Comment

Irradiation of the head and neck in childhood and adolescence for benign lesions has been associated with the subsequent development of both benign and malignant tumours, especially in the thyroid[2] and salivary glands.[3] Radiation exposure of the parathyroids must be similar to that of the thyroid, but there are few reports of hyperparathyroidism occurring after radiotherapy.

In 1975 Rosen *et al*[1] reported a 57-year-old woman with hyperparathyroidism who had undergone radiation for facial hirsutes 10 years before admission. Tissell *et al*[4] presented a series of 170 consecutive patients who had been operated on for primary hyperparathyroidism, 24 (14%) of whom had received radiation in the past. The average time between operation and radiation was 42 years. Triggs and Williams[5] observed parathyroid adenomas arising in 63% of adult rats who received ^{131}I on the second day of life.

This case is of particular interest because both parathyroid glands on the irradiated side of the neck showed hyperplasia. There was also a neuroma and a nodular goitre in this area (both recognised as consequences of radiation).

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[3] David, M C, jun, *American Journal of Surgery*, 1968, **116**, 518.
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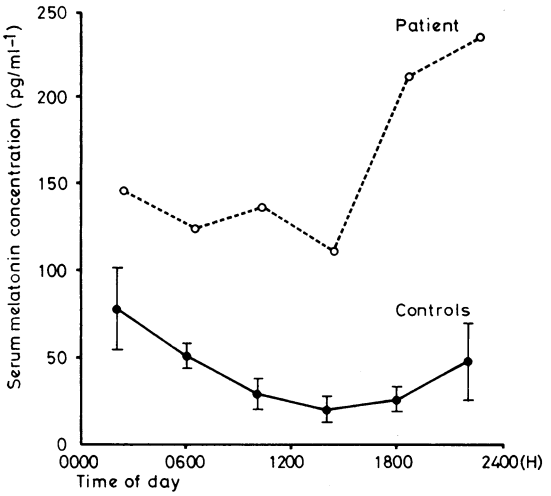
Melatonin as a tumour marker in a patient with pineal tumour

The inaccessibility of pineal tumours makes diagnosis difficult and radiotherapy more popular than surgery. The presence of a tumour marker would radically improve the ease of diagnosis and the monitoring of the efficacy of treatment.

Case history

A 37-year-old motor mechanic presented with a two-month history of occipital headaches, which lasted up to fifteen minutes, were worse in the mornings, and were alleviated by salicylates. For 10 days they had been associated with vomiting and diplopia on downward gaze. Apart from smoking 20 cigarettes daily his medical history had been uneventful. He had bilateral papilloedema with fundal haemorrhages and exudates, slight weakness of his left arm, and a left-sided extensor plantar response. His blood pressure was 120/70 mm Hg. Investigation showed normal serum urea and electrolyte concentrations, a normal blood count, and normal cerebrospinal fluid (CSF) pressure, sugar concentration, and serology. CSF protein ranged from 0·20 to 1·28 g/l. Computerised axial tomography and vertebral angiography showed a cystic tumour in the pineal region which was invading the brain stem. The left internal cerebral vein was occluded. Air ventriculograms showed normal-sized lateral ventricles. Histological examination of biopsy and subsequent necropsy specimens confirmed the presence of an intracranial pineocytoma.

Radioimmunoassay[1] of blood samples taken at four-hourly intervals two months before death showed melatonin concentrations of 147, 126, 138, 112, 213, and 238 pg/ml at 0200, 0600, 1000, 1400, 1800, and 2200, respectively. The figure shows that the daytime levels are raised about five-fold compared with controls. The overall nyctohemeral rhythmicity is retained, though with reduced amplitude. Postmortem analysis[1] of hydroxyindole-O-methyltransferase (HIOMT) in the pineal tumour tissue, an enzyme responsible for the synthesis of melatonin in the pineal, showed activities of 38 and 54 pmol/h/mg protein from two different areas of the tumour. The normal range of HIOMT concentrations in human postmortem pineal glands after sudden death is 268±30 pmol/h/mg protein. Thus these tumour HIOMT concentrations are five to seven times lower than normal. Such low concentrations are unlikely to be due to postmortem decline since bovine and lagomorph studies show that HIOMT activity is stable, even if kept in situ at room temperature up to eight hours after death.[1]



Nyctohemeral rhythm of serum melatonin (pg/ml) in patient with pineocytoma compared with five normal controls.

Comment

The endocrine activity of the pineal gland is well documented, with nyctohemeral variations in circulating melatonin concentrations and pineal enzyme activity,[1-3] though the precise importance of these findings in man is not yet fully elucidated. The pineal appears to have some effect on tumour activity, since in animals extirpation of the pineal increases susceptibility to known carcinogens and tumour growth, while administration of melatonin suppresses tumours.[1 4 5]

The results of investigations in our patient show that nyctohemeral rhythmicity of melatonin concentrations persists when extensive tumour tissue is present. Combined with the apparent absence of normal pineal tissue in necropsy samples this suggests that the activity of this patient's pineocytoma remained under at least some degree of rhythmic control. The presence of a nyctohemeral rhythm of melatonin in this patient indicates that the hospital lighting cycle did not suppress the patient's HIOMT activity. Thus the low enzyme activity found in the tumour tissue may reflect dedifferentiation of cellular biochemical activity in the tumour. In the context of persisting nyctohemeral fluctuation low enzyme activity may represent further evidence for persistence of part of a feedback mechanism which suppresses the enzyme activity of a greatly increased overall mass of melatonin-producing tissue in an (unsuccessful) attempt to maintain normal circulating concentrations of melatonin. Nevertheless, a third explanation is possible—that the large pineal mass is produced to maintain melatonin concentrations in response to a primary loss of HIOMT activity. Only further studies will resolve these difficulties.

Finally, the finding of a rise of daytime rather than night-time concentrations of melatonin in this patient provides convenient evidence that further clinical assessment of melatonin as a tumour marker for pinealomata may be conducted on mid-day serum samples rather than serial four-hourly samples.

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