

Familial Mediterranean Fever, an Amyloid Thyroid Goiter and an Enlarged Parathyroid Gland

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Secondary (AA) amyloidosis is a dreaded complication of familial Mediterranean fever and other chronic inflammatory diseases. The deposition of AA amyloid can cause dysfunction in almost every organ. In patients with FMF, colchicine is an efficient therapy in preventing formation, and subsequent deposition, of visceral AA amyloidosis.

This report details the problems associated with a diffuse thyroid goiter, secondary to AA amyloidosis, in a young renal transplant recipient and also discusses the surprise finding at thyroidectomy of an enlarged parathyroid gland.

PATIENT DESCRIPTION

In August 2011, a 40 year old man underwent elective total thyroidectomy for a diffuse thyroid goiter that had grown rapidly over the previous year. His relevant past history included recurrent attacks of fever and abdominal pain from age 20. FMF was diagnosed at age 28, and colchicine was begun. Colchicine dosage was maintained at 1 mg/day, since any further increase in colchicine dosage caused the patient unacceptable diarrhea. By age 30, he had begun chronic hemodialysis therapy because of chronic kidney disease stage V, presumably due to renal AA amyloidosis. No renal biopsy was performed. In 2003, at age 32, the patient received a living donor renal transplant. Transplant function was immediate, and renal function remains excellent to the present day (August 2011, serum creatinine 1.0 mg/dl). Chronic immunosuppression includes prednisone, cyclosporine and mycophenolate. Post-transplant colchicine dosage was maintained at 1 mg daily.

By 2010, the patient's thyroid gland was growing and starting to cause him discomfort, especially during sleep-time breathing. By 2011, thyroidectomy was deemed necessary

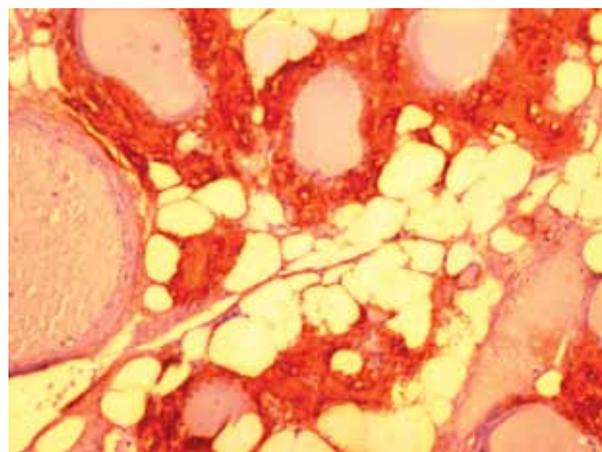
because of increasing difficulties with breathing and swallowing. Preoperative thyroid function tests and serum calcium and phosphorous levels were all normal. In 2008, an intact N-terminal parathyroid hormone level had been normal.

At surgery, total thyroidectomy was performed successfully. The superior right-sided parathyroid gland was markedly enlarged (1.5 x 2 cm) and uneventfully resected. The postoperative recovery was uncomplicated. Postoperative serum calcium and phosphorous levels remained normal, without the need for any calcium-containing medications or vitamin D analogs. A repeat PTH level, in October 2011, was 29 ng/L; again, it was normal. The patient is currently taking colchicine 1.0–1.5 mg daily and oral thyroxine 100 µg daily.

Histopathological findings included diffuse and extensive infiltration of the parenchyma by an eosinophilic amorphous material consistent with amyloid [Figure A]. This material stained intensely with Congo red [Figure B]. An amyloid A immunoperoxidase reaction was positive. Extensive fat cell metaplasia was seen between the thyroid follicles. The parathyroid gland was similarly involved by extensive AA amyloid deposits.

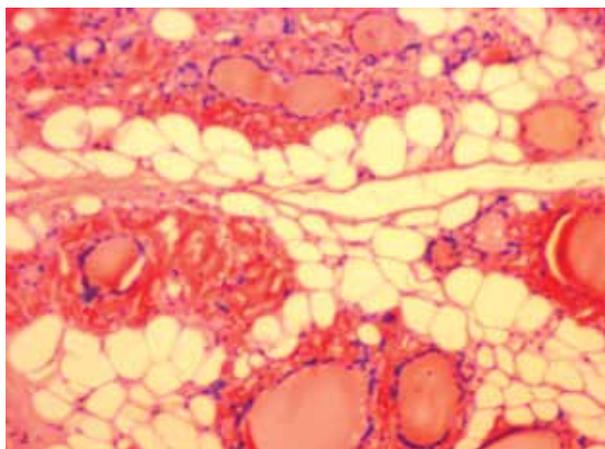
PTH = parathyroid

[A] Thyroid tissue showing extensive stromal infiltration with amyloidosis. Fatty infiltration of the stroma is evident. Some thyroid follicles are enlarged (hematoxylin & eosin, x10)



FMF = familial Mediterranean fever

[B] Congo red stain (x10) of thyroid tissue. A strongly positive Congo red stain for amyloid was confirmed with characteristic apple green birefringence under polarized light (not seen here).



COMMENT

In 1974, Kennedy et al. [1] summarized the literature associated with amyloid involvement of the thyroid gland. They found that small AA amyloid deposits were common in the thyroid gland in patients with rheumatoid arthritis, tuberculosis and bronchiectasis, but these deposits did not lead to overt clinical problems. These authors also described seven patients with amyloid thyroid goiter, six of whom had histopathologically confirmed AA amyloidosis. The goiters were diffuse, rapidly enlarging, and caused pressure symptoms. All seven patients were euthyroid [1]. The amyloid deposits were found in the thyroid stroma and in the small intra-thyroid vasculature.

Despite the extensive infiltration of the thyroid gland by the amyloid goiter, there are only a few cases of primary hypothyroidism. One such case, with plasmatic-type multicentric giant lymph node hyperplasia, was described by Kanoh et al. [2].

AA amyloid goiter can occur in patients with FMF. In 1979, Danovitch and co-workers [3] described three young North African Sephardic Jews* with FMF who later developed renal AA amyloidosis and chronic kidney disease stage V. Rapid thyroid enlargement developed approximately 10 years after the initial diagnosis of FMF and 2–5 years after

* Of North African or Middle Eastern origin

the patients began hemodialysis. Two patients were clearly euthyroid, and the third may have been slightly hypothyroid. Extensive AA amyloidosis was seen on thyroid biopsy in all three patients. Arteriolar and capillary lumens were severely occluded because of amyloid thickening of the vessel walls [3]. Danovitch et al. surmised that “as hemodialysis continues to prolong the lives of patients with systemic amyloidosis, organs not usually associated with amyloid deposition will become involved.” To combat this problem, patients with FMF should continue colchicine therapy, even after they have reached end-stage renal failure. However, colchicine dose is often reduced in these patients because of the fear of colchicine-induced neurotoxicity and myotoxicity.

What of parathyroid amyloidosis? If present, it is rare and of little clinical significance. In 1984, Ellis and Mawhinney [4] studied parathyroid glands obtained postmortem from eight patients who died from chronic renal disease and “generalized amyloidosis.” All eight patients had amyloid involvement of the parathyroid glands. In six patients the deposits were AA amyloidosis [4]. However, no patient had evidence of hypoparathyroidism. In fact, all eight patients had varying degrees of secondary hyperparathyroidism, a common complication of severe chronic renal failure. To the best of our knowledge, only one patient with AA amyloidosis and who presented with polyglandular endocrine failure also developed severe hypoparathyroidism [5]. In that patient, no parathyroid tissue was available for histological examination.

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“The reverse side also has a reverse side”

Japanese proverb

“A superior man is modest in his speech, but exceeds in his actions”

Confucius (c. 551-478 BCE), Chinese teacher, editor, and social philosopher of the Spring and Autumn Period of Chinese history. The philosophy of Confucius emphasized personal and governmental morality, correctness of social relationships, justice, and sincerity