

Bilateral diaphragm paralysis and sleep apnoea without diurnal respiratory failure

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This is a case history of a patient with isolated bilateral diaphragm paralysis. It is presented because it offers insight into possible mechanisms of the respiratory failure which usually develops in this condition.

Case report

The patient, now 40 years old, presented in 1973 with mesangiocapillary glomerulonephritis (hypocomplementaemic with C3 nephritic factor) and subsequently developed progressive renal failure. In 1978 classical neuralgic amyotrophy (brachial neuritis) occurred in both arms and remitted over the next three months, his sister having had similar episodes some years before. Four months later he underwent a successful cadaver renal transplant. Subsequently the patient had several episodes of rejection and suffered from recurrent chest infections during the first year. One year after transplantation he developed avascular necrosis of the left femoral head (presumed to be due to steroids) and the hip was fractured in 1982 after a fall. He returned to work between these episodes and remains fairly active, using a walking stick.

In 1985 he presented with left lower lobe pneumonia after an influenza A infection and he was referred for respiratory assessment. Review of his chest radiographs showed progressively rising diaphragms bilaterally over the previous seven years, starting immediately after the renal transplant; a few linear basal shadows were apparent in the later films. Specific questioning disclosed a history of at least five years' increasing shortness of breath on exertion, substantial orthopnoea, and sleep disturbance. He had been taking azathioprine 175 mg, prednisolone 10 mg, bendrofluzide 5 mg, atenolol 200 mg, and prazosin 6 mg daily since the transplantation.

Examination in the supine posture showed obvious abdominal paradox with inspiration. There was no detectable weakness in any other muscles, although for some time before the renal transplant there had been generalised weakness, presumed to be due to chronic uraemia, and some specific weakness due to the neuralgic amyotrophy. His vital capacity in the upright posture was 3.4 l (60% predicted normal), falling to 1.2 l supine (65% fall). Arterial oxygen (P_{aO_2}) and carbon dioxide tensions (P_{aO_2} , P_{aCO_2}) were 9.7 and 5.4 kPa (73 and 41 mm Hg) respectively (posture not recorded); the alveolar-arterial oxygen gradient (P_{A-aO_2}) was

increased at 3.6 kPa (27 mm Hg) and was presumed to be due to basal atelectasis.

Two months later overnight oximetry was performed (Biox 2A). The awake semirecumbent arterial oxygen saturation (S_{aO_2}) was 93%. Most of the night was spent with a stable S_{aO_2} of about 92%. During three periods of 20 minutes there were regular recurrent dips in S_{aO_2} (rate 45/hour) to about 80% (lowest 69%), presumed to be associated with rapid eye movement (REM) sleep. At this stage no further action was taken except to advise sleeping propped up.

Two full sleep studies were performed 12 and 18 months later. They gave similar results. The patient's height and weight at this time were 1.9 m and 94 kg respectively. Awake values of P_{aO_2} and P_{aCO_2} in the semirecumbent posture were 10.1 and 4.5 kPa (76 and 34 mm Hg) respectively. He fell asleep rapidly and breathed regularly during all stages of non-REM sleep (70 minutes stages 3 and 4 and 211 minutes stage 2), with a stable S_{aO_2} of 90-91%. During 58 minutes of REM sleep he repeatedly showed gross hypoventilation and "central apnoeas" varying from 15 to 28 seconds, reducing the S_{aO_2} to about 80% and leading to arousals (figs 1 and 2). The apnoea rate during REM sleep was about 55 an hour. The transcutaneous P_{CO_2} (Hewlett-Packard 47210A) rose from 7.3 kPa (55 mm Hg) awake and semirecumbent (equivalent to a measured arterial value of 5.4 kPa, 41 mm Hg) to 9.1 kPa (68 mm Hg) by the end of the REM sleep period: an equal rise in arterial P_{CO_2} (1.8 kPa, 14 mm Hg) would be predicted from these transcutaneous measurements.¹ In obese subjects, with very poor inspiratory muscle function, surface measurements may miss small inspiratory efforts against a collapsed pharynx (that is, obstructive sleep apnoea). This man was not, however, obese, he had a reasonable maximum inspiratory pressure, and the abdominal tracing was flat during the apnoeic periods (in the presence of a paralysed diaphragm the abdominal wall movement is an indirect monitor of oesophageal pressure). In addition, his breathing was always absolutely quiet and there was no evidence of upper airways obstruction at any time. We are therefore confident that this was not obstructive sleep apnoea.

His lung volumes lying and standing have not changed since he presented two years ago. Transdiaphragmatic pressures measured in September 1986 by oesophageal and gastric balloons were less than 5 cm H_2O at all times during partial or maximal inspiratory manoeuvres, including sniffs. This therefore confirmed the presence of complete bilateral diaphragm paralysis. Maximum static expiratory mouth pressure at total lung capacity (TLC) was 90 cm H_2O , which is normal, particularly in view of his reduced TLC of 5.3 l (64% predicted normal). Maximum inspiratory mouth pressure at residual volume was 40 cm H_2O . Thus global

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Accepted 15 June 1987

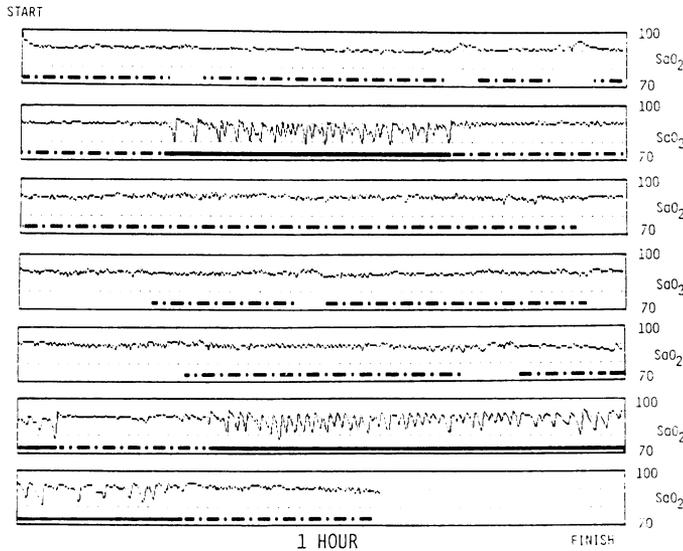


Fig 1 Six and a half hours' continuous tracing of percentage arterial oxygen saturation (SaO_2) from the second sleep study. Sleep stage is indicated by the coded lines under the SaO_2 : no coding indicates wakefulness or stage 1, alternate dots and dashes stage 2, 3 or 4 non-REM sleep, and the solid lines REM sleep. Note the recurrent falls in SaO_2 that occurred only during the REM sleep.

respiratory muscle weakness is very unlikely. The supine and sitting values of $Paco_2$ have varied from 4.5 to 5.4 kPa (34 and 41 mm Hg) but there has been persistent mild hypoxaemia with a Pao_2 as low as 8.5 kPa (64 mm Hg) during infections.

Discussion

We do not know why this man has isolated bilateral diaphragm paralysis. Antinuclear factor tests have given

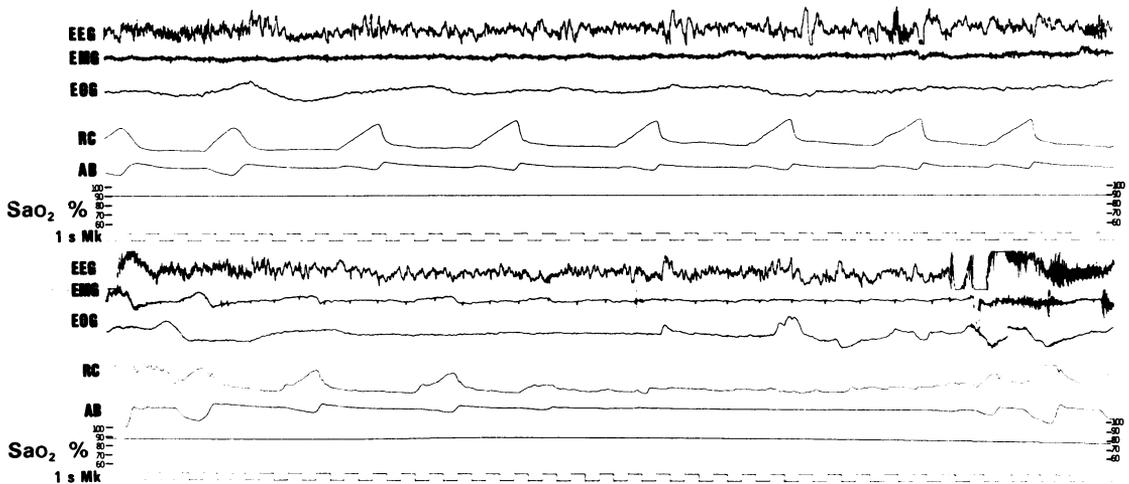


Fig 2 Two lengths of tracing from the second full sleep study each of 35 seconds' duration. The top panel was taken during its rapid progression from wakefulness to stage 1 to stage 2 sleep. Note the normal outward movement of the ribcage (RC), the paradoxical movement of the abdomen (AB) (uncalibrated inductance plethysmograph), and the constancy of arterial oxygen saturation (SaO_2). The bottom panel starts with an arousal from previous apnoea during REM sleep. This rapidly gives way to REM sleep again, with disappearance of RC and AB movement for about 15 seconds, until another arousal occurs. The SaO_2 fell to about 80% during this particular run of apnoeic periods (about 1.5 hours into the tracing in fig 1). EEG—electroencephalogram (C3/A2); EMG—chin muscle tone; EOG—electro-oculogram; 1 s Mk—one second marker.

repeatedly negative results and we do not think he has the "shrinking lungs" of systemic lupus erythematosus. The neuralgic amyotrophy preceded the first evidence of a bilaterally raised diaphragm by some months, with a normal chest radiograph four months later, before the transplantation. The first recognisable rise of the diaphragm occurred a few days after the renal transplant, progressing over the subsequent five years. The inevitable conclusion seems to be that this operation or the anti-rejection drugs (or both) were in some way the cause of the paralysis.

Descriptions of patients with bilateral diaphragm paralysis and their tendency to develop respiratory failure are not new. Newson Davis *et al*² described patients presenting with disturbed sleep whose main abnormality was bilateral diaphragm paralysis and severe lung volume embarrassment with blood gas deterioration when they lay supine. It was not clear why these patients should develop respiratory failure when their vital capacities were above the level usually associated with respiratory failure in neuromuscular disorders.² Blood gas tensions were measured during sleep but the phase of sleep was not identified. Skatrud *et al*³ first described substantial hypoventilation and apnoea with hypoxaemia in a patient with bilateral diaphragm paralysis during REM sleep. They postulated that the normal inhibition of muscles other than the diaphragm during REM sleep⁴ was particularly catastrophic for these patients. This would imply that apnoea resulted not from failure of respiratory centre output but from inability of the respiratory pump to respond; thus they are "apparently central" in that no effort is evident.⁵

It has also been suggested that these recurrent periods of hypoventilation and sometimes frank apnoea during REM sleep may lead to progressive respiratory failure, perhaps by resetting the central and peripheral chemoreceptors.^{3,5,6} The subjects with bilateral diaphragm paralysis reported so far with oximetry and sleep staging have, however, already had persistent carbon dioxide retention.^{3,6} We know that patients with various disorders that produce respiratory failure develop worsening arterial oxygen saturation during REM sleep,⁷⁻⁹ and thus we could argue that the patients with bilateral diaphragm paralysis are behaving no differently. Experimental studies in animals showed that transient diaphragm paralysis produced hypoventilation during REM sleep but not during slow wave sleep and wakefulness.¹⁰ This indicated that, even in the absence of any abnormalities of

resting blood gas tensions or central respiratory control, diaphragm paralysis produces specific REM sleep hypoventilation in dogs.

The findings in this patient also show that bilateral diaphragm paralysis may produce substantial hypoventilation and apnoea with hypoxaemia and hypercapnia during REM sleep before the development of hypercapnia and serious hypoxaemia during the day. This further supports the idea that specific REM sleep induced hypoventilation and apnoea may be the factor that initiates eventual respiratory failure in patients with bilateral diaphragm paralysis. Time will tell if this patient goes on to develop daytime hypoxaemia and hypercapnia.

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