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Addendum: Amino-acid Analysis of Protein Present in a Popliteal Artery Cyst

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The gel obtained from the cyst in Case 2 was stored frozen at −20° C. A portion was analysed by the microKjeldahl method and found to contain 0.52% nitrogen, corresponding to a protein content of approximately 3%. The remainder of the gel was lyophilized and 3 mg. of the dried material was hydrolysed with 1 ml. 6N HCl in an evacuated sealed tube at 115° C. for 20 hours. Hydrochloric acid was removed from the hydrolysate in a rotary evaporator and the residue analysed for amino-acids by Piez and Morris's (1960) modification of the method of Spackman, Stein, and Moore (1958). The results are shown in the Table, where they are compared with values for collagen from human tendon (Eastoe, 1955) and elastin from bovine aorta (Gotte, Stern, Elsden, and Partridge, 1963). The absence of hydroxyproline and hydroxylysine from the hydrolysate was confirmed by paper chromatography with the use of butanol/acetic acid/water (4:1:5) and water-saturated phenol as solvents and both ninhydrin and isatin as staining reagents. The paper chromatograms confirmed the presence of substantial amounts of glucosamine.

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It will be noted that the amino-acid composition of the protein differs markedly from that of a representative collagen, and the failure to detect hydroxyproline suggests that neither collagen nor elastin could be present in more than traces. The presence of glucosamine and the fact that the amino-acids recovered account for only 53.6% of the dry matter suggest that the main constituent may be a mucoprotein. There was insufficient material to investigate this matter further.

Amino-acid Composition of Protein from Popliteal Cyst Compared with Those of Collagen and Elastin

	Cyst Protein	Collagen	Elastin
Aspartic acid	38·4	50·5	15·6
Threonine	24·4	19·3	13·4
Serine	23·2	38·5	10·5
Glutamic acid	52·9	75·5	23·1
Proline	23·6	127·2	117·3
Hydroxyproline	0	96·2	11·4
Glycine	87·0	338·0	318·7
Alanine	41·0	115·6	223·6
Cystine	19·0	0	0
Valine	29·0	26·5	136·7
Methionine	4·3	6·0	2·0
Isoleucine	6·4	9·5	30·5
Leucine	32·3	27·2	67·2
Tyrosine	11·2	3·8	12·7
Phenylalanine	18·8	14·8	36·4
Lysine	42·3	22·5	8·2
Histidine	9·5	5·6	1·9
Arginine	19·9	51·2	9·8
Glucosamine	29·2	—	—
Hydroxylysine	0	9·3	—

Values are expressed as μmoles amino-acid per 10^5 g. dry matter for the unknown protein and μmoles per 10^5 g. protein for collagen (human tendon, Eastoe, 1955) and elastin (bovine aorta, Gotte *et al.*, 1963).

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Medical Memoranda

Chronic Thyrotoxic Myopathy with Involvement of Respiratory and Bulbar Muscles

Brit. med. J., 1967, 3, 415–416

Numerous reports of chronic thyrotoxic myopathy have followed Bathurst's (1895) original description. The incidence of respiratory and bulbar muscle weakness in previously reported cases was extremely rare; furthermore, in most of these cases the diagnosis could be challenged because of lack of proper documentation or correct interpretation. In a review of the condition by Whitfield and Hudson (1961) the respiratory and bulbar muscles were not mentioned, and in a reappraisal by Havard (1962) it was stated that these muscles are little if at all affected.

This report describes a case of chronic thyrotoxic myopathy in which weakness of the respiratory and pharyngeal muscles was a prominent feature.

Case Report

An 83-year-old man was admitted to hospital with nine months' history of progressive loss of weight, generalized weakness and lassitude, shortness of breath on exertion, and difficulty in swallowing.

During that period he was investigated elsewhere but no definite diagnosis was made. Initially he was described as being thin, but he looked fit and active and no abnormal physical signs were noted. Three months before admission he developed oedema of the ankles and distension of the neck veins; he was treated for congestive cardiac failure but his condition continued to deteriorate.

When first seen in hospital he had lost 3 stones (19 kg.) in weight. He was dyspnoeic at rest and so weak that he had difficulty in rising from the sitting or lying position; he was unable to swallow solid food and had difficulty with liquids.

On examination he looked emaciated and ill. The pulse was regular at 90 a minute, was collapsing in character, and the blood pressure was 160/60. The apex beat was forcible but not displaced. The jugular venous pressure was raised and he had oedema of the ankles. Chest expansion was poor and there were a few scattered rhonchi in both lung fields. The liver and spleen were not palpable. The striking findings were confined to the neuromuscular system, which showed profound weakness and wasting of the proximal and distal muscles of the limbs and of the trunk muscles. There were no fasciculations and the tendon reflexes were normal. The cranial nerves were intact and there was no sensory loss.

The thyroid gland was not enlarged and no thyroid bruit could be heard. There were no eye signs, apart from a slight lid lag. His hands were warm and he had fine tremors of the outstretched fingers.

Investigations.—Hb 14 g./100 ml.; white cell count 5,000/cu. mm.; E.S.R. 22 mm. in one hour (Westergren); blood urea 47 mg./100 ml. Serum electrolytes, liver-function tests, and

glucose-tolerance curve were normal. Chest *x*-ray examination showed a normal-sized heart and clear lung fields, and the E.C.G. was normal. Barium studies of the gastrointestinal tract did not reveal any abnormality.

In view of the negative barium studies, the dysphagia was ascribed to weakness of the pharyngeal muscles as part of a generalized myopathy. The diagnosis of chronic thyrotoxic myopathy was confirmed by thyroid function studies which showed protein-bound iodine 12.7 μg./100 ml., radioactive iodine uptake 87.7% at four hours and 70% at 24 hours, and B.M.R. +21% and +24%. Myasthenia gravis was excluded by a negative edrophonium chloride (Tensilon) test.

Respiratory Function Tests

	Before Treatment	After Isoprenaline Inhalation	After Intravenous Edrophonium (10 mg.)	15 Days	3 Months
				After Treatment	
Vital capacity (ml.)	1,550	1,500	1,600	2,500	3,000
Predicted V.C. (ml.)	3,000	3,000	3,000	3,000	3,000
% of predicted V.C.	52	50	53	83	100
% in 0·75 second ..	40	41	43	42	45
M.B.C. (l./min.) ..	25	25	27	42	54
Predicted M.B.C. ..	70	70	70	70	70
% of predicted M.B.C.	36	36	39	60	77
Peak expiratory flow rate (l./min.) ..	185	220	190		270
Arterial blood:					
*p*H	7·404				
CO_2 tension ..	42·5 mm. Hg				
O_2 saturation ..	95·5%				
Po_2	84 mm. Hg				

The respiratory function tests (see Table) showed a moderate degree of airway obstruction with an $F.E.V._{0.75}$ of 40% but a considerable reduction in vital capacity to 52% of the predicted value, presumably due to respiratory muscle weakness. There was no improvement in the vital capacity after isoprenaline inhalation or intravenous edrophonium.

The patient was treated with carbimazole 20 mg. t.d.s. at first, but the dose had to be increased subsequently to 30 mg. t.d.s. Improvement began on the seventh day, and when he was seen three months later his symptoms had completely subsided. The dysphagia was one of the first symptoms to respond, and after two weeks' treatment swallowing had returned to normal. The response of respiratory function was dramatic, and on the fifteenth day of treatment the vital capacity was 83% of the predicted value.

It is interesting to note that as soon as clinical improvement became manifest the patient developed overt signs of hyperthyroidism with motor hyperactivity and a marked lid retraction and lid lag. These signs were presumably masked by the severe muscle weakness.

Discussion

In many respects the clinical features of this case resemble those in previous reports. Thus the relatively short duration of the illness, the masking of signs of thyrotoxicosis, the distribution of muscle weakness and wasting, and the excellent response to treatment have all been emphasized in the past. In addition, the severity of thyrotoxicosis as shown by thyroid-function tests has been stressed.

The B.M.R. is usually high but, as in the present case, it may be only slightly raised (Millikan and Haines, 1953 ; Collings and Lienhard, 1957 ; Gimlette, 1959).

Electromyographic and histological techniques have been extensively studied and frequently reported in the past but have failed to provide any help in the diagnosis ; the findings have been normal, equivocal, or non-specific (Millikan and Haines, 1953 ; Kite *et al.*, 1954 ; Collings and Lienhard, 1957 ; Hed *et al.*, 1958 ; Melville, 1959). It has also been shown that there is no quantitative difference in creatinine excretion in patients with chronic thyrotoxic myopathy or uncomplicated thyrotoxicosis (Quinn and Worcester, 1951). These tests were not carried out in our patient. It is now generally agreed that the diagnosis should mainly depend on clinical assessment, and an essential requirement is a satisfactory response to treatment.

Weakness of the respiratory and bulbar muscles has been described in cases of "acute thyrotoxic myopathy" ; it is doubtful, however, if this condition exists as a distinct entity, and it would appear that such cases were probably examples of myasthenia gravis associated with thyrotoxicosis (Millikan and Haines, 1953).

In chronic thyrotoxic myopathy involvement of these muscles must be exceedingly rare or overlooked in its milder forms. In five previously reported cases there were insufficient data to reliably exclude myasthenia gravis.

Death from respiratory failure has been reported in three cases ; the case reported by McEachern and Ross (1942) was thought to be an example of chronic thyrotoxic myopathy in spite of a myasthenic defect in the electromyogram and a positive response to neostigmine. In the other two cases myasthenia was not excluded (Morgan and Williams, 1940 ; Thorn and Eder, 1946).

Dysphagia was the presenting symptom in the case reported by Leach (1962), but the patient was also suffering from dystrophia myotonica.

Heinrich *et al.* (1962) reported a case of "encephalopathic hyperthyroidism" in a man aged 70 who presented with dysphagia, had most of the features of chronic thyrotoxic myopathy, but, in addition, had a few neurological signs which could well have been due to an associated cerebrovascular disease.

I am grateful to Dr. C. E. Davies for allowing me to report this case.

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