‘Caplan’s Syndrome’ – revisited and lessons learned

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In the mid 1980s, I had just taken up the Neurology Chair at Tufts University in Boston. Dr Ted Munsat, the previous Neurology chairman, said to me that the Tufts' neurology residents would probably not know about Caplan's syndrome. I went to the library and reviewed what was already known at that time about the virus.
a special interest of mine. I have already discussed awakening of interest in posterior circulation strokes in a previous paper in Practical Neurology (Caplan 2004). ‘No’, Munsat said. I refer to the lumbosacral radiculo–myelopathy report in the New England Journal of Medicine (Caplan et al. 1977). I consider that Caplan’s syndrome. Writing and publishing that paper taught me lessons that I hope now to pass on to the readers of Practical Neurology.

During the early 1970s, I was a junior staff neurologist at the Beth Israel Hospital in Boston. I had a joint appointment as Chief of Neurology at the then very beginning years of the Harvard Community Health Plan (HCHP) as well as my post at the Beth Israel. The HCHP was probably the first successful managed care health maintenance organization (HMO). I was an indentured slave for that organization. For $ 2000 dollars a year my duties included consulting of the HCHP.

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THE FIRST TWO PATIENTS

Two patients were admitted from the HCHP within a period of about two weeks. They had almost identical stories. Each was a young male homosexual. Each complained of paraesthesias involving their genitalia and buttocks variously extending into their lower extremities. Each had developed urinary retention, constipation and impotence soon after developing the paraesthesias. Inguinal adenopathy was prominent in one of the patients. Neither had any motor or reflex abnormalities in their lower limbs. Neither had any past neurological or medical illnesses. Spinal taps in each revealed a lymphocytic pleocytosis of about 20 cells with normal chemistry. I was very perplexed. I thought it likely that they had some type of venereal sexually transmitted disease – recall this was a long time before the first AIDS cases were published. But serological tests for syphilis were negative and neither chlamydia nor gonococci grew from cultures. I thought perhaps this was lymphogranuloma venereum, a sexually transmitted disease that I had heard about. However, a visit to the library showed that this was not known to cause the findings in my two patients. Each of the patients required an indwelling urinary catheter. However, within a few weeks, the urinary retention, constipation, and impotence recovered. I had absolutely no idea what the diagnosis was.

THE NEXT CASE

A few years later, another patient came to the hospital and gave me the first hint of the correct diagnosis in my two earlier patients. He was 19-years-old and also homosexual. He presented with fever, headache, and listlessness and had clear painful vesicles on the shaft of his penis with tender enlarged lymphadenopathy. His spinal fluid showed 1209 leucocytes/cc with 12% polymorphonuclear cells and 88% lymphocytes. The clinical picture was clearly that of genital herpes with meningo-encephalitis. He recovered quickly and left the hospital. However he soon returned to see me in the clinic because of numbness in the buttoc and right heel, inability to feel the passage of stool, decreased penile erectile function, and difficulty initiating urination. He then developed urinary retention prompting re-hospitalization. A cystometrogram showed a hypotonic bladder. There were no vesicles in the bladder seen through a cystoscope. The herpes simplex virus (HSV2) complement fixation titre was 1 : 64. I then became very suspicious that my earlier two patients had also had genital herpes due to HSV 2.

THE FOURTH CASE

Shortly afterwards, a young woman consulted me in the clinic and was admitted to the hospital. She had blisters in her vagina and vulva and went into urinary retention. Unfortunately she later developed a Guillain-Barre type of postinfectious radiculo–myelopathy. Cultures from the vesicles grew HSV 2. I inquired of several of my senior gynaecological colleagues if they knew about urinary retention associated with herpes genitalis. They told me that the teaching was that the vesicles and rash were painful and caused secondary urinary retention explained by the pain and local inflammation. They had not considered the possibility that the urinary retention might be due to involvement of the sacral nerve roots or lower spinal cord.

FINDING THE OLD RECORDS!

Now the trick was to identify my two early patients. Foolishly I had not written down their names or kept any information about them. I had to go to the records room and search through all the records of the past 3 years. Of course I knew their sex and approximate ages. I also knew that they were HCHP patients. It took more than a month of searching in my spare time. Of course I had no spare time with 5 children at home, indentured servitude to the HCHP, and an incredibly busy in-patient and out-patient service at the hospital. There were only two neurologists at the Beth Israel Hospital at that time.

Finally I was able to identify 10 potential suspects. I pulled their charts and found my two male homosexuals with urinary retention and impotence. I called them on the telephone and asked to see them. Each came to the clinic. They both told me that they had had a small vesicle on their penis just before the paraesthesias developed. Clearly they had had HSV2 infection like my other male patient with HSV2 followed by meningo-encephalitis and urinary retention and impotence, and my young woman with HSV2 urinary retention and Guillain-Barre. Later I found several other patients with the same syndrome.

WHAT WAS KNOWN OF THE VIRUS?

When I realized that the lumbosacral radiculo–myelopathy syndrome was due to the HSV virus, I went to the library and reviewed what was already known at that time about the virus. The herpes viruses were known to be neuropathic. When inoculated at peripheral sites, the virus could be found in sensory ganglia for prolonged periods of time (Baringer & Swoveland 1974). Primary infection with HSV1 most often caused cold sores on and around the lips and in the oral cavity. Discomfort and paraesthesias in the trigeminal nerve distribution also occurred. The pain and sensory symptoms were due to spread along sensory
branches of the trigeminal nerve. Occasionally the infection was accompanied by a meningo-encephalitis and cells in the CSF. At necropsy HSV1 virus was often found in sensory trigeminal ganglia (Baringer & Swoveland 1973). There was an indication that some cases of trigeminal neuralgia were related to reactivation of HSV1 in the trigeminal ganglia and nerve roots.

The process in the sacral region was similar. The HSV2 virus involves the skin of the genitals or perigenital areas. Lymphadenopathy develops. The virus spreads along peripheral nerves into sacral nerve roots and sensory ganglia. Type 2 virus had been cultured from sacral sensory ganglia in male cadavers shortly after death (Baringer 1974). The HSV2 virus could spread into the spinal fluid as it had in several of my patients. The lumbosacral radiculo-myelopathy produces paraesthesias, urinary retention, and constipation in both sexes and impotence in men. Sexual dysfunction in women has been less often studied. The primary infection is generally self-limited. Recurrent attacks usually cause only a rash and paraesthesias, not urinary retention or loss of sexual function. Oral-genital contact can induce HSV2 in the orphal region or HSV1 in the genital region.

HELP FROM COLLEAGUES
I enlisted the help of two of my urological colleagues who knew much more about neuro-urology than me. They and I looked for more cases of the syndrome. They became coauthors on the paper submitted to the New England Journal that finally contained 8 men and 3 women with the syndrome (Caplan et al. 1977).

BACK TO THE LITERATURE
I searched thoroughly in the past literature for any reference to the syndrome. I did find one article in the French literature that had described the syndrome (Gayral 1953). Gayral had reported two patients. One was a woman with vulvar herpes followed by meningitis, difficulty urinating and reflex loss in the lower limbs. The second patient was a woman with vulvar herpes who had genital and lower limb hypoesthesia, urinary retention, and cells in the spinal fluid (Gayral 1953). A patient reported by Craig and Nahmias within a review of HSV infections also probably had the syndrome (Craig & Nahmias 1973). Their patient had vulvar herpetic vesicles, pain and paraesthesias in the perineum and legs, an inability to void, and a cerebrospinal fluid pleocytosis. Because we did not have culture data from some of the patients, the New England Journal made us attach the words probably secondary to herpes genitalis as the cause of the lumbosacral radiculo-myelopathy.

LESSONS LEARNED
• Become a collector
  I failed to originally note or collect the names and data of my first two strange unknown cases. It was very difficult for me in retrospect to identify them. I recall during my training the collecting practice of Dr Miller Fisher my mentor. To quote one of Fisher’s rules: ‘Collect and categorize phenomena: their mechanism and meaning may become clearer later if enough cases are collected’ (Caplan 1982). Miller Fisher had many, many manila folders that contained various collections: irascible aphasics, patients who answered before the question was completed, abulis, whisperers, mumblers, cerebellar haemorrhages, pallid lesions, patients who intermittently stopped speaking or moving, etc. With time and collecting new cases and with reading the literature, the conundrum or answer to the cases would appear and then a report in the literature would describe the material and the findings. I was deficient in not collecting the data on the original two patients. This cost me much time and energy in the long run when the answer to their conundrum became clear.

• Visit the library often and read the old and original as well as the new
  Residents and fellows these days are very adept at scanning the internet for recent articles and reviews. However, much of the older basic original literature is not yet available by computer. In order to know where the field is and is going one must know where it has been. How did ideas develop? In the case of herpetic lumbosacral radiculo-myelopathy much of the background was available in the older literature. As another of Fisher’s rules states ‘Each generation cannot relive the history of neurology. Take advantage of what has already been clarified in the past’ (Caplan 1982). The French and German literature often contains many clinical pearls and observations. When I was a neurology resident, I read through the volumes of Brain from 1900 to 1966 and many of the old volumes of Revue Neurologique. This has always served me in good stead.

• Much can be learned from colleagues in other fields. Consult them often
  In the case of herpetic lumbosacral radiculo-myelopathy, I learned much from my urological and gynecological colleagues. They helped with basic information about the particular patients. More than that, they helped me learn more about neuro-urology and gynecological infections.

REFERENCES