ARE THE ENDEMIC MOTOR NEURON DISEASES OF GUAM REALLY DISAPPEARING?

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Abstract. Death certificates were reviewed to observe trends in the number of persons on Guam reported to have chronic degenerative motor neuron diseases (amyotrophic lateral sclerosis, parkinsonism-dementia or Parkinson's disease) at the time of death. Additional data, including age and race of the deceased and the name of the certifying physician were also collected. The number of persons having been diagnosed with amyotrophic lateral sclerosis is apparently decreasing while their mean age is increasing suggesting that the etiologic agents or factors causing this disease are less prevalent on Guam today than they have been in the past. Trends with regard to parkinsonism-dementia and Parkinson's disease are less clear.

INTRODUCTION

Although the first published reference to the presence of an unusually high incidence of chronic degenerative motor neuron diseases (CDMND) on Guam to appear in the medical literature was relatively recent (Koerner, 1952), this problem had apparently been present on the island at least since the 19th century. This is suggested by the Spanish derivation of the terms used by island residents for the most common forms of these diseases. "Lytico" (from the spanish "paralytico") is used to describe amyotrophic lateral sclerosis (ALS) and "bodig" (from the Spanish "bodega") is used to describe parkinsonism-dementia (p-d) (GHPDA, 1985). Although a specific diagnosis of ALS was mentioned on a Guam death certificate as early as 1910 (OVS, 1910), the fact that these diseases were occurring among island residents at an unusually high rate apparently escaped the attention of health authorities until much later. This oversight seems puzzling in view of the fact that during the period 1901-1941 military physicians trained in the United States were responsible for the health of all island residents and, by law, all deaths occurring on the island had to be certified as to cause (while deaths occurring in the hospital were generally certified by a medical officer, deaths occurring outside of the hospital were frequently certified by village mayors).

Beginning in 1956 the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) of the US National Institutes of Health established a research center on Guam with the expectation that where the incidence of CDMND was unusually high, the causal factors must similarly be high and therefore could be most readily observed. The research station staff conducted intensive case-finding surveys and provided free treatment for registered patients, including innovative therapies such as the use of levodopa. It was observed that ALS and p-d were occurring on Guam at a rate at least 100 times greater than in most other areas of the world. Studies examining diet histories and the geneologies of patients, examinations of necropsy material and animal transmission experiments were carried out without leading to identification of a definitive cause (Kurland and Mulder, 1954; Reed and Brody, 1975). Yase (1980) later observed that these diseases were associated with an accumulation of aluminum in nervous tissue and Gajdusek (1984) proposed that environmental factors, including diet, may lead to these changes.

Due to a number of considerations including budgetary constraints, the lack of immediate prospects of a dramatic breakthrough in the search for the etiology of these diseases and an apparent decrease in their incidence, in 1983 the Guam research station was closed. At that time it

was predicted that ALS and p-d would disappear from Guam within 10 years (Garruto *et al,* 1985). In an attempt to determine if an apparent decrease in cases since then is real or perhaps only a self-fulfilling prophesy occasioned by the cessation of intensive case-finding efforts, a review of death certificates registered on Guam was conducted.

MATERIALS AND METHODS

Death certificates registered with the Office of Vital Statistics, Guam Department of Public Health and Social Services, for the period 1951-1990 were reviewed. Data listed on the certificate for age at death, sex, ethnicity, diagnoses (if a motor neuron disease was mentioned), whether the diagnosis was listed as an immediate cause of death and the certifying physician were recorded.

The data were summarized by five-year periods and mean age at death for the major CDMND diagnostic groups were calculated.

RESULTS

The number of deaths associated with a diagnosis of ALS peaked during the period 1966-1970 and has shown a steady decrease since then (Table 1). Cases of both Pd and p-d appear to have peaked much later (1981-1985) and, particularly in the case of Pd, have shown only slight decrease in the most recent five-year period.

The mean age at death of persons with CDMND has increased steadily from the period 1951-1955 to the period 1986-1990 (ALS), has apparently hit a plateau (p-d) or first increased but have recently decreased slightly (Pd) (Table 2).

DISCUSSION

The number of apparent classic Parkinson's disease cases (parkinsonism without mention of dementia) recorded on Guam death certificates in recent years would suggest that this manifestation of CDMND may be increasing on Guam. A review of individual death certificates for the past 10 years, however, shows that all such cases were Guamanians, none were diagnosed by neurologists, and 31 of 51 (60.8%) were diagnosed by a single physician. This same physician diagnosed only 8% of p-d cases recorded during the same period. It seems probable then that most, if not all, of the cases reported as Parkinson's disease may actually represent misdiagnosed cases of parkinsonism-dementia.

Table 1

Number of persons with amyotrophic lateral sclerosis, parkinsonism-dementia or Parkinson's disease listed on their death certificate, total chronic degenerative motor neuron disease associated deaths and percent of Guamanian deaths, Guam 1951-1990.

Years	ALS[1]	p-d[2]	ALS/p-d[3]	Pd[4]	Total (%)
1951-55	39	0	0	7	46 (4.3)
1956-60	58	2	3	19	82 (8.0)
1961-65	58	48	4	10	120 (9.9)
1966-70	71	28	1	8	108 (8.8)
1971-75	56	36	6	11	109 (8.6)
1976-80	36	51	12	13	112 (8.7)
1981-85	32	54	7	28	121 (8.8)
1986-90	21	30	7	27	85 (5.3)

[1] Amyotrophic lateral sclerosis
[2] Parkinsonism-dementia
[3] Concurrent diagnoses
[4] Parkinson's disease

Table 2

Mean age at death of persons with amyotrophic lateral sclerosis, parkinsonism-dementia or Parkinson's disease listed on their death certificate, Guam 1951-1990.

Years	ALS[1]	p-d[2]	Pd[3]
1951-55	50.5 (±8.9)[4]	NSD	53.43 (±6.2)
1956-60	51.3 (±11.1)	NSD	55.7 (±5.7)
1961-65	50.6 (±10.5)	56.3 (±11.1)	63.3 (±7.2)
1966-70	53.8 (±10.4)	60.3 (±8.9)	63.0 (±6.7)
1971-75	56.0 (±9.3)	60.8 (±8.5)	66.0 (±10.8)
1876-80	59.1 (±9.8)	66.7 (±9.5)	64.5 (±6.3)
1981-85	57.7 (±10.4)	68.4 (±8.5)	69.0 (±5.9)
1986-90	60.2 (±9.8)	68.6 (±6.4)	67.2 (±9.6)

[1] Amyotrophic lateral sclerosis
[2] Parkinsonism-dementia
[3] Parkinson's disease
[4] Standard deviation

This problem illustrates one of the weaknesses inherent in using death certificates as a surveillance tool. Steps that could be taken to minimize this problem in the future could be providing continuing education on completing death certificates for physicians in differential diagnosis or establishing a permanent case registry for CDMND diseases diagnosed on Guam (perhaps in connection with adding these diseases to the list of officially reportable diseases for the Territory).

In general, deaths on Guam associated with CDMND do indeed appear to be decreasing, both in terms of the percentage of Guamanian deaths they account for and in terms of total numbers of such deaths. One might justifiably suspect, however, that this decrease could be due to less intensive case-finding among living patients following closing of the Guam NINCDS research station. This may have resulted in only the most pronounced typical cases being identified in recent years.

On the other hand, the fact that the mean age at death for at least one major diagnostic group of these diseases is apparently increasing (Table 2) suggests that new cases of these diseases may not be developing among younger persons to replenish the ranks of those already affected. An alternative explanation for this phenomenon could be that improvement in the general level of medical care available on Guam has resulted in an increased survival time of cases, thereby increasing the average age at death for these patients.

It has been proposed that the endemic high incidence of CDMND on Guam is due to the toxic effects of an accumulation of aluminum ions in nervous tissue as a result of an especially aluminum rich but calcium poor diet consumed by Guamanians up to the time of the reoccupation of Guam by American forces in 1944 (Gajdusek, 1984). The subsequent shift from a largely self-sufficient agrarian society to one largely dependent on government employment has resulted in a massive change of diet in which the bulk of food consumed is now imported from other areas of the world, particularly USA. Another theory holds that harvesting of the toxic cycad nut *(Cycas circinalis)* to make a flour used primarily in times of economic hardship (such as following destructive typhoons and during the Japanese occupation of Guam) directly damaged nervous tissue of those consuming it (Whiting, 1964). It also seems possible that both of these proposed mechanisms could be operative: cycad toxin may modify nervous tissue metabolism in such a way that excessive aluminum may later be deposited leading to neuron dysfunction and degeneration.

Both of these theories are similar in that they suggest that cases of the endemic neurodegenerative motor neuron diseases of Guam are unlikely to occur in persons born after World War II and, in fact, this may eventually prove to be the case. All recorded deaths to date in which any of these diseases have been listed on the death certificate have been of persons born in 1944 or before. As these diseases were earlier frequently diagnosed during the third or fourth decades of life and it has now been 47 years since the end of hostilities associated with World War II on Guam, it may indeed be that these diseases are disappearing from the island. Hopefully, in the next few years it may be possible to confirm this trend even in the absence of the active case finding and the more reliable incidence data formerly available.

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