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propranolol and indomethacin did not modify plasma renin activity or plasma aldosterone levels. Further repeated ECG monitoring of heart-rate variation in response to standing and during deep breathing showed unchanged values for both, R-R interval ratio at 30 and at 15 beats, and E:I ratio, suggesting that the symptomatic relief of postural hypotension was not due to improvement of sympathetic function or enhanced renin formation. The patient is now in the 10th month of continuous therapy. No orthostatic falls have occurred, nor have further neurological signs developed.

In conclusion, although the mechanism by which indomethacin acts remains uncertain, we believe that it deserves a trial as an alternative approach to mineral corticoid treatment for the Shy-Drager syndrome. Combined treatment with a β-blocking agent also can be pursued in those rare cases where multiple system atrophy, autonomic failure due to central involvement, and severe supine systolic-diastolic hypertension occur. As far as we know, this is the first report where this drug combination has been used successfully.

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References


Is the “cerebellar” incoordination of Refsum’s disease due to structural lesions in the cerebellum?

Sir: Refsum’s disease is a recessively inherited disorder whose cardinal features are a chronic peripheral neuropathy, pigmentary retinitis and an excess of phytanic acid in various tissues and body fluid lipids.1 Likewise Charcot-Marie-Tooth disease is an inherited chronic peripheral neuropathy in which some patients have a disorder of movement similar to essential (familial) tremor.2

In Charcot-Marie-Tooth disease, if proprioceptive deafferentation is sufficiently marked, incoordination may occur. In other cases, however, incoordination (with or without wasting) mimics cerebellar disease; this latter incoordination has been said to be due to various degrees of deafferentation and essential tremor.3,4 Harding and Thomas,4 when studying the clinical features of Charcot-Marie-Tooth disease assessed ataxia and tremor together because distinguishing between these two features separately often was difficult, a point recently emphasised in a survey of abnormal arm movements.5 Postmortem examination of patients with typical Charcot-Marie-Tooth disease showed that the cerebellum is normal;6 in none of the three cases with incoordination, categorised as cerebellar, that came to necropsy were the cerebellar systems abnormal.7 Patients with essential tremor may have incoordination mimicking cerebellar disease.8 This type of ataxia may be the most obvious manifestation of the disorder of movement for a period of time or may appear years after the onset of obvious essential tremor.9 Incoordination due to essential tremor affects more often the upper limbs alone, less frequently both the upper and the lower extremities together. It is interesting that in Refsum’s disease cerebellar incoordination used to be considered as a cardinal feature of the disorder.10 However, now that the disease is better understood, the cerebellar origin of the ataxia (which could not be explained in some cases on the basis of weakness and/or proprioceptive deafferentation) has been questioned.8 As Refsum pointed out in his review, incoordination is not present in some patients; when it is present, it is may be reminiscent of that in cerebellar disease and is evident either in the upper limbs only or in all four extremities. Other patients with the disease have a disorder of movement similar to essential tremor (see among other cases his summary1 on the patients reported by Rake and Sanders and by Fryer et al). It is worth noting that in the experience of the present author in patients with Charcot-Marie-Tooth disease associated with essential tremor, “cerebellar” incoordination may be absent,1,3 present in the upper limbs only,1,2 or present in all four limbs.2,4,5 Thus there seems to be a striking similarity in the manifestations and distribution of the “cerebellar” incoordination seen in patients with essential tremor, Refsum’s disease, and Charcot-Marie-Tooth disease associated with essential tremor, all of whom may exhibit either normal coordination, “cerebellar” incoordination in the upper limbs only or in all four limbs.

The site of the cerebellum as the cause of the “cerebellar” incoordination in Refsum’s disease may be seriously questioned for two reasons: (1) with the exception of some cases of cerebellar cortical atrophy in which incoordination (which incoordination was limited only to the lower limbs and/or ataxia of gait, the incoordination in the spinocerebellar degenerations affects equally the upper and the lower extremities. In Refsum’s disease the “cerebellar” ataxia may be limited, at least at one stage of the illness, to the upper extremities (see among other cases, the second patient reported by Gordon and Hudson14)2 (2) in the spinocerebellar degenerations presenting with incoordination there is damage to the cerebellum which is almost always more marked pathologically than suspected clinically, and which almost invariably can be seen by the naked eye. In contrast, as pointed out by Refsum, only five necropsy cases of Refsum’s disease have shown some microscopical changes in the cerebellum (see summary by Cammermeyer11). In this respect it has to be remembered that large parts of the cerebellum can be ablated without causing any cerebellar deficit.12 Furthermore some cases with Refsum’s disease show severe “cerebellar” incoordination in all four limbs with ataxia of gait without any pathological
changes in the cerebellum (see among others case III of Refsum reported by Cammermeyer,13 case III of Gordon and Hudson14 and the patient reported by Reese and Bareta15). It should be remembered that in essential tremor, no pathological changes in the cerebellum have so far been found. The present author has examined clinically two patients with Refsum's disease,15 16 and has studied the pathology of three cases; (ref 16, case III of Gordon and Hudson;16 unpublished necropsy, National Hospital Queen Square through the kindness of Professor LW Duchen). In none of these latter three cases was there any structural lesion in the cerebellum. In my view, the coordination difficulties mimicking cerebellar deficit that may occur in Refsum's disease are due to a combination of proprioceptive deafferentation associated with a disorder of movement similar to essential tremor. 

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Matters Arising

Sir: A recent article in your journal1 concerned the differentiation of haemorrhage and traumatic puncture in blood-stained cerebrospinal fluid (CSF) by a variety of methods. Of interest to us was the use of spectrophotometric scanning of CSF; a rather elaborate methodology involving the use of extinction criteria was given. We believe that for routine clinical use, the technique as described is overly complicated; we propose that it can be simplified without significant loss of accuracy, and with much more rapid results. The rationale for spectrophotometric analysis of CSF is as follows: a traumatic puncture results in the presence of red blood cells, and therefore haemoglobin, in the CSF; intracranial haemorrhage (of more than a few hours duration) results in the breakdown of the erythrocytes, with the resultant presence of bilirubin. Both substances are well-defined spectrophotometrically, and are easily detected. Bilirubin shows a peak at 455 nm, and haemoglobin has a characteristic series of peaks at 412 nm (Soret Band), 541 nm, and 576 nm.

Since neither haemoglobin nor bilirubin are normally present in CSF, the presence of either or both substances can readily be determined by a simple scan from 400 to 650 nm. Using a scanning spectrophotometer available in many hospital biochemistry laboratories, results can be obtained within minutes of receiving the sample.

We suggest the following interpretations, which are compatible with those of Buruma et al. An intracranial haemorrhage is suggested by the appearance of a bilirubin peak, and a traumatic puncture by the presence of the characteristic triple peaks of oxyhaemoglobin. A graph with all peaks would suggest a traumatic tap with the concomitant presence of a haemorrhage.

We have run a number of scans on clear CSF, and have shown that it does not contain any substances which could be confused with either bilirubin or haemoglobin at the specified wavelengths.

Our interpretations are based on two suppositions: firstly, that the interval between the onset of the haemorrhage and lumbar puncture is more than two or three hours (which is usually the case); and secondly, that the original intracranial event is self-limiting, in that bleeding does not continue over a prolonged period of time. This is true of most such episodes.

We conclude that adequate and rapid differentiation of haemorrhage and traumatic puncture in CSF can be made by a spectrophotometric scan as described.

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