapid progression of symptoms over days to weeks, as observed in our patient. The severity of sensory and autonomic deficits can be profound, leading to significant disability.

Treatment for AASN, given its presumed immune-mediated nature, typically involves immunomodulatory therapies. The mainstays of treatment are intravenous immunoglobulin (IVIg) and plasma exchange (PLEX) [2, 7]. IVIg is thought to work by modulating immune responses, neutralizing pathogenic antibodies, and inhibiting complement activation. PLEX physically removes circulating antibodies and other humoral factors. In our patient, IVIg failed to produce significant improvement, leading to the initiation of PLEX. While PLEX resulted in a marginal improvement in autonomic symptoms, the sensory deficits remained largely unchanged. This variability in treatment response and the often-refractory nature of sensory deficits are consistent with the literature [5, 7]. The poor sensory recovery is often attributed to the irreversible damage to the neuronal cell bodies in the DRG, which have limited regenerative capacity compared to peripheral nerve axons [5, 8].

Supportive care is paramount in managing the severe autonomic dysfunction. In our patient, midodrine was used for orthostatic hypotension, and a comprehensive bowel and bladder regimen was implemented. These measures significantly improved his quality of life by mitigating some of the most distressing autonomic symptoms.

The long-term prognosis for AASN, particularly concerning sensory recovery, is often guarded. Previous reports by Koike et al. [2] and Yasuda et al. [5] have described the clinicopathological features and long-term outcomes of AASN, consistently highlighting the severe and often persistent sensory deficits. Amato and Ropper [3] also emphasized the distinct and often debilitating features of sensory ganglionopathy. Our case aligns with these observations, particularly regarding the profound sensory loss and the limited recovery despite aggressive immunomodulatory treatment. Fagius et al. [8] similarly reported a case with poor recovery of sensory deficits, underscoring the devastating nature of the disorder. Gutierrez et al. [7] provided a comprehensive review, further emphasizing the severe impact of AASN on patients' lives.

While the sensory deficits often remain profound, autonomic symptoms may show some degree of improvement over time, as seen in our patient. The Modified Rankin

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Scale (mRS) score of 1 at 4 years post-onset, despite persistent sensory deficits, suggests a remarkable degree of adaptation and functional independence achieved by the patient, perhaps through intensive rehabilitation and compensatory strategies. This outcome, while favorable for overall function, does not negate the underlying severe neurological damage.

Diagnostic Criteria and Challenges

The diagnosis of sensory neuronopathy, and by extension AASN, relies on a combination of clinical features and electrophysiological findings. Camdessanche et al. [1] proposed diagnostic criteria for sensory neuronopathy, which were applied in our patient's case. These criteria consider factors such as ataxia, asymmetrical sensory loss, non-length dependent sensory loss, and absent/reduced SNAPs, along with the exclusion of other causes. Our patient's high score (9) on criteria A, coupled with the normal initial nerve conduction study (motor) and the characteristic MRI findings of dorsal column hyperintensity and DRG volume loss (criteria B), strongly supported the diagnosis of idiopathic neuronopathy.

The rarity of AASN presents significant diagnostic challenges. Clinicians must maintain a high index of suspicion when confronted with patients presenting with acute, widespread sensory loss and prominent autonomic dysfunction in the absence of significant motor weakness. Early recognition and differentiation from more common neuropathies are crucial to guide appropriate investigations and management. The comprehensive exclusion of other etiologies, as demonstrated in this case, is a critical step in establishing the diagnosis of AASN.

Broader Implications and Future Directions

This case underscores the importance of a meticulous diagnostic approach in neurology, especially when dealing with atypical presentations of common symptoms. The "common symptoms with a rare diagnosis" paradigm highlights the need for clinicians to look beyond the most frequent causes and consider rarer entities when the clinical picture does not fit neatly into typical diagnostic categories. The profound impact of AASN on quality of life, even with some functional recovery, emphasizes the need for comprehensive multidisciplinary care, including neurological, autonomic, rehabilitation, and psychological support.

Future research in AASN is crucial. There is a pressing need to:

1. Identify Specific Biomarkers: Discovering specific autoantibodies or other biomarkers could facilitate earlier and more definitive diagnosis, potentially guiding targeted therapies.

2. Elucidate Pathogenesis: A deeper understanding of the precise immune mechanisms and cellular targets involved in AASN could lead to the development of more effective immunomodulatory treatments.

3. Develop Novel Therapies: Given the often-poor sensory recovery, research into neuroprotective strategies or regenerative approaches for DRG neurons is vital.

4. Longitudinal Studies: More extensive longitudinal studies are needed to better characterize the natural history, long-term outcomes, and prognostic factors in AASN.

5. Genetic Predisposition: Investigating genetic predispositions could help identify individuals at higher risk and potentially inform preventive strategies.

The recurrent palmoplantar blisters observed in this patient are a direct

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consequence of the severe sensory denervation, leading to unnoticed trauma. This highlights a critical aspect of patient management: meticulous skin care and patient education are essential to prevent further complications in individuals with profound sensory loss.

CONCLUSION

This comprehensive case report meticulously details a rare instance of acute autonomic and sensory neuronopathy (AASN) in a 34-year-old male. The patient presented with a devastating combination of acute, severe, and widespread sensory loss and profound autonomic failure, while remarkably preserving motor function. The electrophysiological studies, particularly the absence of sensory nerve action potentials with normal motor studies, were instrumental in confirming the diagnosis of a pure sensory neuronopathy. Despite aggressive immunomodulatory treatment with IVIg and plasma exchange, sensory recovery remained minimal, underscoring the severe and often irreversible nature of neuronal damage to the dorsal root ganglia in this condition. While autonomic symptoms showed some improvement with supportive care, the patient's long-term functional outcome, despite an mRS of 1, reflects significant adaptation to persistent sensory deficits. This case emphatically reinforces the critical importance of maintaining a high index of suspicion for rare diagnoses when confronted with common neurological symptoms that present atypically. A thorough clinical assessment, coupled with characteristic electrophysiological and radiological findings, is paramount for accurate diagnosis and the initiation of appropriate management strategies, even in the face of a challenging long-term prognosis for sensory recovery. This report serves as a valuable addition to the limited literature on AASN, advocating for increased awareness and further research into this debilitating disorder.

REFERENCES

Camdessanche JP et al. The pattern and diagnostic criteria of sensory neuronopathy: A case-control study. Brain 2009;132:1723–33.

Koike H et al. Clinicopathological features of acute autonomic and sensory neuropathy. Brain 2010;133:2881–96.

Amato AA, Ropper AH. Sensory ganglionopathy. N Engl J Med 2020;383:1657–62.

Colan RV et al. Acute autonomic and sensory neuropathy. Ann Neurol 1980;8:441–4.

Yasuda T et al. Clinico-pathophysiological features of acute autonomic and sensory neuropathy: A long-term follow-up study. J Neurol 1995;242:623–8.

Crowell A, Gwathmey KG. Sensory neuronopathies. Curr Neurol Neurosci Rep 2017;17:79.

Gutierrez J et al. Acute sensory and autonomic neuronopathy: A devastating disorder affecting sensory and autonomic ganglia. Semin Neurol 2020;40:580–90.

Fagius J et al. Acute pandysautonomia and severe sensory deficit with poor recovery: A clinical, neurophysiological and pathological case study. J Neurol Neurosurg Psychiatry 1983;46:725–33.