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Post-Infectious Fatigue

SUMMARY

Post-infectious fatigue or post-infectious neuromyasthenia (PIN) is an illness characterized by persisting fatigue and disability after apparent acute infections. In most cases the illness is attributed to a chronic Epstein-Barr virus infection. Symptoms include weakness and fatigue in the absence of physical findings or significant laboratory abnormalities. These patients are frequently depressed and have considerable disability resulting in prolonged loss of time from work. The illness may be persistent or can be relapsing, but often lingers for two years or more. There is no effective therapy. PIN is probably caused by an acute infection occurring in patients who are psychologically susceptible. They require emotional support, reassurance and explanation. (*Can Fam Physician* 1987; 33:1217-1219.)

Key words: post-infections neurasthenia, chronic Epstein-Barr virus

RÉSUMÉ

La fatigue post-infection ou la neuromyasthénie post-infection (NPI) est une maladie caractérisée par une fatigue persistante et une incapacité suite à des infections apparemment aiguës. Dans la plupart des cas, la maladie est attribuable à une infection chronique par le virus Epstein-Barr. Les symptômes incluent faiblesse et fatigue en l'absence de trouvaillles physiques ou d'anomalies de laboratoire significatives. Ces patients sont fréquemment déprimés et souffrent d'une incapacité qui entraîne une absence prolongée du travail. La maladie peut être persistante ou récidivante, mais durera souvent pendant deux ans ou plus. Il n'existe pas de traitement efficace. La NPI est probablement causée par une infection aiguë se manifestant chez les patients psychologiquement susceptibles. Ils auront besoin de « rassurance », de support émotionnel et d'explications.

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MANY ACUTE viral infections, especially influenza, are charac-

terized by respiratory symptoms, swollen glands, malaise and some degree of disability. This type of illness is familiar to all of us. It may be associated with profound fatigue, lassitude and an inability to carry out daily functions because of weakness, aching muscles, or both symptoms. We have all come to realize and accept that this is a frequent illness, and the symptoms are a normal reaction to the acute viral syndrome. We also know that this illness exists because most of us have experienced it, and it is a well-described condition. During these types of illnesses, an objective measure of muscle strength may be perfectly normal, yet the afflicted feel that they are weak and profoundly fatigued. This type of asthenia is usually known as "flu" or a "flu-like illness" although most of the time this is not actually diagnosed

as influenza; indeed, most of the time it is not influenza. However, if a patient wishes to describe her or his feelings during this episode, it is sufficient to say "I have the flu" because one immediately knows by experience what type of symptoms are present.

What happens if the flu does not go away or if a flu-like illness recurs many times during the year, each time persisting for weeks? This type of illness has been popularized recently and called 'chronic Epstein-Barr virus' (CEBV), "Yuppie plague" or simply "chronic mono". This is a frustrating illness for patients and physicians alike. It is, however, important to try to understand how the illness might occur, and what we can do and should not do for these patients.

I will outline below some of these syndromes, as well as related illnesses

which bear some resemblance to post-infectious fatigue.

Neuromyasthenia

Neuromyasthenia refers to a collection of symptoms, including fatigue, depression, muscle aching and weakness, which occur in the absence of objective physical findings.

Epidemic neuromyasthenia (NM)

This disorder was originally described as occurring in outbreaks, and approximately 30 such epidemics were reported from 1934 to 1977. The epidemics have acquired many different designations according to the area where they took place (for example, Royal Free Disease). These epidemics characteristically took place in hospitals and affected young nurses. A large proportion of these nurses were affected but, by striking contrast, pre-adolescents and adult males were spared, and there was no transmission to family members and friends. The patients had a large number of relatively minor symptoms, but physical findings were unusual in most of the outbreaks. The symptoms continued for years and were present persistently or occurred in a relapsing and remitting form. Most patients, however, gradually improved, and no deaths were attributed to this disease. These outbreaks have defied explanation, though some physicians have attributed them to hysteria or to medical misperception, and some have tried to implicate various viruses including Cocksackie infections. Clearly, however, no etiology has been proven.

Sporadic neuromyasthenia

Although epidemics of this disease are no longer reported, it became apparent that occasional patients present with similar symptoms after an apparent flu-like illness. Because of the remarkable similarities to the epidemic form, I have called this illness 'post-infectious neuromyasthenia' (PIN).

In order to meet the criteria for this diagnosis patients should have a new occurrence of complaints of weakness or exhaustion which persists for more than 30 days after an apparent acute infection. These are the same types of symptoms which occur ordinarily during acute flu-like illnesses and persist for only several days. Patients who have similar symptoms without a defi-

nite acute onset frequently have other illnesses. These illnesses and other serious underlying diseases must be excluded.

The patients who develop PIN tend to be from high socio-economic groups and are well educated. Many are professionals, and a significant proportion are paramedical personnel. Using their own resources, many have done considerable research on this subject. The patients are high achievers in all aspects of life and have usually been very active in physical pursuits such as jogging. They have also tended to be very busy in community activities outside of their work. This has prompted some to call this illness "The Yuppie Plague"; however, a designation such as this tends to trivialize the illness and many patients are offended by this type of characterization.

There is usually an acute precipitating event which triggers PIN. The original infection in some cases is merely a mild flu-like illness, whereas in other cases it appears to have been a more severe flu with muscle aching and excessive tiredness right from the onset. Most patients do not recover at all from the initial infection, although some do experience partial recovery and then relapse when they try to resume their normal activities. This illness does not resemble typical acute infectious mononucleosis by history, by physical findings, or by the usual laboratory criteria. At least half of the patients with PIN appear to have serologic evidence for a recent infection or a relapse of Epstein-Barr virus (EBV) infection (which causes acute infectious mononucleosis). Many patients do however have evidence for other infections such as Cocksackie B and nonviral illnesses (Table 1).

The chronic phase of this illness is characterized by incapacitating exhaustion. Many other symptoms are usually present, and these include weakness, headaches or peculiar sensations which seem to have an intracranial origin, but which are not ac-

Table 1
Common Infectious Agents in PIN

Epstein-Barr virus (EBV) ^a
Cocksackie B
Giardia lamblia
Mycoplasma pneumoniae
Toxoplasma gondii

a. Approximately 50% of patients

curately characterized by the term 'headache' (Table 2). Patients characteristically complain of the worsening of their symptoms for days after any form of physical exertion; they experience difficulty in concentrating on tasks, and they have frequent flu-like illnesses. Many feel that they "get everything that's going around", and that they do not recover normally from apparently mild viral-like infections. They may experience brief periods of confusion and use words in an embarrassingly incorrect way. Anger and depression are very common, and patients attribute this to their failure to carry on a normal life. We have found, however, that many of these patients have a history of depressive episodes even prior to the onset of PIN.

Some patients suffer a constant disability with little in the way of relief. More often the patients follow a relapsing course, with some relatively "good days" followed by a variable period of excessive fatigue and flu-like symptoms. This illness has a devastating impact on these patients, who are unable to continue working at nearly the same level as previously. Many have been forced to quit their jobs and receive disability payments. PIN patients typically had lost very little time from work prior to their illness.

On presentation in the office, PIN patients have some characteristic features. Appointments are often made by a spouse or parent who accompanies the patients and wishes to be present during the interview. The patients often bring extensive notes detailing events, symptoms and feelings, as well as newspaper articles about PIN or chronic EBV infection. It is common for patients to state that they have a friend or a family member with an identical illness. Patients are often tearful during the interview.

An important feature of this illness, however, is the lack of significant

Table 2
More Common Symptoms of PIN

Exhaustion
Malaise
Postexertional exacerbation
Weakness
Headaches
Fever (subjective)
Inability to concentrate
Frequent URIs
Dyslogia
Paraphasia

physical findings. Most patients complain of a feeling of feverishness and swollen tender cervical lymph nodes, but on examination they are afebrile, and the cervical nodes are unremarkable. Despite the feeling of profound fatigue and muscle weakness, the neuromuscular examination is normal.

Routine laboratory tests, including complete blood counts, liver tests, muscle enzymes, urinalysis and the sedimentation rate, are all normal. A low level of anti-nuclear antibody is not infrequent. The serum IgM or IgG may be slightly to moderately elevated. There is therefore no diagnostic lab test.

Serologic tests for viruses are not usually very helpful. Since PIN is commonly believed to be a chronic viral infection (particularly a chronic Epstein-Barr virus infection), the physician could do EBV serology. The monospot test is always negative, but the patients do tend to have a higher antibody level to EBV. The anti-VCA is frequently 1:640 or greater, and the anti-EA is often 1:40 or greater. However, such findings are not uncommon in normal people, and it is difficult to make a sharp distinction between abnormal serology and normal serology. Virtually all adults in North America have had EBV infection, and all of these patients will have antibody titres to at least the VCA component. If the EBV serology is done and is unremarkable, the physician is still left with a patient who presents with the same type of syndrome which may have been caused by another precipitating event.

Treatment

Since neither the cause of PIN nor the way in which symptoms are produced is known, it is obvious that any treatment must be symptomatic. PIN patients tolerate any medications poorly, and many have a history of allergies including drug allergies. There is little evidence for inflammation, and anti-inflammatory agents such as ASA are not helpful. Some patients do have considerable muscle aching as a major symptom, and they may benefit from cyclobenzaprine (Flexeril). Patients with severe depression should receive psychotherapy, and they might benefit from antidepressant therapy. Most do not improve on antidepressants, and they are usually exquisitely sensitive to the side-effects. Anti-virus drugs such as Acyclovir do not help.

PIN patients are seeking an explanation for their illness, and it is useful to refer them to a specialist in neurology, rheumatology or infectious disease, depending on their predominant symptoms. This is recommended only to satisfy their curiosity and to alleviate some of their fears that they might have another serious disease. PIN patients have usually sought out many medical opinions, and they are often labelled as neurotic. Some turn to alternate and unorthodox therapies provided by clinical ecologists and nutritionists.

Ultimately, the most important therapy in this condition is to provide a sympathetic ear and to offer as full an explanation as is possible today. The patients must be reassured that they do not have a life-threatening illness such as cancer or AIDS. However, the uncertainty about the future course of the illness continues to provide considerable anxiety. It is difficult for patients to make long-term plans such as career plans or even short-term plans for social and other activities.

Prognosis

All patients do show some improvement, but it is very slow and may not be consistent. It is important for the physician to be optimistic and to encourage patients to continue some form of activity to the extent of their ability. Taking a vacation does not help very much in the long term, although many patients do feel quite well while they are away. They are not suffering from a contagious disease, and there is no fear of transmission to anyone else.

How does this disease occur?

The most suggestive evidence to date is that this illness represents a chronic or relapsing form of EBV infection. However, many patients have an identical illness without evidence for an unusual antibody response to EBV. PIN may be caused by another unknown virus which either resembles EBV or may reactivate it. It is clear that PIN does occur after other types of infections, and it was described years ago after brucellosis.

In order to formulate ideas as to how this illness occurs, the fact that the patients are depressed and many have mild abnormalities in immune function should be incorporated in the clinical picture given above. My hypothesis is

that PIN is the result of a fairly common form of infection which may trigger an abnormal response in certain types of patients. Many biologic and psychosocial factors come into play. After an acute infection, and perhaps in conjunction with other life stresses, these patients become fatigued, are unable to function normally, and become depressed. This can result in mild immune dysfunction which leads to persistence of the infection, relapses of latent viruses, or acquisition of new infections. This starts a vicious cycle of infection, depression, immune dysfunction and re-infection. In short, it appears that this illness might be an interplay between psychosocial factors and an infective agent.

Similarity to other illnesses

PIN is probably identical to what has been called chronic EBV syndrome. Some patients who have fibrositis also appear to be indistinguishable from patients with PIN. This is especially so if PIN patients have considerable muscle aching and "trigger points".

In summary, there appear to be enough objective abnormalities of organic disease to suggest that PIN is not purely a psychological ailment. It may however, be a result of an interplay between organic and emotional factors. Most of our current therapy should be directed at symptomatic complaints and emotional aspects, since some benefit has been seen from the use of this approach, and no other treatment is currently available. ●

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