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BRIEF COMMUNICATION

Tonic pupils: an unusual autonomic involvement in chronic inflammatory demyelinating polyneuropathy (CIDP)

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Abstract

Background Chronic inflammatory demyelinating polyneuropathy (CIDP) is a neuropathy which affects mainly large myelinated axons and has a typically mild autonomic dysfunction mainly from postganglionic nerve fiber involvement.

Case report We report here an acute onset CIDP initially diagnosed as Guillain-Barré syndrome (GBS), unresponsive to treatment with intravenous immunoglobulin (IVIg), which later responded to plasmapheresis and corticoids. The patient had a markedly distal demyelination, prominent cranial nerve involvement and, interestingly, bilateral fixed dilated pupils. Despite complete clinical recovery, this neurological sign remained.

Conclusions Tonic pupils have previously been described in different neurologic conditions, including GBS, but not yet in acute onset CIDP or in variants with predominantly distal demyelination. It differs from the classical Adie's pupil because it lacks the light-near dissociation. This case report expands the range of possible autonomic signs in acute onset CIDP, which could help physicians establish optimal treatment strategies earlier on.

Keywords Chronic inflammatory demyelinating polyneuropathy · Adie's pupil · Tonic pupil · Autonomic dysfunction · Guillain-Barré syndrome · CIDP

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a clinically heterogenous neuropathy which develops over more than 8 weeks and has inflammatory-mediated demyelination as pathological hallmark [1]. This disease involves mainly large myelinated axons while the autonomic dysfunction is usually mild and predominantly sudomotor, resulting primarily from lesions at the distal postganglionic nerve fibers [2]. We present here a case of acute onset CIDP, with a predominantly distal demyelination and cranial nerve involvement, which included bilateral dilated unreactive pupils due to parasympathetic denervation of the pupil sphincter muscles.

A 23-year-old female house cleaner had watery diarrhea for about 3 days. One week later, she noted numbness in feet and progressive weakness in lower limbs, which in the following 5 days evolved to gait unsteadiness. She was hospitalized and initially diagnosed with Guillain-Barré syndrome (GBS). Intravenous immunoglobulin (IVIg) was administered. Even though no significant improvement was observed, she was discharged from hospital, as symptoms were mild at this point.

In the following weeks, however, the weakness progressed and she developed diplopia and hoarseness, being readmitted to the hospital 5 weeks after symptoms onset. Her examination revealed flaccid tetraparesis and muscle strength was Medical Research Council (MRC) scale grade 2 in proximal muscles and grade 1 in distal muscles from upper and lower limbs. Tendon reflexes were absent. There was bilateral facial palsy, bulbar weakness, and bilateral ophthalmoparesis. Pupils were dilated bilaterally and unresponsive to direct and indirect light stimuli (Fig. 1). Vision was blurry but visual acuity was grossly intact. Other symptoms or signs of dysautonomia were absent. There was distal hypoesthesia to all sensory modalities in the four limbs.

Cerebrospinal fluid (CSF) analysis showed albuminocytologic dissociation (303 mg/dL protein). Routine laboratory tests were normal, including complete blood count, routine blood biochemistry, glucose, copper and vitamins B1 and B12 levels, serum protein electrophoresis, rheumatologic antibodies, paraneoplastic

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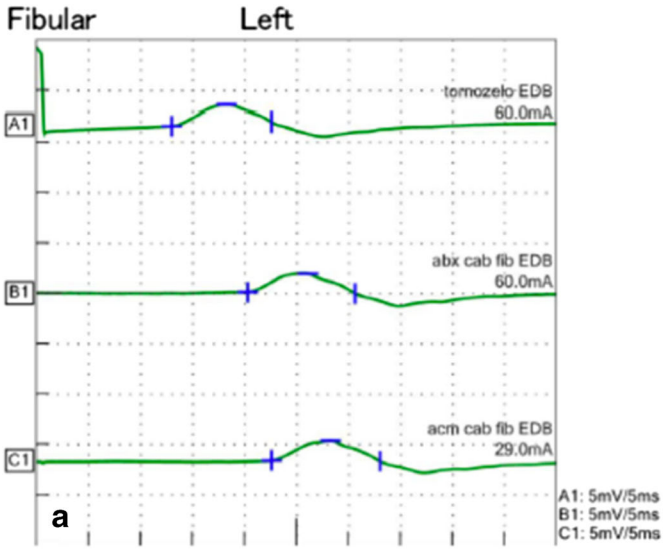

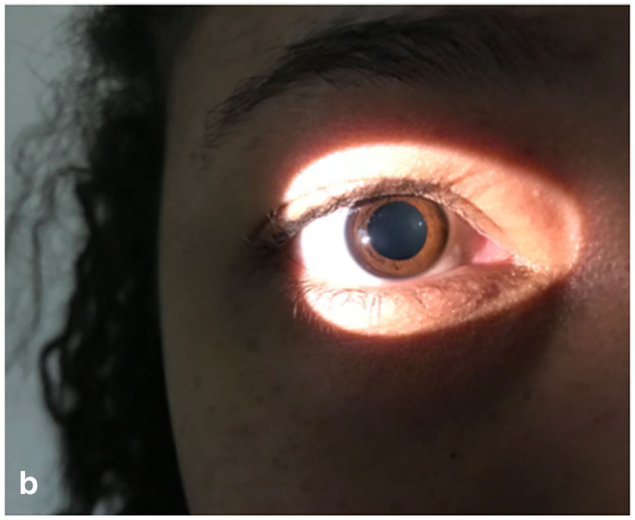

Fig. 1 In (A), a representative waveform from the fibular nerve motor study to the extensor digitorum brevis muscle with severely prolonged distal latencies: 13.1 ms and 2.1 mV amplitude. Conduction velocity was not significantly affected in this nerve. Sweep speed was 5 ms/division and 5 mV/division. In (B), a 7-mm unreactive pupil

antibodies, human immunodeficiency virus types 1 and 2, human T lymphotropic virus types 1 and 2, and viral hepatitis serologies.

A first nerve conduction and electromyography (EMG) study, performed within 2 weeks of symptoms onset revealed markedly prolonged distal motor latencies in the lower limbs while motor nerve velocities were slightly reduced (Fig. 1; Table 1). Sensory nerve conduction study was normal and needle EMG had motor unit action potentials with reduced recruitment and normal morphology. Another study performed about 7 weeks of the initial symptoms revealed diffusely absent sensory potentials, absent sympathetic skin responses, absent motor potentials in lower limbs, and prolonged distal motor latencies in the median and ulnar nerves with mildly reduced conduction velocities. Brain MRI was normal. Spine and nerve root MRI showed no significant hypertrophy.

She received a second cycle of 0.4 g/Kg IVIg within 6 weeks of symptoms onset. But weakness continued to progress, along with frequent episodes of sinus tachycardia, so that 7 weeks later a third pulse of IVIg was repeated, also with no significant response. Then, after 14 weeks of disease onset, she received intravenous corticoids followed by a plasmapheresis cycle, which resulted in a gradual improvement in the following weeks. Because of the response to treatment and clinical improvement, nerve biopsy was not performed. An immune process was considered the main underlying disease mechanism. She was discharged from hospital for ambulatory follow-up in a wheelchair and treated with regular pulses of intravenous corticoids, succeeded by oral corticoids and azathioprine. There was almost complete recovery of muscle strength and sensory function within 6 months of symptoms onset but the pupils remained dilated and unreactive to light. The pilocarpine (0.125% eyedrops) test performed in one of the follow-up outpatient visits caused temporary constriction of the tonic pupils.

The initial diagnosis was GBS as it presented as a severe rapidly progressive tetraparesis with infectious prodrome and cranial nerve involvement. However, the following characteristics challenged this initial assumption and suggested CIDP as more probable: a lack of response to IVIg; clinical worsening beyond 8 weeks of symptoms onset; and good response to the combination of corticoids and plasmapheresis (one cycle). Also, it fulfilled current established criteria for CIDP [3]. Aside from a prominent pupillary dysfunction, other signs of dysautonomia were mild.

The pupil involvement in our patient had no significant light-near dissociation, differing from the classical Holmes-Adie syndrome. This sign is also absent in most individuals with dilated unreactive pupils secondary to neurological disorders [4]. Tonic unreactive pupils have been described as a secondary manifestation of different neurological disorders, including diabetes mellitus, amyloidosis, acute dysautonomia syndrome, and hereditary neuropathies [4, 5]. In most of these situations, other signs of autonomic involvement are usually present while light-near dissociation is absent in most of these individuals [4]. Previous studies quantitating the autonomic dysfunction in CIDP patients characterized it as a mild distal post ganglionic axonopathy [2, 6]. Only rarely a widespread dysautonomia was recognized in this condition [7]. The dilated tonic pupil in our description was probably post-ganglionic, due to dysfunction of the parasympathetic innervation to the iris sphincter, as supported by the pilocarpine test.

Tonic unreactive pupils have been previously reported in some rare descriptions of the GBS and Miller Fisher syndrome

Table 1 First motor nerve conduction study

Nerve	Latency (ms)		Amplitude (mV)		Velocity (m/s)		F wave min. latencies (ms)
	Left	Right	Left	Right	Left	Right	L/R
Median (APB)							
Wrist	3.7	3.7 (< 3.8)	6	9.5 (> 4)			
Elbow	8.2	7.7	5.6	9	56	61 (> 49)	
Ulnar (ADM)							
Wrist	**3.4**	3.1 **(< 3.3)**	**5.3**	7 (> 6)			
BUG	7.1	6.9	4.9	6.6	64	61 (> 49)	
AUG	8.6	8.3	4.7	6.5	69	69	28/29 (< 32)
Peroneal (EDB)							
Ankle	**13**	**9.5 (< 5)**	2.1	3.2 (> 2)			
BFH	20	16	2	3.1	41	44 (> 40)	
AFH	23	18	2	3	44	49	
Tibial (AH)							
MM	**11**	**10 (< 5)**	**2**	**1.7 (> 4)**			
PF	21	21	**1.7**	**1.4**	**38**	**38** (> 40)	60/57 (< 56)

The first nerve conduction study showed prolonged distal motor latencies in the lower limbs. Normal values in parentheses. Abnormal results in bold. *MM,* medial malleolus; *BUG/AUG*, below/above ulnar groove; *BFH/AFH*, below/above fibular head; *PF*, popliteal fossa; *CV*, conduction velocity; *APB*, abductor pollicis brevis; *ADM*, abductor digiti minimi; *EDB*, extensor digitorum brevis; *AH*, abductor hallucis.

[8, 9]. A tonic pupil due to parasympathetic denervation has been described in one patient with a slowly progressive hypertrophic CIDP [10]. Our description differs from this previous one as it is a rapidly progressive neuropathy, in which the markedly prolonged distal motor latencies, mildly affected nerve velocities and lack of significant nerve hypertrophy indicates a predominantly distal demyelination. Indeed, the involvement of post-ganglionic parasympathetic fibers supposedly would be more expected in conditions involving predominantly distal nerves.

Our case expands the range of autonomic signs in CIDP, adding tonic pupils as a possible finding in the acute onset variant of the disease. The knowledge of such an unusual clinical presentation may help physicians adjust treatment strategy early on, when dealing with a rapidly progressive neuropathy, especially when there is no response to first line treatment.

Compliance with ethical standards

Conflict of interest Denis Bernardi Bichuetti has received speaking/consulting honoraria from the Bayer Health Care, Biogen Idec, Merck, Sanofi-Genzyme, TEVA, and Roche.

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