Amyloid goitre and hypothyroidism secondary to cystic fibrosis

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Summary

Although cystic fibrosis (CF) is still the most frequently fatal childhood disease, many adults now survive into their third and fourth decades. Uncommon complications of chronic diseases, such as amyloidosis, while infrequent, may now appear during the course of CF in adulthood. We present a case of a patient with CF who was diagnosed with hypothyroidism due to amyloid deposits in the thyroid.

Keywords: cystic fibrosis, amyloidosis, hypothyroidism

The most frequent complications of cystic fibrosis (CF) are lung infections and respiratory failure. Secondary amyloidosis is an extremely rare manifestation of this disease. Less than 25 cases have been reported in the world literature since the disease was first described in 1938.¹ The most commonly affected organs are the kidneys, liver and spleen.^{2,3} Thyroid infiltration by amyloid deposits in CF is extremely rare.^{4,5} We have found no previous references to these associations with hypothyroidism. We present a case of hypothyroid goitre secondary to amyloid deposits in an adult with CF.

Case report

A 32-year-old male was admitted with dyspnoea, coughing, purulent expectoration, and asthenia. He had been diagnosed as having CF at the age of 7. The symptoms were minimal until the age of 18. Later, he was referred with recurrent respiratory infections. Physical examination revealed a puffy face, cold skin, and central cyanosis. A soft and diffuse goitre was noted. Heart auscultation revealed bradycardia and quiet sounds. On lung auscultation, coarse crackles could be heard, especially in the lower lobes. Moderate hepatomegaly and oedema in the legs were observed. Laboratory findings disclosed a white blood cell count of $13 \times 10^9/l$, haemoglobin 7.8 g/dl, packed cell volume 0.37, platelets $529 \times 10^9/l$, erythrocyte sedimentation rate 115 mm/h, serum glutamic oxaloacetic transferase 88 $\mu\text{mol/l}$, gamma-glutamyl transferase 0.04 $\mu\text{mol/l}$, serum albumin 0.2 mmol/l, creatine phosphokinase 200 U/l and creatinine 61 $\mu\text{mol/l}$. Urine analyses demonstrated pro-

teinuria of 2.4 g/24 h. Basal arterial gasometry: PO_2 7.1 kPa, PCO_2 5.9 kPa, pH 7.39. Thoracic radiology and computed tomography (CT) showed severe bronchiectasis and peribronchial thickening (figure 1). Serum thyroid hormone levels were as follows: triiodothyronine 0.7 (1.2–3.4) nmol/l, thyroxine 100 (51–142) mol/l, free thyroxine 32 (10–36) pmol/l, thyroid-stimulating hormone 32 (2–11) mU/l. Thyroxine-releasing hormone stimulating test revealed an exaggerated response. Thyroglobulin and thyroid microsomal antibodies were not detected. Lung function test disclosed a severe obstructive pattern: force expiratory volume in 1 s (FEV_1) 840 ml (24%), force vital capacity (FVC) 1350 ml (34.7%), FEV_1/FVC 0.62. *Pseudomonas aeruginosa* grew from sputum cultures. On thyroid sonography a diffuse increase of both lobes was seen without nodules or cysts. The fine needle aspiration of the gland showed no evidence of Hashimoto's thyroiditis and secondary amyloid desposits were found (figure 2). On abdominal sonogram, a diffuse homogenous hepatomegaly was observed. Rectal biopsy revealed amyloidosis. On genetic assay, homozygote delta F508 mutation was detected. The patient was treated with L-thyroxine 100 g/day and an amelioration was noted.

Discussion

Although some patients with CF die during early childhood and adolescence, many affected persons lead relatively normal lives into their third and fourth decades. The identification of the gene responsible for CF has improved

Figure 1 CT scan of the thorax: severe and diffuse bronchiectasis and peribronchial thickening

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Figure 2 Thyroid fine needle aspiration: amorphous material without cells, with a mild inflammatory component; stain Congo-red (Papanicolaou 20x)

understanding of the observed clinical variability in CF disease expression.⁶ The typical mutation associated with CF, delta F508, was identified in our patient. As reported by Lester *et al.*,⁶ the presence of the delta F508 mutation allele does not confer a more severe prognosis, nor could it be used to predict disease severity at the time of diagnosis.

Systemic amyloidosis is a rare complication of CF^{1-3,5} because, up to now, the short life expectancy of these patients has precluded the development of this complication. Amyloid infiltration of the thyroid gland in CF is exceptional.⁴ Hypothyroidism associated with amyloid goitre has been previously reported,⁷ and goitre due to amyloidosis in patients with

Learning points

- CF is a childhood disease but nowadays patients may lead normal lives into their third and fourth decades
- amyloidosis had been an uncommon complication of cystic fibrosis due to patients dying early
- associated with the longer survival of CF patients, atypical locations of amyloid deposits, such as in the thyroid, with secondary manifestations (hypothyroidism), should be considered

CF has been described.^{1,3} This case is interesting due to the reduction in thyroid function caused by amyloid deposits in the substance of the gland in a patient with CF. His mild renal and liver function failure were also due to the amyloid deposits. We could find no other cases of hypothyroidism and amyloid goitre in CF.

Until recently, CF patients usually died during the first years of their lives. This accounts for the infrequent occurrence of systemic amyloidosis in CF. Due to therapeutic advances, survival has improved and the pattern of the disease will therefore change, with atypical locations of amyloid deposits due to CF becoming more frequent. Although hypothyroidism due to amyloid deposits in goitre is very rare, its prevalence may increase in adults with CF in the future.

1 Gaffney K, Gibbons D, Keogh B, Fitzgerald MY. Amyloidosis complicating cystic fibrosis. *Thorax* 1993; **48**: 949–50.

2 Travis WD, Castile R, Vawter G, *et al.* Secondary (AA) amyloidosis in cystic fibrosis. A report of three cases. *Am J Clin Pathol* 1986; **85**: 419–24.

3 Castile R, Shawachman H, Travis W, Hadley CA, Warwick W, Missmahl HP. Amyloidosis as a complication of cystic fibrosis. *Am J Dis Child* 1985; **139**: 728–32.

4 Kyle RA, Bayrd ED. Amyloidosis: review of 236 cases. *Medicine* 1975; **54**: 271–99.

5 McGlennen RC, Burke BA, Dehner LP. Systemic amyloidosis complicating cystic fibrosis. A retrospective pathologic study. *Arch Pathol Lab Med* 1986; **110**: 879–84.

6 Lester LA, Krant J, Lloyd-Still J, *et al.* Delta F 508 genotype does not predict disease severity in an ethnically diverse cystic fibrosis population. *Pediatrics* 1994; **93**: 114–8.

7 Kanoth T, Shimada H, Uchino H, Matsamura K. Amyloid goiter with hypothyroidism. *Arch Pathol Lab Med* 1989; **113**: 542–4.