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ACTUALIZACIÓN

Discovery of the Carney Complex, a Familial Lentiginosis-Multiple Endocrine Neoplasia Syndrome: A Medical Odyssey

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Chief Editor's Note: This article is the 1st of 36 that will be published in 2003 for which a total of up to 36 Category 1 CME credits can be earned. Instructions for how credits can be earned appear following the Table of Contents.

Abstract

In 1981, study of the adrenal pathology in four cases of Cushing syndrome led to characterization of a unique disorder termed primary pigmented nodular adrenal disease (PPNAD). Review of the literature showed that the condition occurred in two families. In one, it had affected two siblings; a third sibling who did not have Cushing syndrome died of cardiac myxoma. To test the hypothesis that there was a connection between PPNAD and cardiac myxoma, the Mayo Clinic files and the world literature were searched for patients with both conditions. The search uncovered one Mayo Clinic patient with the two conditions. The patient's record revealed that she was "covered in pigmented moles" and had a myxomatous tumor of the breast. A review of the literature on cardiac myxoma revealed that there were two types of the tumor, nonfamilial and familial, and that rare cases of the latter were variously associated with cutaneous pigmented spots, mammary and cutaneous myxomas, large-cell calcifying Sertoli cell tumor, and growth hormone-producing pituitary adenoma. In 1985, all these conditions were assembled into a unifying syndrome and reported as "the complex of myxomas, spotty pigmentation, and endocrine overactivity" (Carney complex).

Learning Objectives
- Summarize the history of how primary pigmented nodular adrenocortical disease (PPNAD) came to be recognized as part of a discrete syndrome or complex.
- Identify the pathological conditions associated with PPNAD, focusing on cardiac and other myxomas.
- Illustrate the way in which the Carney complex is inherited and its implications for clinical practice.

Cushing Syndrome and Unusual Adrenal Pathologic Findings

In February 1975, a 17-year-old woman with Cushing syndrome underwent bilateral adrenalectomy at Mayo Clinic, Rochester, Minnesota. Biochemical testing indicated autonomous adrenocortical function and, therefore, the probable presence of a cortisol-secreting adrenal adenoma. The localization studies, however, had not shown an adrenal tumor. The

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patient was operated on with the hope that a small adrenal adenoma would be found. Instead, both adrenal glands were similarly abnormal and both were removed. The glands were smaller than normal (total weight, 7 g, normal weight, approximately 9 g) and both had almost complete transformation of the cortex into multiple, small, black, and brown nodules (Fig. 1A [top]). Microscopically, the nodules were generally spherical and located deep in the cortex, often straddling the corticomedullary junction. Some had replaced the normal cortex entirely and impinged on the adrenal capsule causing black discoloration of the external surface of the glands. The cells constituting the nodules were large, sometimes huge, with granular, eosinophilic, pigment-containing cytoplasm (Fig. 1A [bottom]). The extranodular cortex was atrophic.

A New Adrenal Pathologic Entity?

The examining pathologist who did not make a specific diagnosis shared the case with me. Pathologically, the findings were strikingly different from those of other bilateral causes of Cushing syndrome, bilateral cortical hyperplasia (ACTH-dependent), and macronodular hyperplasia. Might they represent a distinct entity, rare or perhaps undiscovered? In the spring of 1975, when I presented the case to the Department of Endocrinology, the follow-

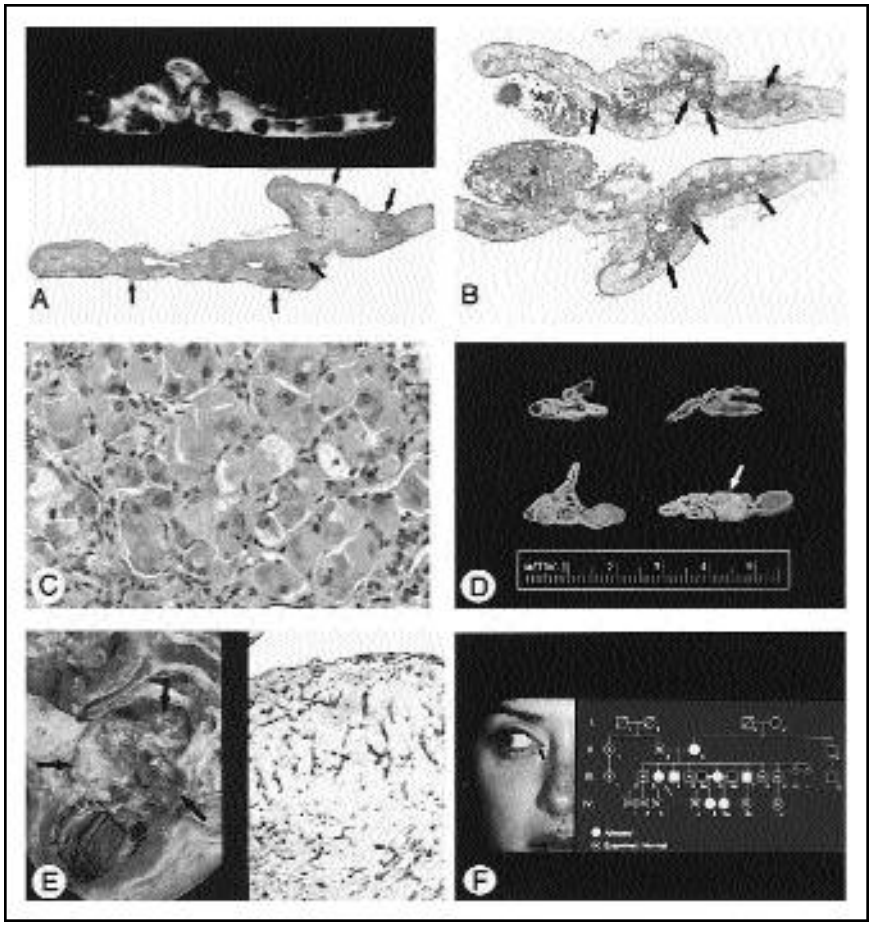

FIGURE 1.A. Primary pigmented nodular adrenocortical disease. Top, The cut surface shows multiple black-and-brown nodules, some con ouent, which have largely replaced the yellow cortex. Bottom,low-power panoramic view of a slice of adrenal, showing multiple cortical nodules (arrows) (Periodic acid-Schiff; 2). **B.** Primary pigmented nodular adrenocortical disease in index patient of Carney complex. Low power photomicrograph of consecutive slices of adrenal shows cortex and medulla. Scattered nodules are present deep in the cortex (arrows). A large nodule (asterisk) has mushroomed from the cortex into the peri-adrenal fat (Periodic acid-Schiff; 2). **C.** Cortical nodule composed of large cells with eosinophilic (pink) cytoplasm and nuclei with occasionally discernible nucleoli. The cytoplasm of most cells contains lipochrome pigment, sometimes disposed in a ring-like fashion.(Hematoxylin-eosin;400.). **D.** Cut surfaces of four slices of adrenal show multiple light and dark brown nodules and one partly yellow nodule (arrow).The nodules measured 1 to 5 mm in diameter. The yellow cortex is readily visible. **E.** Cardiac myxoma in index patient of Carney complex. Left, Opened left atrium is olled with a cauli oower-like, red gelatinous mass (arrows). The trabeculae carneae of the left ventricle and a mitral papillary muscle are seen below the mass. Right, Myxoma featuring mainly capillaries set in a hypocellular matrix and covered by intact endothelium (above) (Hematoxylin-eosin;63). **F.** Dominant inheritance of the Carney complex. Left, Index patient of family with spotty pigmentation of nose and upper lip and typical pigmentation of the conjunctiva covering the lacrimal caruncle. Right, pedigree showing affected and unaffected family member.

ing objections were raised to this notion: (1) there was nothing clinically unusual about the patient's Cushing syndrome (I agreed); (2) adrenal nodules are common (I agreed that they are common, but they are not common at age 19, and certainly not with the characteristics of being multiple, small, black and brown, and bilateral); and (3) I presented only one case (I agreed).

Study of the Adrenal Pathologic Findings: 1981

By 1980, I had encountered two new cases with the same unusual adrenal pathology associated with Cushing syndrome and found a fourth from 1953 in departmental photographic files (Table 1). I began a study of the cases in late 1981 by seeking additional examples of the disorder through a review of the Mayo Clinic files and the world literature. Review of the adrenal slides of the 281 Mayo Clinic patients who had undergone bilateral or subtotal adrenalectomy or bilateral biopsy for Cushing syndrome or for other disorders before 1981 did not reveal any with the peculiar pathology. Search of the literature, however, uncovered 24 cases with pathologic findings similar to the four Mayo Clinic cases. The cases were reported by 18 authors, the first in 1947. Six of the cases occurred in two families [1,2]. This familial occurrence was encouraging evidence that the disorder under study was likely an entity and

TABLE 1. Four Mayo Clinic Patients With Cushing Syndrome and Bilateral Small Pigmented Adrenocortical Nodules

Case (Year)	Sex	Age, y	Suspected cause	Gross Description		Original pathologic diagnosis
				Surgical	Pathologic	
1 (1975)	F	19	Nodular adrenal hyperplasia	Uniformly slightly enlarged	Right, 3.2 g; left, 3.8 g	None
2 (1979)	F	21	Adrenal adenoma vs. bilateral ACTH-independent hyperplasia vs. ectopic ACTH production	Marbled black discoloration with diffuse fine nodularity	Right, 2.3 g; left, 2.5 g; both glands were similar in size and appearance, with a marbled black discoloration and a diffuse, fine nodularity	Bilateral micronodular disease
3 (1980)	M	12	Primary micronodular hyperplasia	Consistent with primary micronodular hyperplasia	Right, 4.9; left, 4.3 g; surfaces were variegated from numerous slightly protruding nodules; black nodules were also seen on the cut surface; he intervening cortex was atrophic	Bilateral micronodular disease
4 (1953)	M	11	?Adrenal adenoma	Right adrenal: diffuse, dark, colored nodules (2–3 mm) throughout. Lt adrenal: similar to Right adrenal, for one 1-cm adenoma and numerous small adenomas	Right, 2.5 g; left, 6.3 g; multiple dark brown adenomas varied in size from microscopic except to 6 mm (Right) and to 1.8 cm (Left); the cortex between the nodules was atrophic	Cortical adenomatosis

ACTH: corticotropin.

TABLE 2. Titles in the Medical Literature in 1983 for the Bilateral Adrenal Pathologic Findings

Author	Name
Chute et al. (1949) [3]	Bilateral nodular hyperplasia of adrenal cortex
Rose et al. (1952) [4]	Bilateral adrenal nodular cortical hyperplasia
Kracht and Tam (1960) [5]	Bilateral small-node adenomatosis
Mosier et al. (1960) [6]	Multinodular adrenal glands
Levin (1966) [7]	Bilateral adenomatous adrenal hyperplasia
Meador et al. (1967) [8]	Primary adrenocortical nodular dysplasia
Tucker et al. (1969) [9]	Nodular adrenal hyperplasia
De Gennes et al. (1970) [10]	Adrenocortical polymicroadenomatosis
Ruder et al. (1974) [11]	Micronodular adrenal disease
Schweizer-Cagianut et al. (1980) [2]	Primary adrenal micro-adenomatosis

that it had a genetic cause. The many names offered for the disorder offered in the 18 reports reflected the uncertainty about its nature (Table 2) [2-11].

Primary Pigmented Nodular Adrenocortical Disease:1982

The opening and closing paragraphs of the discussion in the article reporting the adrenal findings in the four Mayo Clinic cases [12] include the following statements: The clinical and biochemical findings among our four patients were generally similar. The three examined in recent years apparently had ACTH-independent Cushing syndrome, suggesting the presence of an autonomously functioning adrenocortical neoplasm, but radiologic examination failed to uncover a tumor in any of the patients. Each patient had the same unusual and distinctive bilateral adrenal pathologic features: (1) the total adrenal weight was decreased, normal, or slightly increased; (2) the glands were riddled with small, black-brown, red, dark green, or yellow nodules, usually less than 4 mm in diameter; and (3) the extranodular cortex was atrophic and disorganized. Because the basic pathologic process in the adrenals is still not established, because the condition may be heritable, and because the relationship of the disorder to unusual, disparate, extraadrenal conditions (see later) need clarification, to proffer a definitive title for it is premature. It is necessary, however, to have an interim name for this unique adrenal pathology. A descriptive one seems best and we suggest the designation: primary pigmented nodular adrenocortical disease (PPNAD).

Does Primary Pigmented Nodular Adrenocortical Disease have Associated Conditions?

The four Cuban siblings with PPNAD reported by Arce et al. [1] in 1978 had no other conditions. The two Swiss siblings reported by Schweizer-Cagianut et al. [2] in 1980 did have other disorders. One, aged 35, also had an eyelid "fibroma" and became hemiparetic 4 years after adrenalectomy. The other, aged 37 years, was thought to have neurofibromatosis because of skin "fibromas." Might this sibship have been exhibiting a combined syndrome? There was another odd finding in the family a third sibling who did not have Cushing syndrome died of a left atrial myxoma at age 4 years. It seemed remarkable to haply find two disorders, a manifestly rare adrenal disorder (PPNAD) and another rare condition (cardiac myxoma) (and possibly a third [neurofibromatosis]) in a sibship and there not be a connection between them.

Searching for a Patient whit Primary Pigmented Nodular Adrenocortical Disease and Cardiac Myxoma: 1982 to April 1984

But to entertain this hypothesis seriously, it was necessary to find at least one patient with PPNAD and cardiac myxoma. The 28 patients with PPNAD were the obvious candidates for the combination, but none of them had cardiac myxoma. Review of the records of the 131 Mayo Clinic patients who had undergone bilateral or subtotal adrenalectomy for Cushing syndrome up to 1982 showed that none of them had cardiac myxoma.

I tried another approach to the search. I reviewed the approximately 500 reported cases of

cardiac myxoma, seeking case(s) that also featured Cushing syndrome; there were none. Fifty-one patients had been operated on at the Mayo Clinic for cardiac myxoma up to 1981; none of them had Cushing syndrome. Twenty-nine additional Mayo Clinic patients had died of or with cardiac myxoma as an incidental autopsy finding up to that time; none had Cushing syndrome.

Simultaneous with this search for cases with cardiac myxoma and Cushing syndrome, I studied the literature on the tumor itself and quickly learned that there were two types of the neoplasm, nonfamilial and familial, and was surprised to find that the simple distinguishing clinical and pathological features between the two had not been articulated (Table 3) [13].

Continuing the Fruitless Search

As was just mentioned, the Cushing syndrome had not occurred in the 29 Mayo Clinic cases in which cardiac myxoma had been found at autopsy. A review of the pathologic diagnoses in the cases revealed one in which, among 15 other major and minor diagnoses, there was that of "multiple cortical (adrenal) adenomas." The gross description of the glands was: "There are multiple cortical nodules in both adrenals. These are of a yellowish color, but contain some brown and black dots." The bilaterality and color of the nodules were reminiscent of PPNAD. There was no mention of cytoplasmic pigment or of the bizarre cytologic features typical of PPNAD, however; apparently the lesions were small standard adenomas.

Finding the Crucial Case: April 1984

At this point, I had exhausted all the categories of cases that I could think of to search for the PPNAD/ cardiac myxoma combination and had not found a case. In a desperate effort to complete what had been a time-consuming and psychically draining experience before fi nally abandoning the search, I felt obliged to review the adrenal microscopic slides in the 29 autopsy cases. The microscopic slides arrived for study on April 24, 1982. What emotions I felt as I looked at those of the case of "multiple cortical adenomas," and immediately recognized that the patient had PPNAD (Fig. 1B, C, D). At that moment the PPNAD and the cardiac myxoma combination became a reality to me and existed: it never crossed my mind for a moment that the concurrence of the two conditions might have been simply the chance occurrence of two rare disorders in the same patient.

It was surely not accidental that the cardiac myxoma in the case had been attached in the left atrium at the junc-tion of the septum and posterior wall (Fig. 1E), not the fossa ovalis, the usual site for the sporadic neoplasm. There was no mention the Cushing syndrome in the clinical abstract in the autopsy protocol, which was surprising; PPNAD had been functional in all the cases that I had identified up to then. The incongruity was partially explained when I found Crooke changes, telltale signs of hypercortisolemia, in the ACTH cells in the patient's anterior pituitary gland.

The formal clinical record was a revelation. I went through it with mounting excitement and almost disbelief. The medical resident who initially saw the patient noted an unusual skin finding: "deeply pigmented moles cover most of body" (Fig. 2A). The finding was repeated elsewhere: "Pale, tranquil with numerous nevi also (on) mouth/lips"; "she looks pale, somewhat puffy, numerous pigmented nevi"; "many pigmented moles"; "myxomatous mammary fibroadenoma." As I read these observa-

TABLE 3. Differences Between Nonfamilial and Familial Cardiac Myxoma

Featur e	Nonfamilial	Familial
Number	Single	Multiple
Location	Left atrium, attached to fossa ovalis	Any chamber, any site of attachment
Age	Sixth decade	Third decade
Recurrence	No	Yes
Associations*	No	Yes

*Lentigines, breast and skin myxomas, PPNAD, large-cell calcifying Sertoli cell tumor.

tions, I had the eerie feeling that I was reading the description of an unrecognized syndrome-in a medical record, not in a scientific article. It seemed almost impossible (statistically) that all the patient's conditions -PPNAD, unusually situated or multiple cardiac myxomas, numerous pigmented moles, and a myxomatous mammary fibroadenoma- could be encountered together in the particular circumstances in which they had been found and the events be unconnected. They must all be related; they must constitute a syndrome. The search that I was embarked on had to be expanded to include patients with at least two of the following conditions: PPNAD, cardiac myxoma, pigmented-skin spots, and myxomatous breast tumor.

Familial Case of the Primary Pigmented Nodular Adrenocortical Disease-Myxoma Combination: June 1982

In June 1982, less than 2 months later, I was alerted to a case sent to a colleague for his opinion. It concerned a 26-year-old woman who had a hysterectomy for a uterine myxoma. Four right atrial myxomas were found during the preoperative evaluation. In addition, the patient had a past history of bilateral adrenalectomy for Cushing syndrome. I obtained the adrenal slides; they showed PP-NAD. Enquiry revealed that the patient's sister also had bi-lateral adrenalectomy for Cushing syndrome, and she also had PPNAD. I established contact with her in January 1983 only to learn that she had a stroke because of embolization of a cardiac myxoma the previous month. I also learned that she had facial pigmented skin spots, with involvement of the vermilion border of the lips and the conjunctiva at the lacrimal caruncle, and had excisions of an eyelid myxoma and myxoid mammary fibroadenomas.

Late in 1982, Schweizer-Cagianut et al. [14] reported that their previously described patient [2] with PPNAD and hemiparesis died at age 36 years. At autopsy, a left atrial myxoma was found. The histologic features of the patient's skin nodules were reported to be similar to that of the cardiac tumor. Multiple whitish nodules, microscopically benign myxomatous fibroadenomas, were present in both of the patient's breasts. She also had finely freckled pigmentation around the mouth and on the lips. The clinical description of the patient's brother's skin lesions (initially

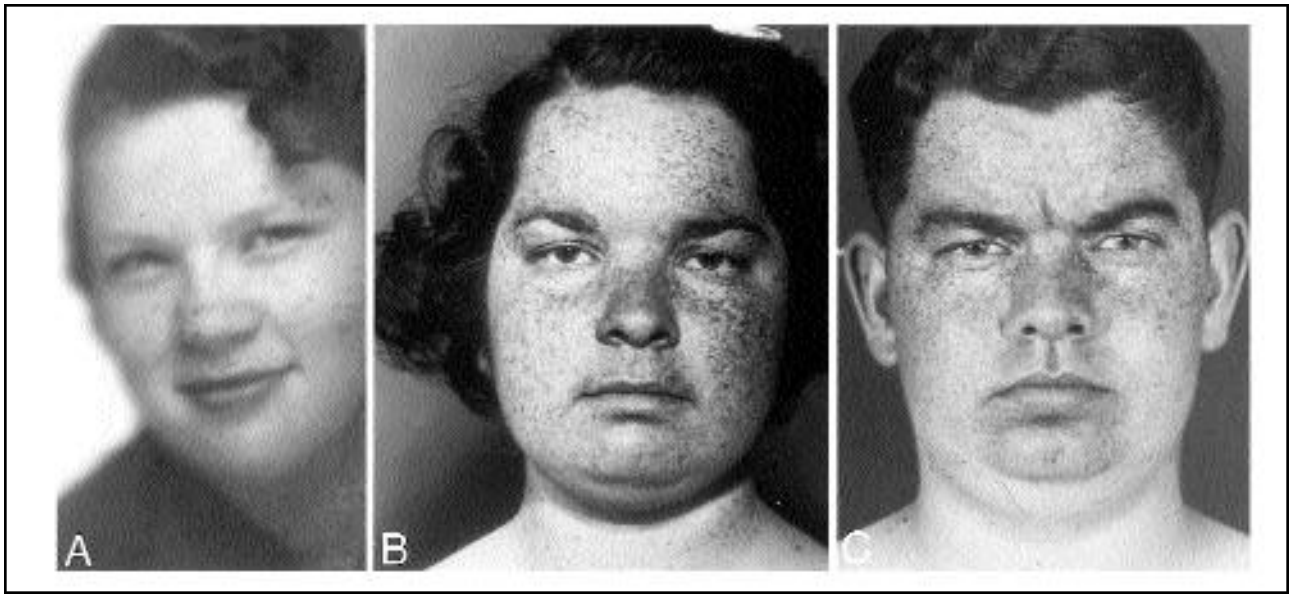

FIGURE 2.A. Index patient of the complex. Enlargement of a portion of a family photograph showing `spotty facial pigmentation when the patient was 17 years old. **B and C.** Fraternal twins with Carney complex. Both patients show a myriad of pigmented spots on face and neck, and a puffy facies with double chin.

interpreted as neurofibromatosis) was amended to indicate that there were multiple skin nodules on his chest, especially around the nipples, on the back, in the left axilla, and on the eyelids, and dark pigmented freckles around the mouth and on the lips.

Selection of the Term "The Complex"

I needed a shorthand way of referring to the Cushing syndrome-cardiac myxoma-pigmented skin spot disorder. I chose the term "the complex," using "complex" in the sense of a whole made up of complicated interrelated parts (see later). Meantime, two acronyms had appeared, each coined for single cases of the complex in which the cutaneous manifestations were striking: NAME (nevi, atrial myxoma, myxoid neurofibroma, and ephelides) [15] and LAMB (lentigines, atrial myxoma, mucocutaneous myxomas, and blue nevi) [16]. Neither patient apparently showed the adrenal involvement that had led me to the syndrome.

Large-cell Calcifying Sertoli Cell Tumor: February 1984

Around this time, I remembered reading about an unusual testicular tumor that had remarkable associations. The article was the original description of large-cell calcifying Sertoli cell tumor (LCCSCT) [17] published in 1980. It described a series of conditions associated with this rare tumor suggesting that LCCSCT was almost certainly another component of the complex (Table 4). Two of the affected patients who will be mentioned later were brothers who had died of cardiac myxoma at a young age.

Significance of Unusual Cardiac Myxomas: March 1984

Earlier in the study, when I realized the significance of unusually located and multiple cardiac myxomas (Table 3), I searched the literature for similar cases and found among others that of a 24-year-old woman with left atrial and ventricular myxomas [18]. In response to my enquiry, Dr. Gary D. Beauchamp confirmed that the patient had black facial spots, including involvement of the lacrimal caruncle (Fig. 1F). She also had myxomatous lesions of an eyelid and both breasts. She had the complex. Dr. Beauchamp introduced me to the patient; she in turn introduced me to her seven siblings and parents. I obtained their medical records, histologic slides, and photographs. Facial and other pigmented spots had occurred in two consecutive generations, raising the possibility that the complex was transmitted as a dominant trait. Histologic slides of biopsy specimens of all family with the skin spots and other cutaneous lesions (myxomas) were available, except from the index patient's mother.

Dominant Inheritance of the Complez: October 1984

The family agreed to participate in a study of

TABLE 4. Conditions Accompanying LCCSCT in 4 Patients (Modi oed from Proppe and Scully [17])*

Patient	Age, y	LCCSCT	Other conditions
5	10	Bilateral, multifocal	Cardiac myxoma (left ventricle); adrenal cortical hyperplasia bilateral †; pigmented skin spots and blue nevi ‡
6	16	Bilateral, multifocal	Cardiac myxoma (left atrium); pigmented skin spots and blue nevi ‡
7	11	Bilateral, multifocal	Adrenal cortical hyperplasia, bilaterally †§
8	11	Single	Growth hormone-producing pituitary adenoma

*LCCSCT, large-cell calcifying Sertoli Cell Tumor.
† Primary pigmented nodular adrenal disease, on review.
‡ Not mentioned in original report.
§ Developed right atrial myxoma at age 31 years.

their pigmentary disorder and undergo examination for cardiac myxoma. Photographs of the mother showed that she had dark facial and labial pigmented spots. Despite the photographic evidence, she became the most important member of the family for me to actually see because she apparently was the first member of the family to manifest the mutated gene and none of her pigmented skin spots had been biopsied.

The late Dr. Hymie Gordon, a colleague, and I met the family at Dr. Beauchamp's office in Kansas City on October 24, 1984. To my chagrin, the mother declined to attend at the last moment. (I eventually did meet her in 1990 and confirmed that she had the classic facial pigmentation of the complex.) However, a 2-year-old member of the third generation was present, the daughter of an affected member of the second generation and she had the typical facial and labial pigmented spots of the complex. Thus, three generations of the family exhibited spotty skin pigmentation in a pattern consistent with dominant inheritance (Fig. 1F). Three also had cutaneous myxomas, one had cardiac myxoma, and one had acromegaly caused by a growth hormone-producing pituitary adenoma. Echocardiograms of all the family members were normal. (The index patient developed PPNAD-associated Cushing syndrome in 1985 and acromegaly in 1995.)

Implications of Dominant Inheritance

As I mentally contemplated the article that would de-scribe dominant inheritance of the complex in the family [19], it seemed important to get further information about the family of the brothers with LCCSCT mentioned earlier who died of cardiac myxoma. If the disorder was a dominant trait, one of their parents must have the complex. Had that parent expressed the disorder? Was the affected parent alive? If neither parent had manifested the condition, it would be important to include this information about penetrance of the trait in an article describing inheritance of the complex.

Dr. Robert B. Scully, Massachusetts General Hospital, Boston, generously shared correspondence related to the deceased boys with me. This led to discovery that pigmented skin lesions, including blue nevi, had been excised from both. The correspondence also provided the father's name, a 1966 home address, his age (he was past retirement age in 1983), and his employer's name. The family had moved and its whereabouts were unknown. The father's employer forwarded a letter from me to him. Within a week I received a phone call from the father.

He was 71 years old, and his wife was 57 years. They had only two children, the deceased boys. Both parents were apparently healthy. Neither had Cushing syndrome or cardiac myxoma, and the father had not had testicular tumors. He had pigmented skin lesions excised but these were seborrheic keratoses microscopically. Photographs did not show obvious facial pigmentation in either parent. After I explained my suspicions regarding the possibility of a familial disorder to them, I arranged to meet at their local hospital in Eugene, Oregon, in December 1984.

While we were introducing ourselves, I scrutinized the father's face and lips for subtle pigmented spots that might not have shown up in the photographs, but none were present.

Then I turned to his wife and immediately realized it was she who was affected! She had fading pigmented spots on her face and lips, and later I saw that a lacrimal caruncle was also affected. These findings took me completely aback because the photograph she had sent me showed a perfectly clear complexion; her pigmented facial spots had been carefully camouflaged for the studio photograph. From this experience, I learned not to rely on just one photograph, particularly one taken by a professional photographer; family photographs are often the most revealing. An echocardiogram performed later in the morning showed that she had a left atrial mass (which proved to be a myxoma). I was not sure how she would react to this potentially devastating news. She said nothing, but a few tears trickled down her cheeks. As we parted, she gave me a hug.

The Complex of Mixomas, Spotty Pigmentation, and Endocrine Overactivity: July 1985

By the end of 1984, I had collected 40 cases with combinations of cardiac myxoma, spotty skin pig-

mentation, skin myxomas, PPNAD, mammary myxoid fibroadenoma, large-cell Sertoli cell tumor of the testis, and growth hormone-producing pituitary adenoma. Through communication with the authors I had obtained additional information relevant to the complex in 21 of the 36 reported cases. The discussion in the article on the series began with the following passage [20]:

The data we have assembled constitute a web of circumstantial evidence that points to a causal connection between several apparently different and unrelated conditions. The conditions included myxomatous masses (cardiac myxoma, cutaneous myxoma, and mammary myxoid fibroadenoma), spotty pigmented lesions of the skin (lentigines and blue nevi), and endocrine disorders (primary pigmented nodular adrenocortical disease, various testicular tumors [large-cell calcifying Sertoli cell, Leydig cell tumor, and adrenocortical rest types], and growth-hormone pituitary adenoma). No patient had all of these conditions; the maximum number of conditions present together was five, and this was observed in only two patients. But each of these is rare, so that the occurrence of variable combinations of even two of them in as many as 40 patients is extremely unlikely to be caused by chance alone.

Nomenclature and Eponyms

Since 1982, I have referred to the combination of spotty skin pigmentation, myxomas, endocrine tumors, and schwannomas as "the complex." There were several reasons for this, one of which was mentioned earlier. In 1977, I described another multitumoral syndrome comprised of gastric epithelioid leiomyosarcoma, functioning extraadrenal paraganglioma, and pulmonary chondroma, [21] which I called the triad of gastric leiomyosarcoma, etc. I decided to title the condition "the triad" of such and such rather than "the syndrome" of such and such, because the disorder was unusual among multitumoral syndromes in not being familial and also "triad" was the more colorful of the two descriptors. I sought through the title to set the disorder apart from other syndromes. In time, two eponymic designations for the condition appeared, Carney triad and Carney syndrome.

When it came time to name the myxoma–spotty skin pigmentation–PPNAD disorder, to avoid confusion with previously used titles, I decided to refer to it as "the complex of myxomas, spotty pigmentation, and endocrine overactivity". Subsequently, the disorder has been referred to as the Carney complex (usually) and as the Carney syndrome (occasionally). In 1985, I had no idea that in 2002 a third syndrome I encountered would need a name [22].

The following was written [23]:

Medical eponyms not only serve to perpetuate the memory of outstanding medical practitioners but also are a useful shorthand notation when communicating about complex medical problems. Eponyms also serve as mnemonics and add color to medical writing.

I will not comment on the authors' first statement, but I agree with the other three.

Final Follow-up: 2002

The index patient of PPNAD, the 19-year-old woman described at the beginning of this article, is alive at age 47 years. She has not developed any other component of the complex; results of a recent echocardiogram are normal. She presumably is a sporadic case of PPNAD.

None of the primary relatives of the 33-year-old index patient of the comfplex have manifested the disorder. The patient presumably was a sporadic case of the syndrome.

The First Cases of the Carney Complex: 1939

To the best of my knowledge, the first documented cases of the Carney complex were seen at Mayo Clinic, Rochester, Minnesota in August 1939 [24]. The patients, a brother and sister who were 17-year-old fraternal twins, had Cushing syndrome and spotty skin pigmentation (Fig. 2). W. F. Young Jr, M.D., a colleague, found their photographs (Fig. 2B, C) in the Department of Endocrinology and brought the cases to my attention in 1986. I had failed to find them in the Mayo files because my search was limited to patients with specimens from both adrenal glands. Adrenal tissue was obtained from only one of the twins, and that was from a unilateral biopsy.

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