Ultrasonically guided fine needle aspiration of suspect parathyroid tissue to determine parathyroid hormone concentration

Since the study of Arima *et al.*,¹ several reports have confirmed that enlarged parathyroid glands can be located preoperatively using ultrasound.² A general problem has been the difficulty of distinguishing nodular thyroid lesions from enlarged parathyroid glands.^{2,3} We report two cases in which parathyroid adenoma was correctly diagnosed using ultrasonically guided fine needle aspiration for determination of parathyroid hormone concentration.

Case reports

CASE 1

A 39 year old woman presented with hypercalcaemia. Two years previously she had had a stone removed from her left kidney, and she had recently had a one day episode of severe haematuria.

On admission serum calcium concentration was 3.66 mmol/l (14.7 mg/100 ml) (normal 2.20-2.70 mmol/l (8.8-10.8 mg/100 ml)); ionised calcium 1.80 mmol/l (7.2 mg/100 ml) (normal 1.13-1.24 mmol/l (4.5-5.0 mg/100 ml)); phosphate 0.49 mmol/l (1.5 mg/100 ml) (normal 0.80-1.50 mmol/l (2.5-4.6 mg/100 ml)); and parathyroid hormone 4.4 µg/l (normal 0.22-0.50 µg/l). Serum creatinine concentration was normal. Intravenous pyelography showed four stones in the right kidney. Parathyroid subtraction scintigraphy of the neck was inconclusive, but ultrasonography showed a 4 × 1.5 × 1.5 cm nodule with a low intensity echogenic pattern posterior to the lower pole of the right lobe of the thyroid gland. Fine needle (22 gauge) aspiration of the abnormal area (parathyroid tissue) and the thyroid gland was performed under ultrasonic guidance after injection of 1 ml isotonic saline. The aspirated specimens (0.1 ml each) were diluted to a final volume of 1 ml with sterile water and centrifuged, and finally the supernatant was analysed by C terminal radioimmunoassay.⁴ Parathyroid hormone concentrations were 150 µg/l in the parathyroid tissue and 2.0 µg/l in the thyroid gland.

At operation the ultrasonic finding was confirmed and a parathyroid adenoma removed. Postoperatively, serum calcium concentration returned to normal.

CASE 2

A 69 year old woman presented with hypercalcaemia and intermittent sinoatrial block. She had had dyspnoea and chest pains on effort for two years.

On admission serum calcium concentration was 3.08 mmol/l (12.3 mg/100 ml); ionised calcium 1.61 mmol/l (6.5 mg/100 ml); phosphate 0.71 mmol/l (2.2 mg/100 ml); and parathyroid hormone 1.14 µg/l. Pyelography and radiography of the chest and skeleton yielded normal results. Echocardiography showed stenosis of the aortic valves. Ultrasonography showed a 1 × 1 × 4 cm, well defined nodule with a homogenous low intensity internal echo pattern inferior to the upper pole of the thyroid gland. Aspiration of the abnormal area (parathyroid tissue) and the thyroid gland was performed under ultrasonic guidance as in case 1; parathyroid hormone concentrations were 200 and 1.5 µg/l, respectively. A parathyroid adenoma was removed, and serum calcium concentration returned to normal post-operatively.

Comment

Distinguishing enlarged parathyroid glands from nodular thyroid lesions is difficult because on ultrasonography both lesions may show the same pattern of echoes, resulting in false positive findings.^{2,3} Fine needle aspiration from masses suspected of being parathyroid glands was described by Doppman *et al.*, who used computed tomography and a mid-region specific radioimmunoassay to determine parathyroid hormone concentrations.⁵ Using a commercially available radioimmunoassay we found a small concentration of parathyroid hormone in the thyroid specimens from our patients, but in both cases the concentrations were different from those in the parathyroid tissue. The difference in concentration between thyroid and parathyroid glands depends on the volume aspirated and dilutional factors. We eliminated these problems by standardising the procedure for aspiration of the two glands.

Ultrasonically guided aspiration of suspect parathyroid tissue may improve the possibility of locating abnormal parathyroid tissue preoperatively. The value of preoperative ultrasonography in patients with clinical and biochemical evidence of primary hyperparathyroidism depends on the surgical approach used. It may also be helpful for

patients requiring re-exploration, those with ectopic or intrathyroidal parathyroid tissue, and those requiring a shortened surgical procedure as in case 2.

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Long term treatment of acromegaly with a long acting analogue of somatostatin

Somatostatin is a potent inhibitor of secretion of growth hormone in patients with acromegaly.¹ The native tetradecapeptide has a half life of less than four minutes, but a long acting analogue (selective mini somatostatin, SMS 201-995, Sandoz) has been shown to be 20 times more potent in inhibiting secretion of growth hormone in animals.² Selective mini somatostatin is an octapeptide protected against degradation by a D-phenylalanyl residue at the N terminus and an amino alcohol at the C terminus. We report initial results of using this analogue in patients with acromegaly.

Patients, methods, and results

Eight patients (six men, two women) gave their informed consent for the trial. Four had not received any previous treatment (cases 5, 6, 7, and 8), three had received only interstitial irradiation (cases 1, 2, and 4), and one (case 3) had received both interstitial and external irradiation and been treated with bromocriptine until two weeks before our study. Sweating was prominent in seven patients, and one (case 3) had severe headache.

Both before and during treatment with selective mini somatostatin growth hormone, insulin, and blood glucose concentrations were monitored at regular intervals for 24 hours in each patient. All subjects received selective mini somatostatin subcutaneously for three days. Three patients were given a 50 µg dose and two patients a 100 µg dose twice daily (at 0800 and 2000). The three remaining patients were treated thrice daily with 100 µg at 0800,

Mean (SEM) circulating concentrations of growth hormone before and after three days' treatment with selective mini somatostatin, and reductions in concentration after treatment

Case No	Age (years)	Mean concentration (mIU/l)		% reduction after treatment	
		Before treatment	After treatment	Mean over 24 h	2-4 h after dosing
50 µg twice daily					
1	53	32.5 (0.4)	11.4 (2.0)	64	81
2	44	29.2 (0.6)	6.4 (0.7)	78	92
3	28	42.0 (1.1)	22.5 (2.1)	46	78
100 µg twice daily					
4	30	27.3 (1.3)	5.9 (0.4)	79	95
5	55	48.1 (2.8)	11.5 (0.8)	76	93
100 µg thrice daily					
6	57	50.4 (1.4)	16.4 (0.8)	68	83
7	26	90.8 (2.0)	60.7 (2.0)	30	50
8	23	234.0 (1.9)	133.0 (9.0)	43	95

1600, and 2400. Student's *t* test was used to compare growth hormone concentrations before and during treatment.

The table shows mean circulating concentrations of growth hormone before and on the third day of treatment. Concentrations ranged from 32.5 to 234 mIU/l before treatment but were suppressed by 30-79% by the third day of treatment ($p < 0.001$). The maximal reduction in growth hormone concentration was achieved two to four hours after administration of the drug and was 50-95% of the basal concentration. After administration of the drug the concentration fell within 30 minutes to 30-83% of the basal concentration in all patients and remained suppressed for up to eight hours.

The patient with an intractable headache experienced relief for periods of two to three hours during the three days of treatment, which reduced his growth hormone concentration by 46%. Placebo was substituted on the fourth day and his headache promptly returned. He was then prescribed long term treatment with selective mini somatostatin in doses up to 100 µg every three hours. After seven months' continuous treatment his symptomatic relief was maintained and his growth hormone concentration was 34% of the concentration before treatment. A further patient (case 4) was treated for five months with selective mini somatostatin 100 µg twice daily. His condition improved, and his mean growth hormone concentration remained suppressed by 80%. Neither patient showed glucose intolerance during treatment or reported any difficulty with self injection or side effects even with the higher dose.

Comment

A clear relation exists between active acromegaly and increased morbidity and mortality.³ We believe that every effort should be made to treat such patients adequately. Complete surgical resection is often impossible, and pharmacological agents (for example, bromocriptine) if effective do not usually stop the secretion of growth hormone, so that concentrations remain raised. Radiotherapy takes a long time to achieve its full effect.⁴ Treatment with selective mini somatostatin seems likely to be a useful, fast acting adjunct in patients whose acromegaly is not rendered inactive by other treatment, because the underlying cause of acromegaly has been postulated to be either excessive growth hormone releasing factor or deficiency in somatostatin.⁵ All patients in our study, irrespective of the dose of selective mini somatostatin given, showed significant suppression of growth hormone concentrations, and two patients followed up for five and seven months were satisfactorily maintained on the drug. Long term trials are required to evaluate this potentially important new treatment.

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Intermediate filaments in the retina and retinoblastoma

Intermediate filaments are fibrillary organelles that are present in almost all eukaryotic cells. There are five different classes of these filaments—namely, keratins in epithelial cells, vimentin in mesenchymal cells, desmin in muscle cells, glial fibrillary acidic protein in astrocytes, and neurofilaments in most types of neurones. When a cell undergoes malignant change it usually retains its intermediate filaments, which can then be used as tissue type specific markers to diagnose and classify malignant neoplasms.¹

The origin of retinoblastoma remains unclear. A neuronal or neuroectodermal origin is presently favoured on the basis of morphological, biochemical, and immunological observations. The type of retinal cell from which the tumour develops, however, is unknown. We studied the types of intermediate filament present in the retina and retinoblastoma in man to try to clarify the histogenesis of retinoblastoma.

Methods and results

We examined 55 specimens of retinoblastoma fixed in formalin and embedded in paraffin, which represented all common histopathological types of the tumour. We used rabbit antiserum against vimentin and monoclonal antibodies to glial fibrillary acidic protein and to the 200 kilodalton neurofilament triplet protein, which were prepared in our laboratory and well characterised. A sensitive immunoperoxidase method of staining was used that makes use of the strong interaction between avidin and reagents coupled to biotin.

Müller's cells in normal retina stained positively for vimentin and often for glial fibrillary acidic protein. These two types of filament were also constantly seen in astrocytes in the inner retinal layers. Processes of ganglion cells in the nerve fibre and inner plexiform layers were stained by the monoclonal antibodies to neurofilaments. Surprisingly, we did not see any reactivity against the intermediate filaments studied in the horizontal cells, which contain vimentin and the three neurofilament triplet proteins in other species.² To verify this finding frozen sections of an eyeball enucleated because of retinoblastoma were studied by indirect immunofluorescence microscopy. The results were identical even though a rabbit antiserum that detected all three neurofilament triplet proteins was used in this experiment.

We did not detect any of the types of intermediate filament studied in retinoblastoma specimens. Vimentin and glial fibrillary acidic protein were seen, however, on many stromal elements within these tumours. In particular, cell processes that stained for neurofilaments could always be traced to infiltrated parts of the retina. A negative reaction was seen in the frozen sections studied by indirect immunofluorescence microscopy.

Comment

The human retina has previously been studied only for the presence of glial fibrillary acidic protein, and results have been inconsistent. The retinal complement of intermediate filaments in seven other species has been studied in detail,² and our results, with minor variations, agreed with these findings. The main difference was that, whereas vimentin and the three neurofilament triplet proteins are found in the horizontal cells in other species,² we could not detect any of the three types of intermediate filament studied in the horizontal cells of man. This emphasises the great interspecies variation in the intermediate filaments contained in horizontal cells.

As in previous studies^{3,4} glial fibrillary acidic protein was not detected in retinoblastoma cells, and these cells were also devoid of the other types of intermediate filament studied. Thus the cells from which retinoblastomas develop may be photoreceptors, bipolar cells, amacrine cells, or horizontal cells, all of which can occur in forms that do not contain intermediate filaments.² Recently, retinoblastoma cells grown in tissue culture were reported to contain glial fibrillary acidic protein.⁵ This observation indicates a need for further research.

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