29. Wann LS, Dillon JC, Weyman AE, et al: Echocardiography in bacterial endocarditis. N Engl J Med 1976; 295:135-139

30. Rubenson DS, Tucker CR, Stinson EB, et al: The use of echocardiography in diagnosing culture-negative endocarditis. Circulation 1981; 64:641-646

31. Sarma R, Prakash R, Kaushik VS, et al: Reliability of two-dimensional echocardiography in diagnosing fungal endocarditis. Clin Cardiol 1983; 6:37-40

32. Vishniavsky N, Sagar KB, Markowitz SM: *Aspergillus fumigatus* endocarditis on a normal heart valve. South Med J 1983; 76:506-508

33. Dillon JC, Feigenbaum H, Konecke LL, et al: Echocardiographic manifestations of valvular vegetations. Am Heart J 1973; 86:698-704

34. Mintz GS, Kotler MN: Clinical value and limitations of echocardiography: Its use in the study of patients with infectious endocarditis. Arch Intern Med 1980; 140:1022-1027

35. Lawrence T, Shockman AT, MacVaugh H: *Aspergillus* infection of prosthetic aortic valves. Chest 1971; 60:406-414

36. Carrizosa J, Levison ME, Lawrence T, et al: Cure of *Aspergillus ustus* endocarditis on a prosthetic valve. Arch Intern Med 1974; 133:486-490

37. Wagner DK, Werner PH, Bonchek LI, et al: Successful treatment of postmitral valve annuloplasty *Aspergillus flavus* endocarditis. Am J Med 1985; 79:777-780

38. Hairston P, Lee WH: Management of infected prosthetic heart valves. Ann Thorac Surg 1970; 9:229-237

39. Gomez RG, Estrada AV, Ortiz RL: Endocarditis por *Aspergillus:* Informe de un caso tratado quirurgicamente con exito. Arch Inst Cardiol Mex 1981; 51:549-553

Alopecia Universalis as a Feature of Polyglandular Autoimmunity Type I

KHALED IMAM, MD
Allen Park, Michigan

MOHAMMED ABDULLAH, MD
New Orleans

JAMES V. FELICETTA, MD
Phoenix

THE OCCURRENCE of two or more endocrine diseases in the same patient has been noted since the 19th century.[1] Numerous workers have described an association of multiple autoimmune diseases of the endocrine organs, including the adrenal glands, endocrine pancreas, thyroid, parathyroid, and ovaries. These endocrine disorders are frequently associated with other disorders of tissue-specific autoimmunity, such as pernicious anemia, vitiligo, and alopecia.

These polyglandular autoimmunity (PGA) syndromes have been classified into two major types, based on familial clustering.[2,3] Type I manifests at least two features from the triad of Addison's disease, hypoparathyroidism, and chronic mucocutaneous candidiasis. Type II is present in patients who have Addison's disease with autoimmune thyroid disease or insulin-dependent diabetes mellitus, or both, but who do not have hypoparathyroidism or candidiasis. Associated immune disorders other than hypoparathyroidism and candidiasis may also be present with either type.

We report here the case of a patient who had the added feature of alopecia universalis as a manifestation of her type I polyglandular autoimmunity syndrome. Although alopecia areata is frequent in patients with the type I form,[2] alopecia universalis is rare. Alopecia universalis was one of the most striking features in our patient, contributing greatly to her morbidity by exacerbating her emotional instability.

(Imam K, Abdullah M, Felicetta JV: Alopecia universalis as a feature of polyglandular autoimmunity type I. West J Med 1988 Sep; 149:338-341)

From the Division of Endocrinology and Hypertension, Department of Medicine, Wayne State University School of Medicine, Detroit, and the Veterans Administration Medical Center, Allen Park, Michigan (Dr Imam); the Division of Endocrinology, Tulane University School of Medicine, New Orleans (Dr Abdullah); and the Medical Services, Veterans Administration Medical Center, Phoenix (Dr Felicetta).

Reprint requests to James V. Felicetta, MD, Chief, Medical Services, Veterans Administration Medical Center, 7th St and Indian School Rd, Phoenix, AZ 85012.

ABBREVIATIONS USED IN TEXT

ACTH = adrenocorticotropic hormone
FSH = follicle-stimulating hormone
HLA = human leukocyte antigen
LH = luteinizing hormone
PGA = polyglandular autoimmunity
PTH = parathyroid hormone

Report of a Case

The patient initially presented to Detroit Children's Hospital in 1962 at age 3 with a history of generalized seizures for one month and a chronic fungal infection of the nails. Laboratory studies at that time showed a serum calcium level of 4.4 mg per dl and a phosphorus of 13.5 mg per dl. A diagnosis of primary hypoparathyroidism was made on the basis of a pronounced phosphaturic response to the intravenous administration of parathyroid hormone and a return to normal of calcium and phosphorus levels after giving the hormone. An adrenocorticotropic hormone (ACTH) stimulation test (cosyntropin test) reportedly showed an appropriate rise in the urinary cortisol level. Therapy was initiated with elemental calcium and vitamin D.

She did well initially except for the progressive development of alopecia areata beginning at age 5. This had progressed to alopecia universalis by age 8, and she always wore a wig after that time. According to her parents, emotional instability of increasing severity first became manifest at the time she began wearing the hairpiece. The diagnosis of hypoparathyroidism was confirmed at Grace Hospital in Detroit in 1979 when she was 20. At that time a C-terminal parathyroid hormone (PTH) level was less than 150 pg per dl (normal 197 to 315), with a simultaneous serum calcium level of 6.4 mg per dl (normal 8.8 to 10.0) and an ionized calcium of 2.56 mg per dl (normal 3.7 to 4.5). An 8 AM plasma cortisol level was 10 μg per dl, a 4 PM cortisol level 8.7 μg per dl, thyroxine 9.8 mg per dl, triiodothyronine resin uptake 40%, follicle-stimulating hormone (FSH) 12 mIU per ml, and luteinizing hormone (LH) 66 mIU per ml. Calcium supplementation and vitamin D therapy were continued.

At age 23, she presented to a North Carolina hospital with nausea, vomiting, weakness, dizziness, salt craving, increasing skin pigmentation, and an 18-kg (40-lb) weight loss over three months. Her blood pressure was 80/40 mm of mercury. Her serum calcium level was 6.5 mg per dl; an 8 AM cortisol level was undetectable. An intravenous ACTH stimulation test elicited values of less than 1 μg per dl at baseline, 30 minutes, and 60 minutes. Her baseline ACTH level was more than 250 pg per ml (normal 20 to 100). A computed tomographic scan of the head revealed bilateral basal ganglia calcification, consistent with hypoparathyroidism. A regimen of calcium carbonate; calcitriol, 0.5 μg daily; and cortisone acetate, 37.5 mg daily in divided doses, was started.

She was first admitted to Wayne County General Hospital in Detroit in December 1981 because of profound somnolence and weakness. According to her boyfriend, she had been extremely sporadic in taking her medications. She had also been experiencing considerable emotional stress related to her alopecia universalis and had noted intermittent amenorrhea and irregular menstrual cycles for more than two

TABLE 1.—*Manifestations of the Polyglandular Autoimmunity Syndrome Type I in a Female Patient and Her Brothers*

Feature of Syndrome	*Index Patient Born 1958*	*1st Brother Born 1961*	*2nd Brother Born 1970*
Hypoparathyroidism	Onset age 3½ yr	Onset age 8 yr	Onset age 4½ yr
Addison's disease	Onset age 23 yr	Onset age 16 yr	Onset age 11 yr
Mucocutaneous candidiasis	Yes	Yes	Yes
Vitiligo	Yes	No	Yes
Alopecia	Universalis	Areata	No

years. Her blood pressure while supine was 88/56 mm of mercury with a pulse of 102 per minute, and while sitting 76/54 mm of mercury with a pulse of 120 per minute. Her temperature was 36°C (97°F). Abnormal physical findings were limited to skin hyperpigmentation, onychomycosis of the fingernails, cheilosis, oral mucosal candidiasis, and alopecia universalis. The family history revealed that two living brothers also manifested the type I syndrome, as shown in Table 1. Two sisters, aged 29 and 23, had no history of endocrinopathy; her mother, aged 47, and her father, aged 48, were also said to be free of any endocrine pathologic disorder.

A laboratory evaluation elicited the following values: sodium 129, potassium 4.6, and carbon dioxide 18 mEq per liter; creatinine 1.2, glucose 27, calcium 8.0, and phosphorus 5.9 mg per dl; PTH 0.8 pg per ml (normal 1.97 to 3.15); cortisol 2.5 μg per dl; immunoglobulin A 128 mg per dl (normal 75 to 312); normal thyroid function values; FSH 8 and LH 10 mIU per ml.

After initial therapy with intravenous hydrocortisone, she was placed on a maintenance regimen of hydrocortisone, 30 mg a day in divided doses; calcium carbonate; dihydrotachysterol (Hytakerol), 0.25 μg three times a day; and ketoconazole, 200 mg a day. Although we did not look for organ-specific antibodies, we presumed that the Addison's disease and hypoparathyroidism were on an autoimmune basis.

The patient was lost to follow-up until March 1983, when she presented with seizures and a blood glucose level of 30 mg per dl. She again admitted to noncompliance with her medications, as well as depression related to her alopecia. She had similar admissions in May, September, and October 1983. On each occasion noncompliance led to hypoglycemia, hypocalcemia, seizures, and hypotension.

In mid-December 1983, the patient was unexpectedly found dead in a friend's apartment. Once again the history of noncompliance was obtained. Vitreous fluid chemistry tests done 30 hours postmortem revealed a potassium level of 10.1 mEq per liter, a calcium of 6.0 mg per dl, and a blood cortisol level of only 0.2 μg per dl. Vitreous fluid chemistry levels are thought to correlate closely with blood levels at the time of death.

On postmortem examination there was an enlarged pituitary gland with hypertrophy of the basophilic and chromophobic cells. The parathyroid glands could not be identified, while the adrenal glands showed substantial atrophy and total replacement of the cortex by fibrous tissue. On microscopic examination there were scattered chronic inflammatory cells, primarily lymphocytes, within the dense cortical stroma (Figure 1). The adrenal medulla consisted of normal cells without atrophy or hypertrophy. The ovaries contained few developing follicles and only rare scattered oogonia. Chronic inflammatory infiltrate consisting of lymphocytes and plasma cells was found throughout the ovarian cortex, and no corpora albicantia were seen. Neither the thyroid nor the pancreatic islets showed any abnormalities.

Discussion

Sporadic cases of associated endocrinopathies and dermatologic disorders have been reported over the years. Thorpe and Handley reported in 1929 an association between hypoparathyroidism and chronic mycelial stomatitis.[4] Talbot and co-workers were the first to describe (in 1943) the association between Addison's disease, mucocutaneous candidiasis, and superimposed hypoparathyroidism.[5] In 1954 Papadatos and Klein reported the additional association of alopecia areata in patients with Addison's disease and hypoparathyroidism.[6] The full triad of familial juvenile hypoadrenocorticism, hypoparathyroidism, and superficial moniliasis was again reported by Whitaker and associates in 1956.[7] They suggested that the superficial moniliasis was the result of dystrophic lesions of the mucosa, skin, and nails due to hypoparathyroidism. Our patient apparently is the first to have alopecia universalis as a feature of the polyglandular autoimmunity syndrome type I.

Sutphin and colleagues in 1943 were the first to suggest a hereditary component to the PGA syndrome.[8] The first genetic study, however, was not reported until 1968, when Spinner and co-workers concluded that PGA type I is inherited as an autosomal recessive trait. They noted that the age of onset is young and that male and female patients are affected in equal numbers.[9] Because the aggregation within siblings involves both sexes, Eisenbarth and associates have suggested an autosomal recessive inheritance.[10] The type I syndrome is not human leukocyte antigen (HLA)-associated

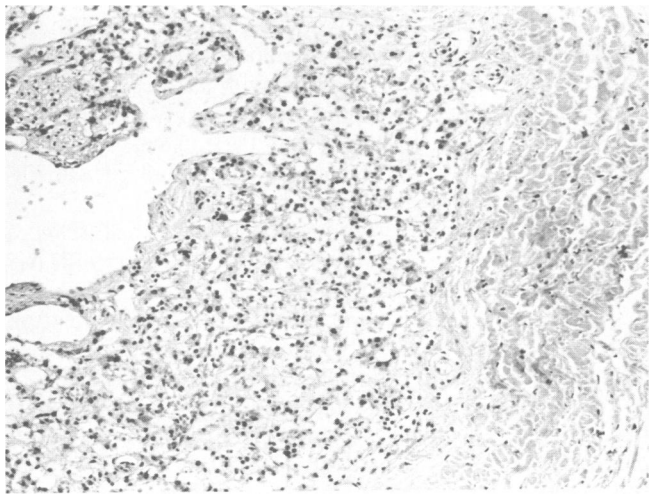

Figure 1.—Adrenal gland shows normal medullary tissue (left side) and dense cortical stromal replacement of the cortex (right side). Viable cortical cells were not identified. Scattered lymphocytic cells are present within the fibrous tissue replacing the cortex (original magnification × 300).

at a population level,[11] nor does it correlate with HLA inheritance in involved families.[12] This is in contrast to the type II PGA syndrome, which appears to be linked to the HLA system and especially to the inheritance of the HLA-B8 (Dw3) haplotype.

An autoimmune basis for the polyglandular syndromes was first suggested by Williams and Wood in 1957.[13] Wuepper and Fudenberg have also presented evidence of faulty immunologic responsiveness.[14] They found organ-specific antibodies in a patient with mucocutaneous moniliasis and multisystem endocrine diseases, and they identified similar antibodies in 17 members of the patient's family. Castells and co-workers have also shown defective delayed hypersensitivity in three siblings with mucocutaneous candidiasis, decreased adrenal reserve, and hypoparathyroidism.[15]

Recent reports suggest that patients with the type I PGA syndrome have an underlying defect in cell-mediated, thymus-derived (T-lymphocyte) immunity.[16,17] Arulanatham and colleagues reported that suppressor T-lymphocyte functions are defective in such patients.[18] Delayed hypersensitivity by skin testing is commonly defective in those with chronic mucocutaneous candidiasis. The frequent observation of IgA deficiency in type I PGA is also in keeping with an abnormality in thymic function. Attempts at thymus transplantation have led to some clinical improvement,[19,20] and the use of a transfer factor coupled with amphotericin B has afforded considerable improvement in some patients with chronic mucocutaneous candidiasis.[21] These findings incriminate the thymus as the defective organ in the type I PGA syndrome.

The type I PGA syndrome is characteristically recognized clinically in early childhood. Chronic mucocutaneous candidiasis often occurs first with accompanying hypoparathyroidism, followed later by adrenal insufficiency.[2] Decades may elapse in between the diagnosis of one disease and the onset of another. The peak age of onset of Addison's disease, however, is before 10 years. Within a given kinship, some persons may express only one or two of the three manifestations of the type I syndrome.[2] In the family presented here, the age at which Addison's disease began ranged between 11 and 23 years (mean, 16.7 years) and for hypoparathyroidism between 3½ and 8 years (mean, 5.3 years).

In addition to her classic type I triad, our patient also had intermittent amenorrhea and oligomenorrhea. Her ovarian findings at autopsy were consistent with the recent report by Gloor and Hurlimann[22] and the previous study by Irvine and Barnes[1] in which more than 25% of patients with idiopathic Addison's disease had premature gonadal failure with increased levels of gonadotropins.

Our patient suffered from severe psychiatric disturbances that contributed significantly to noncompliance with her medication regimen. Her psychiatric disturbances were probably multifactorial. One factor was a low self-esteem and an extremely poor body image related to her alopecia universalis. A second factor, however, may have been hypoparathyroidism. Denko and Kaelbling report that the mental disturbances associated with hypoparathyroidism may include intellectual impairment, organic brain syndrome, functional psychosis, pseudoneuroses (hysteric, hypochondriacal), and nonspecific symptoms such as depression and nervousness.[23] A third etiologic factor could have been her Addison's disease. The mental disorders associated with Addison's disease include apathy, somnolence, insomnia, troublesome dreams, and dulling of the intellect.[24] Indeed, Thomas Addison himself noted that as Addison's disease progresses, the mind frequently wanders. His first patient, a man, had a childish demeanor and spoke with an "intolerable whine."[25]

The immediate cause of death in our patient was clearly noncompliance with her medical regimen. Fraser and Clark have managed a similar patient with Addison's disease and autoimmune hypothyroidism with nurse-supervised therapy, using a regimen of oral thyroxine weekly, intramuscular methylprednisolone weekly, and intramuscular deoxycortisone pivalate monthly.[26] Such an approach might have prolonged our patient's survival.

Our patient's disease was aggravated and her death partially related to the emotional stress of her alopecia universalis. Alopecia of this severity is never a trivial disorder. In addition to its cosmetic significance, alopecia universalis has the potential to create or to exacerbate psychiatric disease.

REFERENCES

1. Irvine WJ, Barnes EW: Addison's disease and associated conditions, chap 46, *In* Gell PGH, Coombs RRA, Lachmann PJ (Eds): Clinical Aspects of Immunology, 3rd Ed. Oxford, Blackwell, 1975, pp 1301-1354

2. Neufeld M, Maclaren NK, Blizzard RM: Two types of autoimmune Addison's disease associated with different polyglandular autoimmune (PGA) syndromes. Medicine (Baltimore) 1981; 60:355-362

3. Neufeld M, Maclaren N, Blizzard R: Autoimmune polyglandular syndrome. Pediatr Ann 1980; 9:154-162

4. Thorpe ES, Handley HE: Chronic tetany and chronic mycelial stomatitis in a child aged four and one half years. Am J Dis Child 1929; 38:328-338

5. Talbot NB, Butler AM, MacLachlan EA: The effect of testosterone and allied compounds on the mineral nitrogen and carbohydrate metabolism of a girl with Addison's disease. J Clin Invest 1943; 22:583-593

6. Papadatos C, Klein R: Addison's disease in a boy with hypoparathyroidism. J Clin Endocrinol Metab 1954; 14:643-660

7. Whitaker J, Lamding BH, Esselborn JM, et al: The syndrome of familial juvenile hypoadrenocorticism, hypoparathyroidism, and superficial moniliasis. Clin Endocrinol 1956; 16:1374-1387

8. Sutphin A, Albright F, McCune DJ: Five cases (3 in siblings) of idiopathic hypoparathyroidism associated with moniliasis. J Clin Endocrinol 1943; 3:625-634

9. Spinner MW, Blizzard RM, Childs B: Clinical and genetic heterogenicity in idiopathic Addison's disease and hypoparathyroidism. J Clin Endocrinol Metab 1968; 28:795-804

10. Eisenbarth GS, Wilson PW, Ward F, et al: The polyglandular failure syndrome: Disease inheritance, HLA type, and immune function. Ann Intern Med 1979; 92:528-533

11. Eisenbarth G, Wilson PW, Ward F, et al: HLA type and occurrence of disease in familial polyglandular failure. N Engl J Med 1978; 298:92-94

12. Thomsen M, Platz P, Andersen OO, et al: MLC typing in juvenile diabetes mellitus and idiopathic Addison's disease. Transplant Rev 1975; 22:125-147

13. Williams E, Wood C: Syndrome of hypoparathyroidism and steatorrhea. Arch Dis Child 1959; 34:302

14. Wuepper KD, Fudenberg HH: Moniliasis, autoimmune polyendocrinopathy and immunologic family study. Clin Exp Immunol 1967; 2:71-82

15. Castells S, Fikrig S, Inamdar S, et al: Familial moniliasis, defective delayed hypersensitivity, and adrenocorticotropic hormone deficiency. Pediatrics 1971; 79:72-79

16. Kaffe S, Pettigrew CS, Cahill LT, et al: Variable cell-mediated immune defects in a family with 'Candida endocrinopathy syndrome.' Clin Exp Immunol 1975; 20:397-408

17. Rickards AG, Barrett GM: Non-tuberculous Addison's disease and its relationship to giant-cell granuloma and multiple glandular disease. Q J Med 1954; 23:403-423

18. Arulanatham K, Dwyer JM, Genel M: Evidence for defective immunoregulation in the syndrome of familial candidiasis endocrinopathy. N Engl J Med 1979; 300:164-168

19. Ballow M, Hyman LR: Combination immunotherapy in chronic mucocutaneous candidiasis: Synergism between transfer factor and fetal thymus tissue. Clin Immunol Immunopathol 1977; 8:504-512

20. Levy RL, Bach ML, Huang SW, et al: Thymic transplantation in a case of chronic mucocutaneous candidiasis. Lancet 1971; 2:898-900

21. Kirkpatrick CH, Greenberg LE: Treatment of chronic mucocutaneous candidiasis with transfer factor, *In* Khan A, Kirkpatrick CH, Hill NO (Eds): Immune Regulators in Transfer Factor. New York, Academic Press, 1978

22. Gloor E, Hurlimann J: Autoimmune oophoritis. Am J Clin Pathol 1984; 81:105-109

23. Denko JD, Kaelbling R: The psychiatric aspects of hypoparathyroidism. Acta Psychiatr Scand 1962; 38:7-70

24. Smith EK, Barish J, Correa J, et al: Psychiatric disturbance in endocrinologic diseases. Psychosom Med 1972; 34

25. Maisey I, Stevens A: Addison's disease at Guy's hospital—A pathological study. Guy Hosp Rep 1969; 118:373-385

26. Fraser AR, Clark F: Replacement therapy in uncooperative patients with endocrine-deficiency states (Letter). Lancet 1979; 1:667

Reversal of Severe Osteopenia in a Patient With Hyperprolactinemia Treated With Bromocriptine

MAJ JILL S. LINDBERG, MC, USA
Fort Sam Houston, Texas

FELIX O. KOLB, MD
ROBERT A. BLAU, MD
MALCOLM R. POWELL, MD
San Francisco

This paper was read in part before the Adult Clinical Working Group, American Society for Bone and Mineral Research Annual Meeting, Anaheim, California, June 22, 1986.

HYPERPROLACTINEMIA IS OFTEN due to a prolactin-secreting pituitary adenoma or to idiopathic hypersecretion of prolactin. Since 1971 when prolactin was distinguished from growth hormone,[1] hyperprolactinemia has been found to be a common condition. It is seen in 15% to 30%[1-3] of cases of amenorrhea and 60% to 70% of all tumors previously thought to be functionless.[4]

Initially the clinical effects of hyperprolactinemia were believed to be mainly galactorrhea, infertility, and amenorrhea. More recently, hyperprolactinemic patients have shown decreased bone mineral content by single-photon measurement of radial bone mineral, by computed tomographic measurement of vertebral bone mineral, and by dual-photon measurements of the vertebral bone mineral.[2,3,5,6] Osteopenia has also occurred in men with hyperprolactinemia.[7,8] Increased radial bone mineral content in hyperprolactinemic women on therapy with bromocriptine was recently reported.[9] Increased spinal bone mineral content by quantitative computed tomography also has been reported by Schlechte and co-workers.[10]

We report the case of a 48-year-old woman with persistent hyperprolactinemia and idiopathic hypercalciuria concurrent with severe radial and lumbar spine osteopenia who had reversal of the spinal osteopenia by long-term bromocriptine therapy. The reversal was documented by serial dual-photon absorptiometry.

(Lindberg JS, Kolb FO, Blau RA, et al: Reversal of severe osteopenia in a patient with hyperprolactinemia treated with bromocriptine. West J Med 1988 Sep; 149:341-343)

From the Department of Medicine, Letterman Army Medical Center, Presidio of San Francisco (Dr Lindberg); the Department of Medicine, University of California, San Francisco, School of Medicine (Dr Kolb); and the Nuclear Medicine Associates, San Francisco (Dr Powell). Dr Blau is in private practice in San Francisco. Dr Lindberg is presently with the Department of Medicine, Nephrology Service, Brooke Army Medical Center, Fort Sam Houston, Texas.

Reprint requests to Maj Jill S. Lindberg, MC, USA, Nephrology Service, Department of Medicine, Brooke Army Medical Center, Fort Sam Houston, TX 78234-6200.

Report of a Case

A 45-year-old nulliparous woman presented with a 14-year history of amenorrhea and galactorrhea that began after a miscarriage. At age 36, sellar tomography and a pneumoencephalogram were normal. A year later, an elevated prolactin level of 330 ng per ml (normal less than 23) was found, and repeat sellar tomography showed anterior, inferior, and posteroinferior sellar erosion. Amenorrhea, galactorrhea, fatigue, and mild obesity persisted, but she had no vision complaints, and the findings of a general physical examination were normal. Osteoporosis and scoliosis were noted on a chest roentgenogram. She underwent transsphenoidal exploration of the pituitary gland. No evidence of adenoma was found at operation, and a biopsy revealed normal pituitary tissue. The patient was treated briefly with a regimen of bromocriptine mesylate after her operation.

She was not seen again until November 1984 when, at age 45, she reported persistent fatigue, galactorrhea, amenorrhea, and back pain. Multiple rib fractures and a compression fracture of the seventh thoracic vertebra were seen on plain films of her chest. These had occurred in spite of her intermittent use—missing five to ten days of medication every six months—of 0.625 mg of conjugated estrogens daily with cyclic doses of 10 mg of progesterone, which caused withdrawal bleeding, plus 1 gram of calcium carbonate per day over several years. She had a history of hypothyroidism treated with the administration of 0.15 mg of liotrix (Thyrolar-2) daily. Her family history was remarkable only for nephrolithiasis in a cousin.

The patient weighed 74 kg (178 lb), was 158 cm (62¼ in) tall, and had an arm span of 165 cm (65 in). Galactorrhea was inducible with breast manipulation. Visual fields were normal. Serum electrolytes and hemogram values were normal. A serum calcium level was 10 mg per dl and phosphate was 3 mg per dl, both values being within the normal range. A prolactin level was 495 ng per ml (normal 2 to 20). An intact parathyroid hormone level was 19 pg per ml, and the 25-hydroxyvitamin D level was 38 ng per ml, both being within normal limits. The urine calcium content was 332 mg per 24 hours (normal 50 to 250), and creatinine, uric acid, and 24-hour urine phosphate levels were normal.

Postsurgical sellar changes were seen on a computed tomographic scan of the head and neck, but the pituitary gland was considered to be normal and without evidence of adenoma. The patient's radial bone density in the "cortical area" at the junction of the distal and middle thirds was 0.65 grams per cm, 3.37 standard deviations (SD) below the mean for women aged 40 to 49 years.[11] Her spinal bone mineral measurement of the second through the fourth lumbar vertebrae was 0.77 grams per cm^2, 3.67 SD below the mean for women aged 40 to 49 years (see Table 1).[12]

In January 1984, bromocriptine mesylate, 5 mg a day, and 50 mg of triamterene and 25 mg of hydrochlorothiazide were added to her long-term cyclic therapy with conjugated estrogens and medroxyprogesterone acetate plus calcium carbonate. The patient had regular withdrawal menstruation. Her prolactin level decreased from 400 ng per ml to 83 ng per ml on a regimen of 7.5 mg of bromocriptine mesylate per day. After increasing the dose to 10 mg a day, her prolactin level was reduced to 37 ng per ml. A repeat spine mineral assessment by dual-photon absorptiometry showed an increased density of 29%, going from 0.770 grams per cm^2 in December 1983 to 0.997 grams per cm^2 12 months later