

# Gastric Carcinoma Presenting With Chronic Inflammatory Demyelinating Polyneuropathy

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## Abstract

Although paraneoplastic neuropathy is usually associated with lung cancer, this report describes an association with gastric adeno-carcinoma. We report on a patient with chronic inflammatory demyelinating polyneuropathy (CIDP) manifesting as a paraneoplastic complication of gastric carcinoma. Due to motor and sensory deficits in the lower limbs his ambulation was severely limited. The onset was subacute, followed by a slow progression. Electrodiagnostic examination and sural nerve biopsy were consistent with CIDP. The patient received chemotherapy and experienced clinically meaningful improvement of symptoms. We thus conclude that CIDP should be considered in patients known to have gastric adenocarcinoma who present with a polyneuropathy. To our knowledge this is the first reported case of paraneoplastic CIDP secondary to gastric adenocarcinoma.

## INTRODUCTION

Paraneoplastic processes are well established causes of neuropathies. These neuropathies have been associated with small cell carcinoma of the lung, ovarian or uterine cancer and rarely with cancers of the digestive system organs. We describe a unique patient with CIDP who was later diagnosed and treated for gastric adenocarcinoma with a subsequent improvement of symptoms.

## CASE REPORT

The patient was a fifty five-year-old, right-handed white male with a 6-7 week history of progressively worsening numbness. The numbness started in the right leg below the knee, and subsequently involved the left leg below the knee as well as in both hands. There was an associated worsening of a right foot drop dating from prior back surgeries. He denies any upper respiratory or gastrointestinal illness prior to the onset of his symptoms. He had diarrheal episodes after he was hospitalized. Patient continued to progress gradually for few months after his initial symptoms. His past medical history was significant for a melanoma removed in 1976. He had multiple other previous surgeries, including cervical fusion, lumbar laminectomies, bilateral knee and hip replacement, bilateral shoulder replacement and multiple ankle surgeries. A review of systems was significant for a 50 lb. weight loss over the previous 6 months.

Neurological examination revealed a normal mental status

with intact cranial nerves bilaterally. Motor examination revealed intact strength except for right foot dorsiflexors and everter 0-1/5 and mild bilateral hip flexor weakness. Mildly decreased tone in the right foot. Deep tendon reflexes been 2 and equal bilaterally in the upper extremities, reduced bilateral patellar and absent at the ankles. Sensory examination showed decreased pin sensation bilateral up to the mid-thighs and mid-arms bilaterally. There was decreased vibration bilaterally up to the elbows and decreased position at the toes. Finger-to-nose and heel-to-shin testing was unremarkable. Plantars were flexors. The patient walked with a steppage gait on right side. There was positive Romberg.

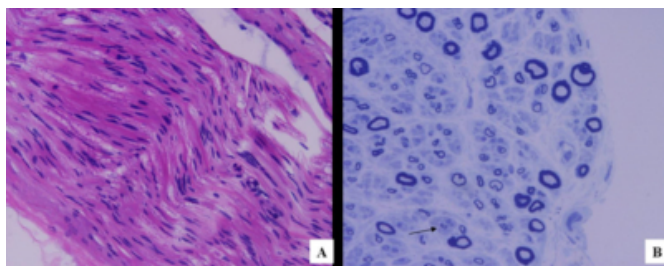
Laboratory tests with normal ranges are shown in the Table. The sural nerve biopsy is shown in Figure-1 A & B. Electrodiagnostic findings revealed a multifocal process with demyelinating changes. A cerebrospinal fluid analysis was not performed. There was no history of exposure to neurotoxins. The clinical history, findings on physical examination and laboratory studies did not support an infectious or metabolic neuropathy. The patient's megaloblastic blood picture with borderline elevated liver functions was attributed to alcohol use.

As the patient continued to lose weight and appetite, his workup was repeated. Initial gastro-intestinal workups was negative but repeat gastro-intestinal workups including

endoscopy and colonoscopy 8-9 months after the start of his neurologic symptoms revealed gastric adenocarcinoma. The patient's neuropathic symptoms continued to progress for the 8-9 months until his gastric adeno-carcinoma was diagnosed. He was then treated with chemotherapy with partial resolution of his neurologic symptoms. The patient refused plasmapheresis or IVIgG. He has remained stable for the last year and a half.

**Figure 1**

Figure 1A (H & E Stain) showing chronic inflammatory cells, Figure 1B (Toluidine blue stain) showing loss of myelin from most of the axons and arrow pointing at onion bulb formation, suggestive of chronic demyelination and remyelination changes.



**Figure 2**

Table 1

VALUES	RESULTS	NORMAL RANGE
MCH/MCV	35.4/102	(26-34)/(80-100)
AST	226	10-37
ALT	102	10-65
ESR	7	0-20
ANA	Negative	Negative
B12	414	211-911
Folic acid	9.0	2.5-15.6
HbA1C	5.1	4.4-6.4
T4/TSH	1.09/1.18	(0.71-1.85)/(0.49-4.7)
SPEP	IgG=1110, IgM=123, IgA=282	IgG=700-1600, IgM=40-230, IgA=70-400
RPR	Non-reactive	Non-reactive
Serum Arsenic	None detected	None detected
Serum organophosphorous	None detected	None detected
Anti-Hu antibody	Negative	Negative
Chest x-ray	Unremarkable	Unremarkable
Stool guaic	Positive	Negative
CT abdomen & pelvis	Hepatomegaly	Normal
EMG-NCS	Multifocal process with demyelinating features	Normal
Sural nerve biopsy	Lymphocytic infiltration in the endoneurium & perineurium, extensive demyelinating & minimal axonal changes.	Normal

**DISCUSSION AND LITERATURE REVIEW**

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a commonly diagnosed disorder first described in 1975 (Dyck et al. 1975). The diagnosis of CIDP may be established by a combination of clinical, laboratory CSF, histologic, and electrophysiological features (Ad Hoc AAN). The onset is subacute with proximal weakness a characteristic feature. Symptoms

progres for at least 2 months in contrast to the Guillain-Barre syndrome where symptoms progress less than 4 weeks (Ad Hoc AAN, Barohn et al., 1989, Mendell 1993). Several authors have suggested that in patients who progress for 4 to 8 weeks, the disorder should be labeled “subacute inflammatory demyelinating polyneuropathy” (SIDP) to differentiate it from both Guillain-Barre syndrome and CIDP (Hughes et al., 1992).

The association of CIDP with malignant disease is rare but has been described in association with several malignancies. Paraneoplastic polyneuropathy is usually associated with small cell carcinoma of the lung (Graus et al) and neoplasm of the ovary or uterus (Sugai et al). Malignancies associated with CIDP include Hodgkin's lymphoma (Barohn et al., 1989; Mendell, 1993), carcinomas of the colon, pancreas and cholangiocarcinomas (Barohn et al., 1989, Antoine et al 1996), carcinomas of the larynx, lung (Barohn et al., 1989; Mendell, 1993, Sugai et al), hepatocellular carcinoma (Sugai et al., 1997), and malignant melanoma (Bird et al., 1996; Weiss et al., 1998). CIDP has been described in association with inflammatory bowel disease, connective tissue disorders, chronic active hepatitis, and monoclonal gammopathy of unknown significance (MGUS) (Barohn et al., 1989; Mendell, 1993). A predominantly sensory polyneuropathy has also been described in a patient from the UK (Calvey et al., 1983).

Since the clinical presentation of CIDP is so varied, confirmatory testing must be performed to ensure the validity of the clinical diagnosis. The diagnosis of CIDP must be confirmed by either electrodiagnostic testing or nerve biopsy (Ad Hoc AAN, 1989, Barohn et al., 1989). Because the abnormalities found in CIDP are multifocal, up to 18% of patients with CIDP have normal nerve biopsies, and only 48% of patients have typical pathological findings (Barohn et al., 1989). Sural nerve biopsy should be considered when a clinical suspicion of CIDP remains in patients who do not meet the proposed EDX criteria for demyelination (Haq et al). Our patient met the clinical, electrodiagnostic and sural nerve biopsy criteria for CIDP.

Carcinomatous neuropathy (CN) was first reported by Denny-Brown (Denny-Brown, 1948). Though Denny-Brown's CN was sensory neuropathy, sensorimotor neuropathy is a more common clinical pattern of a peripheral neuropathy associated with a malignant tumor than a pure sensory neuropathy (Croft et al., 1967). The pathogenesis remains poorly understood, and evidence for cell-mediated and humoral mechanisms with anti-onconeural antibodies

disimmune mechanisms are involved (Dalmau et al., 1997). There are pathological changes in the dorsal root ganglia (Ohnishi et al., 1986). Sensorimotor dominant paraneoplastic polyneuropathy is characterized by degeneration of the dorsal column of the spinal cord and axonal degeneration (Rowland, 1995). Carcinomatous sensory neuropathy associated with gastric carcinoma has been described (Yamamoto et al 1989) but CIDP as a manifestation of gastric adenocarcinoma has not been reported.

Some paraneoplastic neuropathies are part of complex syndromes involving simultaneously the central and peripheral nervous systems, the most frequent of which is subacute sensory neuronopathy/paraneoplastic encephalomyelitis (SSN/PEM). This disorder, when occurring with small cell lung cancer, is almost invariably associated with anti-Hu antibodies (Dalmau et al., 1997). An antinuclear autoantibody, named anti-Hu antibody, has been found in patients with CN (Croft et al., 1967; Anderson et al., 1988). Type 1 antineuronal nuclear antibodies (ANNA-1, sometimes called "anti-Hu") were initially recognized in serum of patients with sensory neuronopathies associated with small-cell lung carcinoma (Graus et al., 1985; Kimmel et al., 1988). Although most patients with anti-Hu antibodies have had SSN (Dalmau et al., 1992), recent studies indicate that neuropathies associated anti-Hu antibodies can be heterogeneous (Younger et al., 1994; Oh et al., 1997). Nevertheless, ANNA-1 seropositivity appears to be highly specific for small-cell lung carcinoma in patients with sensory neuronopathy (Chalk et al). Seronegativity in a patient with sensory neuronopathy does not exclude cancer (Chalk et al., 1992).

Each of the well-established paraneoplastic neurological syndromes also occurs without cancer (O'Neill et al., 1988). Although attention has been mainly focused on antibody positive cases, there also exist true paraneoplastic neuropathies and no known antibodies (Graus et al., 1985), such as in our patient. Again, as in our patient, the cancer associated with a paraneoplastic neuropathy is often occult (Chalk et al), and an initial negative work-up for cancer is common. In patients without antibodies, neuropathies that occurred within 2.5 years of carcinoma were probably paraneoplastic and corresponded mainly to inflammatory disorders whereas in neuropathies in which the cancer appeared after many years the association was probably coincidental (Antoine et al). Depending upon the criteria up to 50% of patients with carcinoma develop a peripheral neuropathy (McLeod 1993). In our patient the cancer

appeared within 9 months after the appearance of neuropathic symptoms. In patients with axonal polyneuropathy of otherwise unknown origin, 4%-5% of patients develop cancer within the first years after the appearance of the neuropathy and an additional similar proportion with protracted follow up (Antoine 1999).

Recognition of CIDP is important because it remains the most common of the treatable neuropathies (Wilson et al 2000). Treatment of CIDP is aimed at the suspected autoimmune etiology and consists of immunosuppressive therapy. Corticosteroids have been associated with an initial response in 95% of patients with a mean time of response of 1.9 months (Mendell, 1993). Plasmapheresis and intravenous immunoglobulin have been used as initial therapy for CIDP with high response rates. Long-term immunosuppressive therapy is necessary due to the high relapse rate of CIDP. For cases with disease resistance to initial therapy, cyclosporine A and cyclophosphamide have been used successfully (Barohn et al., 1989; Mendell, 1993).

Treatment of paraneoplastic neuropathies remains unsatisfactory. Some patients improve with treatment of the cancer. Our patient received chemotherapy with significant resolution of symptoms but he declined any further medical therapy. This report therefore emphasizes the primary etiological role of cancer in paraneoplastic neuropathies even for those who meet accepted criteria for CIDP.

### **CONCLUSIONS**

The present report suggests that CIDP may be a paraneoplastic syndrome associated with the presence of gastric adenocarcinoma. CIDP should be considered in patients known to have gastric adenocarcinoma who present with a compatible clinical picture suggestive of polyneuropathy.

### **References**

1. Ad Hoc Subcommittee of the American Academy of Neurology. Research criteria for diagnosis of chronic inflammatory polyneuropathy (CIDP). *Neurology* 1991; 41: 617-618.
2. Anderson NE, Rosenblum MK, Graus F, Wiley RG, Posner JB. Autoantibodies in paraneoplastic syndromes associated with small-cell lung cancer. *Neurology* 1988; 38: 1391-1398.
3. Antoine JC, Mosnier JF, Lapras J et al. Chronic inflammatory demyelinating polyneuropathy associated with carcinoma. *J Neurol Neurosurg Psychiatry* 1996; 60: 188-190.
4. Antoine JC, Mosnier JF, Absi L, Convers P, Honnorat J, Michael D. Carcinoma associated paraneoplastic peripheral neuropathies in patients with and without anti-onconeural antibodies. *J Neurol Neurosurg Psychiatry* 1999; 67: 7-14

5. Barohn RJ, Kissel JT, et al. Chronic inflammatory demyelinating polyradiculoneuropathy : Clinical characteristics, course, and recommendations for diagnostic criteria. *Arch Neurol* 1989;46: 878-884.
6. Bird JS, Brown MJ, Shy ME et al. Chronic inflammatory demyelinating polyneuropathy associated with malignant melanoma. *Neurology* 1996; 46: 822-4.
7. Calvey HD, Melia WM, Williams R. Polyneuropathy: An unreported non-metastatic complication of primary hepatocellular carcinoma. *Clin Oncol* 1983; 9: 199-202.
8. Chalk CH, Windebank AJ, Kimmel DW, McManis PG. The distinctive clinical features of paraneoplastic sensory neuronopathy. *Can J Neurol Sci* 1992; 19: 346-351.
9. Croft PB, Urich H, Wilkinson M. Peripheral neuropathy of sensorimotor type associated with malignant disease. *Brain* 1967; 90: 1-66.
10. Dalmau J, Graus F, Rosenblum MK, et al. Anti-Hu associated paraneoplastic encephalomyelitis/sensory neuronopathy. A clinical study of 71 patients. *Medicine* 1992; 71:59-72.
11. Dalmau J, Posner JB. Paraneoplastic syndromes affecting the nervous system. *Semin Oncol* 1997; 24: 318-28.
12. Denny-Brown DE. Primary sensory neuropathy with muscular changes associated with carcinoma. *J Neurol Neurosurg Psychiatry* 1948; 11: 73-87.
13. Dyck PJ, Lais AC, Otha M, Bastron JA, Okazaki H, Groover RV. Chronic inflammatory demyelinating polyradiculoneuropathy. *Mayo Clin Proc* 1975; 50: 621-637.
14. Graus F, Cordon-Cardo C, Posner JB. Neuronal antinuclear antibody in sensory neuronopathy from lung cancer. *Neurology* 1985; 35: 538-543.
15. Haq RU, Fries TJ, et al. Chronic inflammatory demyelinating polyradiculoneuropathy: A study of proposed electrodiagnostic and histologic criteria. *Arch Neurol* 2000;57:1745-1750.
16. Hughes R, Sanders E, Hall S, Atkinson P, Colchester A, Payan P. Subacute idiopathic demyelinating polyradiculoneuropathy. *Arch Neurol* 1992; 49: 612-616.
17. Kimmel DW, O'Neill BP, Lennon VA. Subacute sensory neuronopathy associated with small cell lung carcinoma : diagnosis aided by autoimmune serology. *Mayo Clin Proc* 1988; 63: 29-32.
18. McLeod JG. Paraneoplastic neuropathies. In: Dyck PJ, Thomas PK, eds. *Peripheral Neuropathy*. Philadelphia: Saunders 1993;II: 1583-90.
19. Mendell JR. Chronic inflammatory demyelinating polyradiculoneuropathy. *Ann Rev Med* 1993; 44: 211-219.
20. Nicolas G, Maisonobe T, et al. Proposed revised electrophysiological criteria for chronic inflammatory demyelinating polyradiculoneuropathy. *Muscle & Nerve* 2001;25:26-30.
21. Oh SDI, Dropcho EJ, Claussen GC. Anti-Hu associated paraneoplastic sensory neuronopathy responding to early aggressive immunotherapy: report of two cases and review of literature. *Muscle Nerve* 1997; 20: 1576-82.
22. Ohnishi A, Ogawa M. Preferential loss of large lumber primary sensory neurons in carcinomatous sensory neuropathy. *Ann Neurol* 1986; 20: 102-104.
23. Rowland LP. *Merrit's Textbook of Neurology* 9th ed. Williams & Wilkins, Baltimore, 1995, p. 662.
24. Sugai F, Abe K, Fujimoto T, Nagano S, Fujimura H, Kuyanoki Y, Oshikawa O, Yamasaki E, Kawata S, Matsuzawa Y, Yanagihara T. A case of inflammatory demyelinating polyneuropathy accompanied by hepatocellular carcinoma. *Intern Med* 1997; 36: 53-55.
25. Weiss MD, Luciano CA, Semino-Mora C et al. Molecular mimicry in chronic inflammatory demyelinating polyneuropathy and melanoma. *Neurology* 1998; 51: 1738-41.
26. Wilson JR, Park Y, Fisher MA. Electrodiagnostic criteria in CIDP: comparison with diabetic neuropathy. *Electromyogr. Clin. Neurophysiol* 2000;40:181-185.
27. Yamamoto K, Ohnishi A, Noda S, Umezaki H, Yamamoto T. An autopsy case of carcinomatous sensory neuropathy associated with gastric adenocarcinoma. *Clin Neurol* 1989; 29: 493-496.
28. Younger DS, Dalmau J, Inghirami G, et al. Anti-Hu associated peripheral nerve and muscle microvasculitis. *Neurology* 1994; 44: 181-2.

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