FOR DEBATE....

Restless Legs Syndrome in Chronic Pulmonary Disease

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Summary: Eight consecutive patients referred for neurological opinion because of very severe "restless legs" all suffered from chronic pulmonary disease. It was considered that the restless legs syndrome was not a metabolic consequence of respiratory failure but a nervous manifestation of their invalidism.

Introduction

There must be few clinicians who have not been puzzled by the symptom or syndrome described by Ekbom in 1944, which he first entitled "irritable legs," amending it to "restless legs" in 1945. The salient clinical features are well known and in a mild form he found they occurred in 5% of a series of 500 healthy adults. Strang (1967) recorded an incidence of 2·5%. For the majority it is only an occasional experience, occurring perhaps in circumstances where there are long periods of enforced immobilization, as when travelling in a car, train, or aeroplane. To others it is something which makes a winter evening disagreeable. Tight trousers, television, and ultra-modern furniture exact their toll. It is particularly troublesome in bed. In such patients the complaint is usually incidental, emerging in a case history of some other disorder.

On the other hand restless legs may be a complaint of such persisting severity that it can lead to suicide, as in one of my patients. There are highly disagreeable pains and sensations in the lower limbs which are felt in the legs rather than the feet, deep in the tissues rather than superficial, resulting in an overwhelming urge to move the limbs. It interferes with rest and sleep, and the patient is usually forced to get out of bed several times during the night and walk about until the symptoms subside. Relief may be sought by bathing the feet in cold water, walking on cold tiles, rubbing and massaging the limbs, or stamping about. One of my patients, whose father also suffered from this complaint, found for a time that putting his feet into a refrigerator eased the torment. Myoclonus is not uncommon and insomnia is inevitable. There are no abnormal signs.

All patients agree that it is no ordinary pain which they feel in their legs. It does not resemble any other pain they have experienced. They use words such as "creeping, pulling, stretching, twisting, like toothache," and so on in trying to describe it, or else they stress its severity with adjectives such as "awful, dreadful, tormenting, gnawing, indescribable." Tingling, numbness, cramp, or burning feet are not often mentioned. But whatever words and phrases are used by the sufferers they all aver that, once the discomforts and pains have begun, they know that sooner or later they will be forced to move their limbs and get out of bed. The urge to do so is overwhelming.

A heredofamilial tendency has been noted (Ekbom, 1945), sometimes in association with iron-deficiency anaemia (Nordlander, 1953), pregnancy (Murray, 1967), or following partial gastrectomy (Ask-Upmark, 1959). It has also been described in various forms of neuropathy—idiopathic diabetic, amyloid, and uraemic (Callaghan, 1966)—and, more recently, during haemodialysis (Hampers and Schupak, 1967).

Most writers on the subject regard it as an organic disorder. A few think it is neurotic. Sedatives, vasodilators, and anticonvulsants all have their advocates. Perhaps the most useful drug is diazepam 5 to 10 mg. before retiring at night (Ekbom, 1965, Morgan, 1967).

Behrman (1958) thought that relaxation rather than immobility of the limbs was the provocative factor. Gorman and his colleagues (1965) at the Mayo clinic found that 13 out of 27 patients were thought on clinical grounds to suffer from depression. This was confirmed in eleven cases by application of the Minnesota Multiphasic Personality Inventory. Ekbom (1960) flatly stated that "the pathogenesis is unknown but the ailment is not psychogenic." Lugaresi and his colleagues (1965) also thought that the syndrome was organic in origin after they had used simultaneous electroencephalography, electromyography, and oculography, while the patients were falling asleep, during sleep, and on wakening. They thought that muscular jerking of the legs prevented the patient falling asleep, disturbed light sleep, but disappeared during deep sleep and in paradoxical sleep.

That the syndrome is no twentieth-century blues, a form of restlessness peculiar to modern life, is illustrated from this quotation from the writings of Thomas Willis in 1685, an observation rescued from the past by Macdonald Critchley in 1955: "Wherefore to some, when being a Bed they betake themselves to sleep, presently in the arms and leggs, leapings and contraction of the tendons, and so great a restlessness and Tossings of their members ensue, that the diseased are no more able to sleep, than if they were in a Place of the greatest Torture."

In its severe form it is not a malady commonly seen by neurologists, so that one's curiosity was aroused when eight consecutive cases, in four years, proved also to be chronic respiratory cripples. An examination of the possible significance of this relationship forms the basis of this communication.

Case Histories

Case 1.—Ex-miner, aged 61 years. Gastroenterostomy for duodenal ulcer 20 years previously. Chronic bronchitis and emphysema 10 years. Restless legs with nocturnal myoclonus and severe insomnia for five years. Sedatives, anticonvulsants, and thalidomide had failed to help him. Admitted to a Miners' Chest Disease Treatment Centre with an acute exacerbation of bronchitis. Iron-deficiency anaemia (haemoglobin 57%) with poor response to oral iron and a good response to intravenous iron. No improvement of the restless legs syndrome. Neurological examination was negative. An electroencephalogram remained normal during an afternoon repose despite persisting restless legs and myoclonus. Moderate relief from diazepam 20 mg. on retiring, but symptoms returned on leaving hospital and persisted until his death two years later.

Case 2.—Man, aged 58 years, a former greaser, unemployed for five years, disabled with chronic bronchitis and emphysema for 15 years. Referred by his practitioner with a diagnosis of Ekbom's syndrome of two years' duration. In patient psychiatric treatment three times in the previous four years with anxiety, depression, and insomnia. Little response to nocturnal sedation and parenteral phenytoin sodium 250 mg. Neurological examination was negative.

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Slept deeply during electroencephalography, when it was noted that leg jerking occurred during the light stage of sleep with arousal response. Leg jerking ceased during deep sleep. No epileptiform activity preceded or coincided with the myoclonic movements. Table I summarizes the observations of a night nurse, indicating the tormenting nature of his complaint.

TABLE I.—*Night Nurse's Observations in Case 2*
"Oh sleep! it is a gentle thing,"—COLERIDGE

P.M.	
11.00	Sleeping
11.30	(L) leg jerking in sleep; ceased on waking at 11.36
11.48	Sitting up; holding head in hands; both legs jerking
A.M.	
12.10	On bedside rubbing legs; groaning
12.21	Standing by bed; taking few steps
12.37	Returned to bed
1.30	(L) leg jerking; did not wake
2.00	On back; legs flexed; jerking
2.15	On bedside; rubbing legs
2.35	Standing; arching his back; walked round ward three times
2.45	Returned to bed. Sleeping
3.40	(R) leg jerking in sleep
3.45	Woke up; moving legs about; moaning
4.00	Sat up; smoked cigarette
4.20	Asleep
5.30	Asleep

Case 3.—A former power station worker aged 51. Chronic bronchitis with emphysema for 10 years. Unemployed for five years. Psychiatric treatment for spasmodic torticollis six years previously. Admitted to hospital on three occasions during the previous two years for acute respiratory failure. The last admission was an emergency following oversedation for insomnia. There was incipient CO_2 narcosis. Neurological examination negative. Electroencephalography (during intermittent oxygen inhalation) showed fluctuating irregular diffuse slow waves in the theta and delta range in all leads. Moderate response to nocturnal diazepam 20 mg. He died two years later.

Case 4.—A retired fitter, aged 66 years. Partial gastrectomy for peptic ulcer 13 years previously. Partial left pneumonectomy for chronic tuberculosis 10 years previously, followed one year later by thoracoplasty. Now suffering from marked emphysema and shortness of breath. Restless legs syndrome two years' duration. Poor response to diazepam 20 mg. at night.

Case 5.—A farmer, aged 63 years. Chronic pulmonary fibrosis with emphysema of 12 years' duration. No story of hypersensitivity to mouldy hay. The fibrosis was in both upper zones, nodular in pattern, with bronchiectatic cavities; thick calcified pleura. Restless legs syndrome with severe insomnia for four or five years. Neurological examination negative. Initially there was a good response to diazepam 10 mg. at night. His practitioner soon found that no relief was obtained with 10 to 20 mg. diazepam at night. He subsequently became somewhat addicted to the preparation Diconal (dipipanone hydrochloride 10 mg. and cyclizine hydrochloride 30 mg.)

Case 6.—Retired miner, aged 72 years. Pneumoconiosis 22 years. Radiographs showed bilateral progressive massive pulmonary fibrosis. Five-year history of restless legs. Neurological examination negative, electroencephalography normal, diazepam completely ineffective.

Case 7.—An ex-miner, aged 66 with pneumoconiosis and emphysema who had been unable to work for the previous 13 years. Restless legs syndrome for five years. Neurological examination negative; radiographs disclosed considerable consolidation with collapse involving both upper lobes and emphysema in both lower lobes. Very satisfactory response to treatment with diazepam 5 mg. in the morning and 20 mg. at night.

Case 8.—An ex-miner, aged 67, who had been forced to retire at the age of 60 because of chronic bronchitis with emphysema. Restless legs syndrome of one year's duration. Neurological examination negative. He was referred by Dr. C. E. C. Wells for nerve conduction studies and, although these were normal, Dr. J. G. Graham noticed that during the test there were slight, apparently involuntary, fanning movements of the toes of both feet. During four weeks' observation in hospital these movements were confirmed by all observers. They were intermittent, waxed and waned, and were at least partially under voluntary control. He was quite unaware of the movements until his attention was directed to them. By an effort of will he could practically abolish the movements for a few minutes at a time. Neither the pains and discomfort in his legs nor the movements of his toes were in any way relieved by sedatives, diazepam, chlordiazepoxide, or carbamazepine. A left lumbar sympathetic block with 1% lignocaine was performed by Professor W. W. Mushin, without relief of pain or influence on the toe movements. Dr. J. M. Anderton, of the Department of Anaesthetics, found that the pains and toe movements were not influenced by altering the blood gas levels of oxygen and carbon dioxide. The patient subsequently committed suicide.

Discussion

It is clearly impossible to define a clinical syndrome in which there are no clinical signs and which may vary from one of mild transitory discomfort to a state of persisting nocturnal torment and insomnia. Seven of this series of eight patients were studied in hospital and no signs of disease of the nervous system were discovered. Electromyography and nerve conduction studies were carried out by Dr. J. G. Graham in four of them (Cases 5, 6, 7, 8). The results were normal in Cases 7 and 8 and showed only minor and questionable abnormalities in Cases 5 and 6. There was no peripheral neuropathy nor any evidence of peripheral vascular disorder.

On the other hand they were all suffering from chronic pulmonary disease and seven were severely disabled. Two patients (Cases 1 and 3) have since died. These eight patients are the only ones I have seen in recent years, and were referred to me solely because of their restless legs. I recollect others in whom there was no clinical indication of pulmonary disease, but, with the exception of a depressed patient who committed suicide many years ago, they are the severest examples I have encountered.

When one comes to consider a possible relationship between these two disorders several points can be made. Firstly, if there were some causal relationship between respiratory failure and restless legs we would expect to see it more often. The majority of respiratory cripples do not suffer from restless legs. In the literature of the Restless Legs Syndrome over the past 25 years there is no mention of chronic respiratory disorder. Secondly, it became clear from the cases studied in this series, that the restless legs syndrome was not influenced by the exacerbations and remissions of pulmonary failure which the patients experienced. Relief of the latter had no appreciable effect on their leg complaints. It is well known that in chronic pulmonary insufficiency hypoxia and hypercapnia may result in headache, confusion, and papilloedema. Twitching and tremors of the extremities may also occur, as in hepatic encephalopathy, but their cause is not known (Austen *et al.*, 1957). In accounts of the neurological complications of respiratory failure, restless legs are not described (Bickerstaff, 1967). On the other hand, peripheral neuropathy in chronic obstructive bronchopulmonary disease has been described (Appenzeller *et al.*, 1968). In eight patients with chronic pulmonary disease those authors found evidence of peripheral neuropathy in seven, but symptoms arose in only one patient. The remainder retained their deep tendon reflexes, but there were mild motor and sensory deficits and electromyography and nerve conduction studies were abnormal. A sural nerve biopsy on the patient with clinical neuropathy showed degenerative changes with Schwann cell proliferation.

Neurologists have been reminded of the clinical value of the P_{CO_2} measurements Table II. "It is the 'blood urea' of respiratory medicine" (Campbell, 1967). As in Case 3, sedatives may lead to further CO_2 retention with narcosis. My original impression in the early cases was that hypoxia or hypercapnia or some other metabolic disturbance was the likely explanation for the restless legs, but this appears doubtful.

Is the restless legs syndrome of psychogenic origin? I suspect that it is, and that the severe form met with in chronic progressive respiratory disease is a result of the wretched

nature of the suffering. Certainly, a visit to a ward of respiratory cripples is a depressing experience even for a neurologist. By contrast, patients severely disabled with arthritis or multiple sclerosis are rarely so demoralized.

TABLE II.—*Lung Function Studies in Restless Legs Syndrome*

Case No.	Vital Capacity (litres)	Forced Expiratory Volume (litres)	Maximum Breathing Capacity (l./min.)	P_{CO_2} (mm. Hg.)
1	1·8	0·45	15·75	53
2	1·75	1·20	42·0	53
3	1·6	0·475	16·6	85
4				
5	2·2	1·2	41·0	43
6	4·05	1·45	51·0	43
7	2·5	0·6	21·0	55
8	2·85	1·30	45·5	36

These tentative observations formed the basis of a communication to the Association of British Neurologists (Spillane, 1969) and their publication has been prompted by three recent contributions on the psychiatric aspects of patients with chronic respiratory disease. Burns and Howell (1969) found that breathlessness in airways disease cannot always be fully explained by the degree of airways obstruction. Anxiety, depression, and hysterical reactions frequently contribute to the inordinate breathlessness experienced. Psychiatric treatment contributed to resolution of the breathlessness.

Clark and Cochrane (1970) studied the personality of patients with chronic airways obstruction and found that it played an important part in determining the alveolar ventilation developed in face of the mechanical hindrance to breathing. The highly extrovert patient did better. Oswald *et al.* (1970) applied personality testing to a large series of patients with chronic respiratory disease. They found that all categories of patients showed a tendency towards neuroticism, anxiety, and introversion, and that these increased with progressive respiratory disability.

It is probably better to refer to the symptom rather than the syndrome of restless legs, as suggested by Strang (1967). He found 40 instances (30 mild, 10 severe) in a series of 600 cases of Parkinson's disease, but concluded that it was not psychogenic in nature and that the sensations were not usually painful. (He misquotes Gorman *et al.* (1965) in reporting that they found anxiety and depression were not common associated symptoms; they were). Again, however, the patient with Parkinsonism is often anxious or depressed and is rarely able to adjust himself to his fate. His immobility he finds intolerable.

Twitching and jerking movements of the feet and legs in this malady have been commented on by many writers, including Ekbom. It disturbs sleep and aggravates insomnia. The wives of my eight patients had long since sought another bed. In Case 8, however, there were movements of the toes which occurred in otherwise motionless legs and which appeared to be involuntary. Bornstein (1961) noted the difficulty in deciding whether the twitching and jerking movements of the legs described by the patient or witnessed by observers were voluntary or involuntary. Some patients say the legs "jump and jerk" or "twitch" "on their own" or "by themselves," while others state that "I have to do it" or "I cannot stop it." Each patient is by no means consistent in his opinions about the movements. He is often just as perplexed as his physician. There may be something akin to the toe movements seen in other cases of obscure pains in the legs (Spillane, 1969). Nocturnal myoclonus may of course be a presenting complaint unassociated with restless legs (Symonds, 1953).

The patient who enters the consulting-room shyly clutching a small cushion, which, it is said, is essential for sitting, and accompanies him everywhere, invariably complains of disagreeable sensations in the buttocks and not the legs, and is not troubled in bed. If restless legs syndrome was first dubbed "Anxietas tibiarum" (Ekbom, 1945) then the cushioned patient might be said to have "Anxietas ischiorum."

The lung function studies were carried out in the Miners' Chest Diseases Treatment Centre at Llandough Hospital, the M.R.C. Pneumoconiosis Unit at Llandough Hospital, the Pulmonary Function Laboratory at Sully Hospital, and the Cardiff Royal Infirmary. I am grateful to my colleagues for their advice and co-operation.

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