



Multifocal Fibrosclerosis Presenting with Panhypopituitarism, Diplopia, and Cranial Nerve Palsy

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Introduction

Multifocal fibrosclerosis is a rare cause of pituitary gland dysfunction. In our case report, we present a man with panhypopituitarism who is felt to have this condition. A discussion of previous cases follows.

Case History

The patient is a 68-yr-old man who presented to our clinic in April 2005 for evaluation of osteoporosis. He had a history of an orthotopic liver transplant in 2002 for primary sclerosing cholangitis and had been on prednisone, 5 mg daily, as part of his transplant anti-rejection regimen. He was subsequently found to have multiple vertebral compression fractures. Before seeing us in clinic, an attempt had been made to taper the patient's prednisone. He soon developed symptoms consistent with adrenal insufficiency, including nausea, vomiting, and proximal muscle weakness. A random cortisol level at 12 pm was 3 $\mu\text{g}/\text{dl}$. Serum sodium was low at 116 mmol/liter (normal 135–145 mmol/liter). Potassium was normal. Soon after resuming his prednisone, all of his symptoms resolved, as did his hyponatremia.

The patient had been diagnosed with diabetes insipidus and hypogonadotropic hypogonadism in 1996, and magnetic resonance imaging (MRI) at that time had shown pituitary stalk thickening. He had been started on testosterone replacement, and his diabetes insipidus had resolved spontaneously. The patient had been diagnosed with a benign orbital tu-

mor in 1985. This was treated with external beam radiation to the orbit. Past medical history was otherwise significant for chronic renal insufficiency of unclear etiology, asthma, gastroesophageal reflux disease, and an abdominal aortic aneurysm. In addition to his prednisone and testosterone, the patient was taking tacrolimus as part of his transplant anti-rejection regimen, pantoprazole, alendronate, and calcium. His mother had been diagnosed with osteoporosis. Family history was otherwise unremarkable.

On review of systems, the patient noted chronic cold intolerance. He had no fatigue, difficulty with concentrating, or mood disturbances. He had no symptoms of diabetes insipidus. He had no changes in shaving frequency and no erectile dysfunction, although he felt his libido was decreased. He had no headaches and no changes in his vision. He had no constipation or changes in his skin or hair. The patient's physical exam revealed a well-nourished appearing male, with a blood pressure of 147/91 mm Hg, heart rate 65 beats per min, weight 158 lbs, and height of 5 ft, 6.25 in. He had some thinning of the skin over his extremities, and some ecchymoses. Visual fields were intact to confrontation. Thyroid exam was unremarkable. He had 5/5 proximal muscle strength. Cardiovascular, pulmonary, and abdominal examinations were unremarkable.

Laboratory studies revealed a TSH of 2.07 $\mu\text{IU}/\text{ml}$ (normal 0.45–4.5 $\mu\text{IU}/\text{ml}$), and a

free T_4 of 0.6 ng/dl (normal 0.8–1.8 ng/dl). A second free T_4 measurement was 0.5 ng/dl, and it was felt that the patient's labs were consistent with central hypothyroidism. A total testosterone (just before his injection was due) was low at 160 ng/dl (normal 210–810 ng/dl) with a normal sex hormone binding globulin of 47 nmol/liter (normal 13–71 nmol/liter). IGF-I was low-normal at 73 ng/ml (normal 71–290 ng/ml).

There was concern that his adrenal insufficiency was related to either his long-term glucocorticoid use or his history of external beam radiation. His prednisone was changed to hydrocortisone 10 mg each morning and 5 mg each afternoon. The patient had an 0800 h cortisol level drawn off of his hydrocortisone that was low at 1 $\mu\text{g}/\text{dl}$. His testosterone therapy was changed to testosterone cypionate and increased to 100 mg weekly, and then to every 10 d. He eventually began taking thyroid hormone as well.

Given his history and laboratory findings, a pituitary MRI was performed. This showed "marked thickening and enhancement of the pituitary stalk. . . [measuring] 7 \times 8 \times 15 mm." Overall this imaging was unchanged when compared with his earlier MRI. The differential diagnosis for the stalk pathology included a granular cell tumor, germ cell tumor, lymphoma, astrocytoma, sarcoidosis, or metastatic disease.

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LETTER FROM THE EDITOR

As the newly appointed Editor-in-Chief of *EndoTrends*, I would first of all like to thank Dr. Arnold Moses, our former Editor-in-Chief, for all his hard work and his vision in making this the premier publication for endocrine fellows.

As a member of the Board of EFF since its inception, I have seen *EndoTrends* grow and develop into truly a fellow's publication where most of the content comes from all of you. We would like to continue this trend, and we encourage you to keep submitting interesting case reports and reviews that will be of interest to all your colleagues.

I would also like to thank all our Associate Editors for their past commitment and support of *EndoTrends*, and I look forward to maintaining and growing our collaboration.

The Associate Editors and I welcome any comments and suggestions you may have, and we can be reached through the EFF office.

Sincerely Yours,
Ramachandiran Cooppan, M.D., FRCP(C) FACE
Editor-in-Chief



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EndoTrends

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Multifocal Fibrosclerosis Presenting with Panhypopituitarism, Diplopia, and Cranial Nerve Palsy

In February 2007, the patient developed double vision. Visual field testing revealed a mild, symmetric bitemporal visual field defect. He was also found to have a new left cranial nerve III palsy. He was having new headaches, pain behind his left eye, and nausea. On physical exam, the patient had diplopia with right inferior gaze and a right inferior temporal visual field defect on confrontation. An MRI was performed (Fig. 1). This showed an increase in the thickening of his pituitary stalk, a mass effect on the optic chiasm, and fullness of the left cavernous sinus. The patient was seen urgently in the neurosurgery clinic, and given his symptoms and radiographic findings, he was scheduled for a transsphenoidal biopsy of the mass.

At surgery, “very firm gray. . . tissue” was encountered within the pituitary gland. The portions of this tumor found within the sella were removed, and intraoperative pathologic analysis was consistent with a “lymphohistiocytic neoplastic process.” Almost immediately after surgery the patient had resolution of his visual symptoms. Final pathologic analysis (Fig. 2) revealed anterior pituitary gland almost completely replaced by extensive

nonnecrotic granulomatous inflammation. The differential diagnosis included an infectious process, including a fungal infection or tuberculosis, and less likely, sarcoidosis. Stains for acid-fast bacteria and for fungi were negative. The dura mater was also involved by the intense inflammatory process and fibrosis, consistent with a pachymeningitis. Before the patient’s discharge, a lumbar puncture was done and this showed no evidence of infectious disease.

These findings were felt to be most consistent with multifocal fibrosclerosis given his history of other conditions associated with this disease. Our patient considered therapy with higher doses of steroids, but he decided to wait and have his pituitary lesion monitored over time. His most recent MRI from November of 2007 showed a decrease in the size of his stalk thickening, and he will have another MRI in 6 months.

Discussion

Multifocal fibrosclerosis was first defined by Comings *et al.* in 1967 (1). In their article, the authors described two brothers who shared combinations of fibrosing conditions including primary sclerosing

cholangitis, retroperitoneal fibrosis, Riedel’s thyroiditis, mediastinal fibrosis, and orbital pseudotumors. Later case reports described similar patients with involvement of other organs, including the kidneys, stomach, thyroid, lacrimal glands, lungs, parotid glands, bone, breasts, testicles, skin, parathyroid glands, heart, pancreas, and small bowel (2–7). Multifocal fibrosclerosis is quite rare. Retroperitoneal fibrosis may be the most commonly observed component, and has an incidence of 0.1 per 100,000 people (8). Multifocal fibrosclerosis is most often diagnosed in middle-aged individuals (9). The pathogenesis of the fibrosclerosis is unclear. Recent reports have suggested that abnormally high levels of IgG4 may be involved, although the exact mechanism by which it causes disease is unknown (10).

The clinical presentation of the disease depends upon the organs involved. An elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell count, and eosinophilia may be present (11, 12). Various imaging modalities can be used to visualize areas of involvement including plain films,

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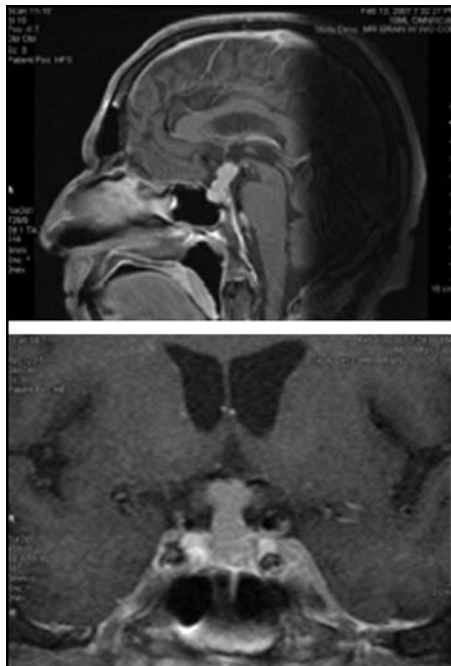


Figure 1. Pituitary-protocol brain MRI performed after patient developed double vision. Both sagittal (upper panel) and coronal (lower panel) images demonstrate thickening of the pituitary stalk with mass effect on the optic apparatus.

computed tomography scans, and magnetic resonance imaging. Multiple therapies have been utilized in treating fibrosing diseases, with varying results. These include radiation therapy, glucocorticoids, various immunomodulating drugs such as cyclophosphamide, cyclosporine, azathioprine and methotrexate, and combinations of these modalities (5, 9, 13). Some fibrosing diseases may go into remission after therapy, and then return years after therapy has been discontinued, making follow-up mandatory (7).

Cases of multifocal fibrosclerosis involving the pituitary and hypothalamus have been described, with and without pituitary dysfunction (12, 14–17). In 1969, Hissong and Freimanis described a 16-yr-old male patient with a fibrous growth of the sellar area, who was found to have fibrosis of multiple organs, including his gastrointestinal tract, spleen, liver, thyroid, adrenal glands, bladder, and testes, at autopsy (18). Grossman *et al.* reported a 29-yr-old man with retroperitoneal and testicular fibrosis who presented with multiple pituitary hormone abnormalities. Craniotomy revealed a tough yellowish intrasellar tumor that was removed, and final pathology showed a mass with fibrosis and calcification (14). Olmos *et al.* de-

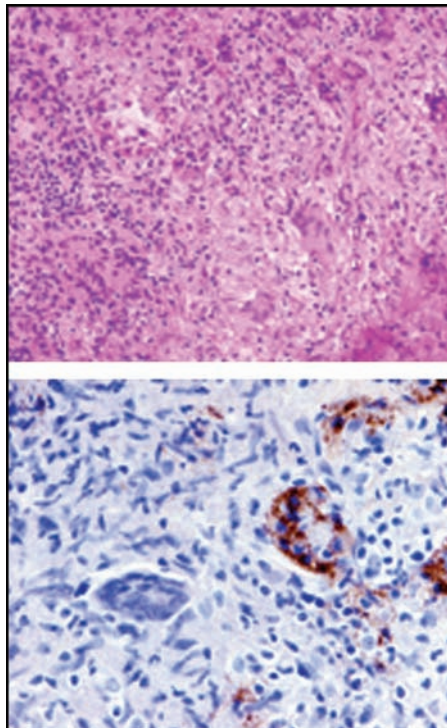


Figure 2. Histopathology of the patient's pituitary gland biopsy reveals non-necrotic granulomatous inflammation replacing normal tissue (viewed at low- and high-power magnification, upper and lower panels).

scribed a 64-yr-old woman with a history of a left orbital pseudotumor who presented with acute anterior pituitary failure, and a mass in the sella consisting of a mixture of both a yellowish, fibrous tissue and calcified tissue (17). The patient was treated with radiation therapy. She later developed multiple cranial nerve palsies and was treated successfully with glucocorticoids. Most recently, Kishimoto *et al.* (12) described a 53-yr-old man with a history of an orbital pseudotumor who developed panhypopituitarism and central diabetes insipidus. His MRI showed a mosaic image of the pituitary gland and swelling of the pituitary stalk. He was initially treated with steroids and intranasal 1-desamino-8-D-arginine vasopressin. He eventually required L-T₄ as well. As with previous cases his ESR and CRP were both elevated.

Conclusion

Systemic infiltrative inflammatory and/or fibrosing diseases can affect the pituitary gland and hypothalamus, and can lead to a deficiency of one or more of the pituitary hormones. Rare conditions, including Wegener's granulomatosis, sarcoidosis, giant-cell granuloma

and eosinophilic granulomatous disease may involve this region. Other more localized infiltrative diseases to consider include hemochromatosis, multiple infectious agents including fungal pathogens and tuberculosis, metastatic neoplasms (especially lung and breast), and lymphocytic hypophysitis (which most often occurs in women during or just after pregnancy) (19). Here we describe a rare case of multifocal fibrosclerosis involving the pituitary gland, leading to pituitary dysfunction, diplopia, and cranial nerve palsy.

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Case Report

Use of Exenatide as an Alternative to Initiation of Insulin in a Commercial Truck Driver

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Introduction

Working as an endocrinologist, one is often referred patients who have worsening glycemic control on oral hypoglycemics—from primary care providers who struggle to decide whether or not to initiate insulin. It can be the case, however, that the patient's fear is not necessarily of the needle (as most doctors initially suspect), but rather of losing his job as a result. This is a case of an important clinical scenario where exenatide has been useful—in a commercial truck driver with type 2 diabetes who by law, is not permitted to use insulin without relinquishing his license and losing his job.

Case

M.R. is a 66-yr-old white male who was referred to the endocrinology clinic at a large midwestern academic medical center for management of his type 2 diabetes. He supported himself, his wife, and his mother by working as a long-distance truck driver. He was frightened that he was going to lose his commercial driver's license if he had to initiate insulin. He was taking a combined metformin/glyburide medication with worsening hemoglobin A1c values over the last year. He experienced intermittent episodes of hypoglycemia on this regimen, sometimes even while driving. He would drive for prolonged periods without eating and would eat at very irregular times as he hauled loads from New Jersey to California and back.

His weight had risen to 271 lbs as he was unable to exercise consistently.

At his initial visit, the decision was made to discontinue the glyburide, increase his activity, and arrange an appointment with a dietician to teach him about carbohydrate counting and limiting his caloric intake. The logic behind these changes was to decrease his risk of hypoglycemia by stopping the sulfonylurea (SU) and to improve his chances of weight loss through lifestyle interventions. It was determined that his goal was to lose 50 lbs.

He returned approximately 7 wk later having lost approximately 7 lbs of weight. He increased his exercise via walking, stopped the SU, and was taking metformin 500 mg three times daily. At that time he was educated and instructed on the use of byetta 5 µg sc twice daily.

He returned approximately 7 wk later having lost an additional 4.5 lbs since adding byetta. He experienced no significant episodes of hypoglycemia on this new regimen. His hemoglobin A1c was decreased to 6.0%. He was excited about this and extremely grateful to continue to be able to drive trucks while keeping his blood glucose values near normal.

Discussion

On first glance, this seems to be a fairly straightforward case of type 2 diabetes

and its medical management; however, it brings to light several issues faced by patients that don't have straightforward answers:

1. Why is insulin prohibited for use by commercial truck drivers?
2. What is the treatment of choice for these patients?

Question no. 1 has been the subject of considerable debate for decades and a source of great frustration for commercial truck drivers in the United States. According to the U.S. Department of Labor, there were about 2.8 million truck drivers in 2004. With a prevalence of diabetes in the United States of approximately 7.0%, (www.diabetes.org), one can infer that approximately 196,000 truck drivers are diabetic. However, this number is likely higher for several reasons: truck drivers comprise an older subset of the population, their work is largely sedentary, and they likely have difficult eating a nutritious diet "on the road." The natural history of diabetes is characterized by gradual loss of β -cell function and death, and thus the majority will progress to insulin dependence over time. Under current federal regulations, however, they would be forced to relinquish their commercial driver's license, causing financial hardships for themselves and their families.

So it begs the question: why are insulin-treated diabetics prohibited from hold-

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ing a commercial driver's license? One might argue that there are no restrictions on non-commercial drivers taking insulin, and there are far more of them on the road, accounting for far more miles driven per year. Additionally, the incidence of hypoglycemia with SUs is not trivial, yet their use is not restricted among commercial drivers. The UK Prospective Diabetes Study Group reported a 6-yr incidence of significant hypoglycemic events to be 17% among those on SUs compared with 37% among those taking insulin (1).

The presumptive reason for concern about drivers who take insulin is that they are at risk of developing hypoglycemia while driving. Hypoglycemia leads to inattention, poor coordination, slower reaction times, or even blackouts or seizures—causing an increase in motor vehicle collisions, injury, or even death. It remains a matter of dispute, however, whether overall traffic accident rates are higher in insulin-treated diabetic drivers than in the general population. Some studies show an increase in accident rates (2), whereas the majority do not (3–6). The increase in accident rates among insulin-treated diabetics found in the Cox study, however, was limited to type 1 diabetics on insulin and not seen in type 2 diabetics, who likely comprise the majority of diabetic commercial truck drivers in the United States. Additionally, Harsch *et al.* (7) found that comparing diabetics on oral therapy, conventional (once or twice daily) insulin therapy, intensive insulin therapy (three or more shots), or insulin pumps, there was no significant differences in the incidence of hypoglycemia-induced accidents between the groups.

Although many doctors provide recommendations to their diabetic patients to monitor their blood glucose before driving and to wait until their glucose has normalized before driving, there is evidence that diabetics are poorly compliant with these recommendations. A study in Scotland of 202 drivers with insulin-dependent diabetes (115 with type 1 diabetes) showed that 31.7% had experienced hypoglycemia while driving, 38.1% reported never carrying a glucose meter while driving, 59.9% reported never testing their blood glucose before

driving or only if symptomatic (8). Waiting for symptoms to develop is inappropriate due to the prevalence of hypoglycemic unawareness in this population. In a study by Weinger *et al.* (9), 38% of subjects felt able to drive safely with a blood glucose of 2.8 mmol/liter (50.4 mg/dl) although previous studies (10–11) have shown that cognitive functions critical to driving are impaired below blood glucose values of 4.0 mmol/liter (72 mg/dl). Unfortunately, at low blood glucose levels, a diabetic driver may have impaired judgment and truly believe himself capable of driving well. Cox *et al.* (3) investigated the correlation between presence of diabetes with number of traffic violations and crashes. In seven U.S. cities and four European cities (which is important as in many other countries commercial truck drivers are permitted to use insulin), three different groups were compared: type 1 diabetics (n = 341), type 2 diabetics (n = 342), and nondiabetic spousal controls (n = 363). Their findings indicated that type 1 diabetic drivers are at increased risk for driving mishaps, but type 2 diabetic drivers, even on insulin, appear not to be at a higher risk than nondiabetic individuals. The risks that arise seem to be that often diabetics are not compliant with recommended safe practices.

Question no. 2 may be answered a variety of ways as well. With respect to choice of medications to treat diabetes short of insulin, there are an increasing number of options. SUs, glitinides, thiazolidinediones (TZDs), acarbose, metformin, exenatide, and sitagliptin are all approved for use to treat diabetes. If avoiding hypoglycemia is the paramount concern, then SUs and glitinides should be avoided as they work via increasing insulin secretion by the pancreas. TZDs work via decreasing peripheral insulin resistance but are expensive and have come under increasing scrutiny in the last year due to concern for potential increased risk of cardiac events and increased incidence of heart failure. Acarbose does not cause hypoglycemia but is poorly tolerated due to malabsorption in many patients. Metformin works primarily via decreasing hepatic glucose production and has a low incidence of hypoglycemia. Exenatide should also be considered in patients who wish to avoid

hypoglycemia because, although it increases insulin secretion, it does so in a glucose-dependent fashion, and is not associated with an increase in hypoglycemic events (12). Additionally, it may have the benefit of inducing weight loss, improving endogenous insulin sensitivity.

The recent FDA approval of several continuous glucose monitoring devices may be clinically important as well. This would allow the wearer to know his or her blood glucose value with less frequent fingerstick monitoring and to anticipate trends of high or low blood glucose. These devices are primarily used currently in patients with severe hypoglycemic episodes on intensive insulin therapy and hypoglycemic unawareness, but may be considered in the future for commercial drivers who require insulin therapy as a way of reducing the incidence and risk of severe hypoglycemia.

Recommendations

Further studies still need to be done to better define the risks associated with tight glycemic control with respect to adverse driving events and to determine whether there is a true cause-and-effect relationship between the two in both type 1 and type 2 diabetes. Just as the goal hemoglobin A1c value is a compromise between limiting long-term microvascular complications and short-term morbidity from hypoglycemic events, we must collectively determine better safe guidelines to allow our diabetic drivers, especially those with commercial licenses, to appropriately treat their illness without losing their livelihood.

Doctors have a responsibility to teach patients about the risks of hypoglycemia and driving. Diabetic patients have the responsibility to heed this advice and monitor their blood glucose closely and avoid driving at low blood glucose levels, regardless of symptoms.

Exenatide is an excellent adjunctive therapy to metformin and lifestyle changes in treatment of type 2 diabetes because it causes blood glucose lowering with a glucose-dependent mechanism of action, without increased risk of hypoglycemic events.

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Hypogonadism Associated with Progressive Neurologic Deterioration in a 19-Year-Old Male

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Introduction

In this case report, we describe the clinical and biochemical presentation of a 19-yr-old male with a complex association of endocrine and neurologic disturbances.

This 19-yr-old male was recently reviewed at the Adult Metabolic Disease Clinic in Vancouver, British Columbia, Canada for evaluation for possible pituitary disease. Specifically, a question of hypogonadotropic hypogonadism was raised to us. This patient has been seen by several pediatric specialists including neurology, biochemical diseases, and medical genetics over many years.

Past Medical History

This young man is the second child born to healthy, unrelated Canadian parents of Caucasian background. The pregnancy was complicated by bleeding due to partial placenta previa, but did continue to 42 wk of gestation. Delivery was by SVD without complication. Apgar scores were not available, but birth weight was approximately 9 lbs.

The neonatal period was uneventful as was early psychomotor development.

Detailed developmental milestones could not be recalled very well by parental history. However, sitting was achieved around 5 months of age, crawling at age 10 months and independent walking at 14 months. His gait was described as “clumsy” and he was unable to walk down stairs. Achievement of fine motor skills and development of speech perception and active speech were stated to be normal. The parents believed that he talked somewhat less well and in shorter sentences compared with his older brother. The first concerns surrounding motor skills arose during the third to fourth of life when the parents began to notice increasing unsteadiness and frequent falls.

The patient's first neurological assessment at the age of 4 1/2 yr revealed ataxia (with preserved one leg standing), brisk reflexes, mild head titubation, and abnormal saccadic eye movements. A magnetic resonance imaging (MRI) head scan revealed deep white matter changes in both cerebral and cerebellar hemispheres, abnormalities of the basal ganglia, and mild cerebellar tissue loss. He was also found to have significant refractory errors in his vision and received glasses for myopia. Numerous metabolic

investigations failed to reveal an underlying cause for his slowly progressive disease. Cell counts, renal, liver and lipid profiles were normal. Karyotype was normal. Lead and zinc levels were normal as were vitamin B12 values. His workup included normal urine organic acids and serum amino acids. N-acetylaspartate, very long chain fatty acids, hexosaminidase A, single myelinase and betaglucosidase are reported as having been normal. Electroencephalogram and electromyogram tests were normal, and a lumbar puncture revealed normal cerebrospinal fluid. At this age, a diagnosis of Pelizaeus-Merzbacher was considered but neither be ruled in or out due to lack of available genetic testing.

At the age of 5 1/2 yr, his ataxia had progressed and he had developed horizontal and upward nystagmus, mild dysmetria, and difficulty with repetitive hand movement. His intellect was deemed to be normal. Testing at that age included an MRI, which showed no interval changes to the previous exam. A skin biopsy was performed and tests for pyruvate dehydrogenase, pyruvate carboxylase and cytochrome c oxidase were normal.

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One year later, at 6 1/2 yr of age, he had entered a modified school program. There is no information on his clinical status otherwise, but an MRI again showed diffuse, symmetric white matter disease, basal ganglia changes and cerebellar atrophy.

By the time the patient was 9 yr old, the parents were finding considerable worsening of symptoms during illness and associated fatigue. His speech was slower and he was having difficulty with academic tasks. Interval investigations included normal biopsies of both bone marrow and muscle. Neuropsychiatric testing revealed average intellect, but score were primarily impaired by poor motor response.

At age 15, the patient was described as having immature behavior and dysarthric speech that was explosive and scanning. Upwards gaze was limited and horizontal, and vertical nystagmus were present. Tone was increased and reflexes were brisk; however, the presence of spasticity was questionable. His gait was broad-based and ataxic, and he had dysmetria with dysdiadochokinesia.

At the age of 19, his current age, he has had progression of his symptoms, particularly the worsening with fatigue and also with high ambient temperatures. He does participate in numerous sporting activities but has had some difficulty with injuries due to impaired motor coordination. He tends to require the use of handrails when climbing stairs.

Once again, the diagnosis of Pelizaeus-Merzbacher was raised, and although some of the criteria were met, the presentation was atypical. Formal testing for this was initiated as for mutation analysis for Pelizaeus-Merzbacher-like disease. In addition, in light of recent publications suggesting a syndromic link, specific history regarding dentition was reviewed. The patient's teeth, to the recollection of his father, erupted very late and some required dental dissection. There is also a component of primary pubertal failure as a result of hypogonadotropic hypogonadism that is part of the aforementioned syndrome.

Present Illness

With respect to the specific question of endocrinopathy, the patient developed axillary and pubic hair around the age of 12–13 yr. He has not developed any facial hair requiring shaving. He has recognized only one or two spontaneous morning erections and does achieve erection with stimulation. It is not clear whether he had any ejaculate as the concept was somewhat difficult for him to understand. There was no history of vasomotor flushing or sweating and he uses deodorant. There was no information on growth curves available, but his father suggested there was never an express concern about vertical growth. His father's height was 174 cm, and his mother's was estimated to be 172 cm. Thus, a predicted mid-parental height of 180 cm.

He had no symptoms suggesting adrenal or thyroid disease, diabetes insipidus, or galactorrhea. There were no complaints of morning headache or of an obvious change to his vision. His sense of smell was reported to be normal.

He did not have any prescription medications and denies alcohol, tobacco or other illicit drugs. He denies use of exogenous anabolic steroids. He had no drug allergies.

The family history was unremarkable for diabetes, hemochromatosis, or other significant illness. His elder brother, by the same parents, is healthy and does not have any cognitive or motor difficulties. However, it was suggested that he also has very little body hair, shaves infrequently, and has a body habitus similar to the patient, somewhat different from the family in general.

Physical Examination

The patient's height was 181 cm, arm span was 181 cm, weight was 78 kg, and body mass index was 23.8 kg/m². Blood pressure was 130/70 supine, 135/70 standing with resting pulse of 80 bpm and no postural change. General appearance was that of a healthy young male, with a somewhat gynoid body habitus. Visual fields were full to confrontation, and pupils were equal and reactive with vertical and horizontal nystagmus. Facial movement was normal. The upper-

second incisors were abnormal in shape. The thyroid was unremarkable as were the respiratory and cardiac examinations. There was a suggestion of gynecomastia bilaterally but no true breast tissue and no galactorrhea. Abdominal examination was soft and nontender with no hepatosplenomegaly. Genital exam was Tanner 4 for phallus and pubic hair development. The testes were 12–15 ml bilaterally and of normal texture. There was scant, coarse axillary hair, but otherwise no other androgenic hair growth over the body. His skin texture, temperature, and pigmentation were normal. The neurologic exam was consistent with that of the past with paratonia but no spasticity, a wide-based gait, and an inability to walk heel-toe. Finger-nose and heel-shin were impaired bilaterally, and he had dysdiadochokinesia bilaterally. Reflexes were brisk with no clonus and toes were plantar bilaterally. Sensation was globally normal, but smell was not specifically evaluated.

Investigations

Specific testing with respect to the question of hypogonadotropic hypogonadism and any associated pituitary deficiencies was performed.

Baseline Investigations

Electrolyte profile and renal function and albumin were normal. Serum iron 13 μmol/liter (9–30), TIBC 52 μmol/liter (45–73), iron saturation 0.25 (0.20–0.55), and ferritin 55 μg/liter (20–300), were all well within normal.

TSH was 2.40 mU/liter (0.34–4.82), and free T₄ was 15.2 (11.0–22.0). PRL was 6.1 μg/liter, morning cortisol was 503 nmol/liter, ACTH was 10 pmol/liter (<11), and IGF-I was 240 μg/liter (155–548). Total testosterone was 5.6 nmol/liter (9.7–30.5), LH was 1.9 IU/liter (1.2–8.6), and FSH was 1.8 IU/liter (1.3–19.3).

Dynamic endocrine testing (modified triple bolus) was performed as follows: cosyntropin 1 μg iv, TRH 200 μg iv, and GnRH 100 μg iv (Table 1).

Interpretation

This 19-yr-old male with a chronic, progressive neurologic disease compatible

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Table 1
Endocrine Testing

	Baseline	30 min	60 min
Cortisol (nmol/liter)	503	683	538
Stimulated salivary free cortisol (nmol/liter)	8.1	27.9	10.2
TSH (mIU/liter)	2.40	16.07	10.76
LU (IU/liter)	1.5	2.9	3.1
FSH (IU/liter)	1.9	1.7	1.6
Prolactin (6.1 µg/liter)	6.1	28.1	14.1
Total testosterone nmol/liter	10.5 (10–38); range difference due to separate laboratory method		

with a leukodystrophy and a history of hypodontia has clinical and biochemical evidence of hypogonadotropic hypogonadism with otherwise normal pituitary function. The decision was made to introduce testosterone replacement therapy on a gradual basis in light of requirements for male health. There was no expectation of effect on his neurologic impairment.

Discussion

Despite concerted efforts since the age of 4 1/2 yr at diagnosis, little progress has been made in this difficult patient's case. The characteristic imaging features are in keeping with those first described in 2002 (1). In light of two publications (2, 3), this patient has been reviewed and it is possible that he may have a unifying diagnosis. Wolf *et al.* (2) describe a series of four unrelated females with early-onset progressive ataxia, hypodontia with delayed dentition, and MRI findings of hypomyelinated white matter and cerebellar atrophy. This case series involved prepubertal patients with age ranges from 3 to 7.6 yr, and thus no suspicion was raised with respect to hypogonadism. It was their belief that this constellation comprised an entirely separate entity from previous descriptions involving delayed dentition and progressive, primarily cerebellar, degeneration—a group known as ectodermal dysplasias (EDD). Timmons *et al.* (3) describe a similar dysmyelinating leukodystrophy with hypodontia as the previous study with the additional finding of pituitary hypogonadotropic hypogonadism. Four unrelated patients (three female, one male) ages 20–30 yr are presented. These patients had neuroimaging results compatible with those of the patient under discussion and also had abnormal response to GnRH stimulated testing. Sural nerve biopsy results

served as a unifying factor in this group with otherwise very similar clinical presentations. A putative moniker for the syndrome is also suggested—4H (hypomyelination, hypogonadotropic hypogonadism, and hypodontia). However, little information surrounding growth and development from the perspective of endocrine disease, and in particular hypogonadotropic hypogonadism, is given. To date, there is no information suggesting a putative target gene or gene product that incorporates the phenotypic presentation. We believe this to be the first well-described case of an individual with “4H” in whom thorough endocrine review has been performed.

In the context of syndrome illnesses of endocrinology and metabolism that include hypogonadotropic hypogonadism, Gordon-Holmes syndrome (OMIM #212840), a heterogeneous group of disorders with both cerebellar ataxia and hypogonadotropic hypogonadism can be considered. This disorder has a variable age at presentation, but most reports suggest the second to fourth decades. Inheritance appears to be autosomal recessive in nature, differentiating this syndrome from what appears to be sporadic appearance in 4H. Both primary and secondary hypogonadotropic hypogonadism are described. Pelzaeus-Merzbacher disease (PMD, OMIM no. 12080) and Pelzaeus-Merzbacher-like disorders (PMLD, OMIM no. 608804, #260600) have been considered in this patient primarily because of the neurologic manifestations and progressive nature of his disease. Again, however, there are clear patterns of autosomal recessive inheritance and no description of dental abnormalities or of hypogonadotropic hypogonadism. The neurologic abnormalities of both PMD and PMLD, when arising in early childhood, tend to be more rapidly progres-

sive than that of this patient and often are fatal in childhood or adolescence.

One of the primary considerations in male patients with hypogonadotropic hypogonadism is the diagnosis of Kallmann Syndrome (KS), classically described as being associated with anosmia. However, within the realm of idiopathic hypogonadotropic hypogonadism (IHH), there are clear descriptions of normosmia and heterogeneity of pubertal development ranging from complete lack of pubertal development to near-normal testicular volume. In addition, there are other associated defects including cleft palate, dental agenesis, septo-optic dysplasia, eye movement abnormalities, and cerebellar abnormalities. The cerebellar dysfunction does not appear to be one of a chronic, progressive or myelination disorder as currently described. Thus, a diagnosis of KS or IHH with normosmia is unlikely (4, 5).

This patient, by history and investigation, does not appear to have an acquired hypogonadotropic hypogonadism. His iron studies do not suggest hemochromatosis and otherwise normal anterior pituitary function make a significant structural lesion unlikely. Pituitary-specific imaging remains pending to definitively rule this out.

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Case Report

Aggressive Pheochromocytoma: Is There a Place for Innovative Medical Therapies?

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Brief Description

In this case report, we will describe a 21-yr-old male with Von Hippel Lindau (VHL) Syndrome and recurrent pheochromocytomas. He has the RET mutation, activating tyrosine kinase, consistent with VHL. He has had multiple surgical resections but has persistent/recurrent disease. Currently he has labile blood pressure, tachycardia, and a retroperitoneal mass associated with elevated catecholamines. The patient was presented to the University of New Mexico Health Sciences Center (UNMHSC) tumor board.

After significant discussion, the board decided that the patient may benefit from Sorafenib, a tyrosine kinase inhibitor, as an experimental trial. We will discuss the potential utility of Sorafenib in patients with neuroendocrine tumors.

Introduction

LG is a 21-yr-old male who has been followed in the endocrinology clinic at the UNMHSC since 1994. He initially presented at age 8 yr with headache, sweating, and palpitations. He was hypertensive and tachycardic. An extensive workup led to a diagnosis of a right-sided adrenal pheochromocytoma measuring 2 × 3 × 3 cm (Table 1). He underwent a right-sided adrenalectomy. Surgical exploration further demonstrated a left-sided paraganglioma in the mesentery that was invading the left renal vein. A subtotal resection was performed.

Family history was significant for Von Hippel Lindau in his mother. She also had a history of a pheochromocytoma. The patient underwent genetic testing and a mutation on exon 3 at nucleotide 794 with a valine substitution for glycine consistent with the RET oncogene mutation associated with Von Hippel

Lindau syndrome was found. Later in his course, an older sister developed a pheochromocytoma.

The patient did well over the next 2 yr but presented with a hypertensive episode in 1996. His diagnostic evaluation was significant for elevated urinary catecholamines and imaging that revealed a 4 × 5 × 5-cm mesenteric mass, and a left-sided adrenal mass. Both masses were resected.

He was lost to follow-up until May 2003 when he presented with a hypertensive crisis. Labs revealed elevated serum normetanephrines, and metaiodobenzylguanidine scan (MIBG) imaging revealed a recurrent left sided pheochromocytoma. The mass was resected, resulting in adrenal insufficiency. Hydrocortisone and fludrocortisones were started.

One year later, surveillance monitoring was significant for elevated serum catecholamines followed by an abnormal MIBG scan showing a 6 × 2-cm retroperitoneal mass. He was referred to UCSF for further evaluation. The tumor was resected and he was being considered for an experimental chemotherapy clinical trial. However, he was lost to follow up until 2007, when he re-presented to the clinic with complaints of dizziness, sweating, and labile blood pressure. Labs revealed elevated urine catecholamines, and magnetic resonance imaging (MRI)/MIBG imaging revealed a 2.0 × 3.0-cm mass at L2-L3 anterior to psoas and left aorta consistent with a recurrent pheochromocytoma.

The patient was presented at the Tumor Board at the UNMHSC. Extensive discussion ensued, and it was suggested that our patient might benefit from a new medication Sorafenib, a tyrosine kinase inhibitor.

Discussion

Surgery remains the main treatment for pheochromocytomas. In some situations, more aggressive tumors and malignant pheochromocytomas, external radiation therapy or cryoablation can be used to treat painful skeletal metastases. Recently, I-131 MIBG has been used in research protocols. However, I-131 MIBG has been reserved for patients with malignant pheochromocytomas who have metastases. Radiofrequency ablation can be used in select patients with hepatic and bone metastases. Chemotherapy has also been used in certain patients who have aggressive tumors and decreased quality of life.

Many neuroendocrine tumors, including some pheochromocytomas, are associated with c-kit expression, found in tumor types (1–16). C-Kit, a proto-oncogene, encodes a transmembrane tyrosine kinase receptor on chromosome 4, which is thought to be involved in tumor genesis. Tyrosine kinase inhibitors including, Gleevec (Imatinib mesylate) have been used with success in patients with tumors expressing KIT. Gleevec targets both KIT and platelet-derived growth factor (PDGFR), PDGFR also localizes to chromosome 4. PDGFR, a tyrosine kinase receptor, is a receptor for PDGF, which in turn helps regulates cell growth and division. Newer tyrosine kinase inhibitors, including Sorafenib, can target several receptors simultaneously, including KIT, PDGF, EGR-R, VEGF, and RAF (17, 18).

KIT expression in pheochromocytomas has been shown by Went *et al.* (4) to be around 14%. Indeed in previous studies, the response of neuroendocrine tumors to Gleevec has had variable success. Patients with malignant pheochromocytomas are difficult to treat and have a

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Table 1
Clinical Course

June 1994	October 1996	May 2003	May 2004	2006/2007
Symptoms: Malignant HTN	HTN	HTN crisis	Asymptomatic	Dizzy, sweating, labile blood pressure
Labs: None available	Elevated 24 h VMA per progress note	Plasma normetanephrine: 10.40 (N: 0–0.89) Plasma metanephrine 35 (N: <0.5)	Plasma: Dopamine 72 (N: 0–20) Norepinephrine 3446 (N: 80–520)	Urine norepinephrine 727 (normal: 0–45) Urine metanephrine 2095 (normal: 0–400)
Imaging: 2- × 3- × 3-cm R adrenal pheo Superior mesenteric mass (+ margins)	4 × 5- × 5-cm mesenteric mass L adrenal pheo (per old records)	L recurrent adrenal Pheo (imaging not available)	MIBG scan: 6- × 2-cm retroperitoneal mass	MRI/computed tomography chest/pelvis/MIBG: 2.0- × 3.0-cm mass L2-L3 anterior to psoas and left aorta consistent with recurrent pheochromocytoma
Treatment: Partial right adrenalectomy (found paraganglioma in mesentery invading left renal vein, subtotally resected)	UCSF resection of mesenteric pheo, left adrenal pheo noted, and hemi-adrenalectomy done.	Laparotomy at UNM, resection recurrent L adrenal pheo, both adrenals removed.	At UCSF this mass is resected –1/7/05: MIBG scan shows bilobed mass inferior to resected mass.	Possible further surgery planned, also being evaluated for newer medical management (possible Gleevec, I-131 MIBG)

HTN, Hypertension; L, left; N, normal.

5-yr survival that is less than 50%. While our patient does not have signs of metastases at this time, his tumor behaves in an aggressive manner, as noted by his multiple relapses. Indeed, if our patient's tumor demonstrates KIT expression, Gleevec or newer agents, including Sorafenib, may be an effective chemotherapeutic agent for him.

Conclusion

This case illustrates a 21-yr-old man with Hippel Lindau syndrome due to RET oncogene and recurrent pheochromocytomas. Since diagnosis at age 7, he has undergone four surgeries but has persistent/recurrent disease. Search for novel chemotherapeutic agents to attempt to treat and cure his disease are needed. Recent work has centered on tyrosine kinase inhibitors, and their use in neuroendocrine tumors that show KIT expression. Our patient is currently being evaluated by oncology for the potential benefit of Sorafenib. This case demonstrates a potential novel treatment modality for patients like ours whose pheochromocytoma is not likely to be cured by surgical resection alone.

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Keeping Older Adults with Endocrine Disorders Safe in the Community

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Introduction

Older adults with endocrine disorders are often affected by mobility disabilities, making it more difficult to remain safe in the community. People with type 1 and type 2 diabetes have an increased risk of falls, in part due to neuropathy and retinopathy, and women with diabetes have a higher risk of hip fractures than those without diabetes (1). Muscle weakness, making ambulation and activities of daily living (ADLs) more difficult and unsafe, is associated with several endocrine disorders including hypothyroidism, hyperthyroidism, and hyperparathyroidism (2). Over 90% of hip fractures are the direct result of a fall (3) and those who suffer a hip fracture have increased morbidity and mortality during the following year, (4) making safe mobility a great concern for those with osteoporosis. This article will describe the demands required for an older adult to safely move about in the community, review assessments commonly performed by physical therapists (PTs) and occupational therapists (OTs) to determine mobility disabilities and explain interventions that can improve mobility in the older adult with endocrine disorders.

The Demands for Safe Community-Dwelling

Shumway-Cook *et al.* (5) evaluated older community-dwelling adults and determined the physical demands that must be met to safely move about in the environment. Thirty-six older community-dwelling adults (age ≥ 70 yr), who lived independently in their home or in an independent living retirement center, and routinely made at least three trips into the community, were included in the study. Performance measures to determine mobility disability included a mobility test (3-min timed walk test with turns), a balance test (Berg Balance Scale or BBS), and a lower extremity performance battery (Short Physical Perfor-

mance Battery or SPPB). Typical community mobility was measured by questionnaire to provide information regarding community trips taken including number of trips per week, type and quantity of activity done per trip, transportation used, and whether they were accompanied or unaccompanied by another person. Field observations were then performed with a researcher observing three trips into the community including going to a grocery store, a health care practitioner visit, and a recreational trip. Environmental challenges were documented including distance covered, outside and inside lighting conditions, ambient temperatures, weight of packages carried, and postural transitions performed by the subjects.

Those with mobility disabilities tended to take fewer trips, perform fewer activities per trip, and were accompanied by another more often on their trips. Both groups were required to walk approximately 1000 ft per trip to complete their activity. Those without disabilities were different than those with disabilities in the ability to move at a pace equal to those around them; encounter busy streets; carry heavier packages (weighing 6.7 lbs compared with 1.6 lbs for those with disabilities); traverse two flights of stairs, take elevators, move on grass, and around obstacles; avoid collisions with other pedestrians; and make postural transitions with changing head directions, reaching above shoulder height, reaching beyond arms length, reaching below knee height, and changing movement directions when necessary. Gait speed in the group without mobility disabilities was 1.2 m/sec (22 min/mile) compared with 0.4 m/sec (67 min/mile) in the disability group.

Assessments to Determine Mobility Disabilities

Assessments can be performed by a physical therapist (PT) or an occupa-

tional therapist (OT) in the home or in a clinic to determine a patient's ability to accomplish many of the tasks stated above. Rikli and Jones tested over 7000 older adults nationwide, aged 60 to 94 yr, to provide normative data for independent-living males and females (6). The Senior Fitness Test (SFT) was developed to assess physical mobility parameters including endurance, strength, flexibility, agility, balance, and body composition. A 6-min timed walk test and 2-min timed step test evaluate a person's endurance. For the 6-min walk test, the individual walks for 6 min over a measured area and the total distance covered is recorded. The 2-min timed step test involves marching in place for 2 min, counting each time the right knee is raised. The 30-sec chair stand test quantifies lower extremity strength that is required for standing from a chair, climbing stairs and curbs, and squatting down. The person stands from a sitting position without using the upper extremities for assistance, and then returns to sitting as many times as possible in 30 sec. The total number of chair stands is the score. A 30-sec arm curl test assesses biceps strength that is necessary to lift and carry packages. For this test, females use a 5-lb dumbbell and males use an 8-lb dumbbell. From a seated position, the person lifts the weight from a hanging position near the hip to the shoulder and then back down as quickly as possible. The back scratch test provides a measurement of general upper extremity flexibility that is required for reaching ADLs and self-care tasks including bathing and dressing of the upper body. The test is performed by having the person reach one hand up in the air and then bending the elbow to touch the back as if to pat the upper back. The opposite hand reaches down toward the ground and then with a bend of the elbow, reaches up the back as far as possible. A mea-

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surement from the middle fingertip of each hand provides a flexibility measurement. A chair sit and reach test measures lower extremity flexibility which can help a person reach down to get things from the floor and to perform self-care tasks such as donning and doffing pants, socks, and shoes. The person sits on the front edge of a chair, extends one leg out straight, and then reaches both hands toward the toes of the extended foot. The 8-ft up and go test entails standing from a chair, walking forward to an obstacle, circling around the obstacle, returning to the chair and sitting down as quickly as possible. This is performed to assess a person's agility and balance that are needed for community ambulation around other people and obstacles and for crossing a busy street quickly and safely. In addition to the SFT, PTs and OTs commonly perform the Berg Balance Scale, a test that can be completed in 10 to 15 min that incorporates typical movements (sit to stand transitions; static sitting and standing; standing with feet close together, eyes closed, heel to toe, and on one foot; reaching forward; picking up an object from the floor; turning to look behind; turning around in a circle; and alternately touching the feet up to a step) and has been shown to be valid and can reliably predict fall risk in older adults (7). Gait speed is another quick test which can be performed by a PT or OT to evaluate a person's comfortable

and fast walking speed (8). The person is asked to walk along a measured distance (usually 4–10 m) at comfortable pace and then as quickly as possible and the result can be converted to meters/second. Fast gait speed improves safety in the community when crossing a street at a traffic signal and to walk well in the vicinity of others.

Interventions to Improve Mobility

Once a person's ability to move is evaluated, PT and OT interventions can target deficits, to improve an individual's independence in the community. Endurance can be improved through performance of aerobic exercise such as walking, riding a bicycle, swimming, and aerobic exercise. Upper and lower extremity strength can be improved through resistance training on weight machines, with free weights, with exercise tubing/bands, or by using the body's weight against gravity. Gait speed can be improved through lower extremity power training which would include strength training at a fast pace. Agility and balance can be improved through lower extremity strength training and challenging balance-specific activities (including Tai Chi). Flexibility is gained by specific stretches to the affected body region. The aging adult with endocrine disorders should initially be instructed in appropriate exercises and monitored periodically to ensure a safe and effective program.

Older adults must have a certain level of endurance, strength, balance, and agility to safely remain in the community. Many patients with endocrine disorders have mobility limitations, are challenged with normal activities, and can suffer catastrophic consequences if they fall. Through a task-oriented assessment and guided intervention, a person can work to improve their status as an independent, community-dwelling person.

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EMPLOYMENT OPPORTUNITIES

Single practicing physician (Endocrinologist) looking for associate doctor—full-time—in Beverly Hills, California, Office. Large practice. Salary is commensurate with time of postgraduate training. Please fax bios to: (310) 652-2269. For information: please call (310) 657-1780.

Board Certified or Board Eligible Endocrinologist

San Antonio, Texas. We are seeking a Board Certified or Board Eligible Endocrinologist doctor to work in an eight-physician Endocrine group at the Texas Diabetes Institute (TDI). The TDI is a 153,000 square foot state-of-the-art facility devoted to the care of patients with diabetes and includes all medical and surgical subspecialties devoted to the compre-

hensive care of the diabetes patient. The Endocrine physicians must be capable of interacting with a large Diabetes/Endocrine group at the University of Texas Health Science Center including seven other Endocrine physicians. The physician will have a faculty appointment as a Clinical Assistant Professor at the UTHSCSA. The University of Texas Health Science Center at San Antonio (UTHSCSA) is an equal opportunity affirmative action employer. The UTHSCSA offers a competitive salary and generous benefits package. **All faculty appointments are designated as security-sensitive positions.** Interested candidates should contact Ralph A. DeFronzo, M.D., Deputy Director at TDI, Professor of Medicine, and Chief of the Diabetes Division, UTHSCSA (210-567-6691), and e-mail a copy of their CV to Albarado@uthscsa.edu.



ENDOCRINE FELLOWS FOUNDATION ANNOUNCES ITS RESEARCH GRANT RECIPIENTS FOR THE SPRING CYCLE OF 2008

Derek LeRoith, M.D., Ph.D., Director, Grants Program

The Endocrine Fellows Foundations received 32 grant applications for the spring cycle. Awardees receive \$7,500 to facilitate their research. Applications were received covering projects on diabetes/obesity, bone, pituitary, PCOS, thyroid, and growth. Among the 49 experts who were asked to review these applications, the EFF received 100% participation from across the country. The average grant received three separate reviews. Using an NIH-based priority system, many grants were very favorably received. We are pleased to announce that six grants were approved for funding. The awardees are listed below:

Jennifer Bell, M.D.—Baylor College of Medicine
“Androgen Receptor Signaling in Children with Hypospadias”
Program Director, Morey Hammond, M.D.

Marissa Grotzke, M.D.—University of Utah
“Associate between Iron and Adiponectin”
Program Director, Donald McClain, M.D.

Jyotsna Keni, M.D.—University of California—Los Angeles
“The Role of Humanin in Beta Cell Survival”
Program Director, Kuk-Wha Lee, M.D.

Gregory Ku, M.D.—University of California—San Francisco
“An RNAi Screen for Regulators of the Insulin Promoter in Pancreatic Beta Cells”
Program Director, Michael German, M.D.

Lindsey Nicol, M.D.—University of Wisconsin
“Fetal Programming of PCOS by Androgen Excess: A Developmental Etiology for Changes in Islet Cell Mass and Subsequent Manifestation of Decreased Insulin Secretion”
Program Director, David Allen, M.D.

Airani Sathananthan, M.D.—Mayo Clinic
“OCT1 and Response to Metformin”
Program Director, Neena Natt, M.D.



Contribute to *EndoTrends* . . .

Submit a patient case study, journal review, or research update to *EndoTrends*. It is an innovative, quarterly newsletter for endocrine fellows sponsored by the Endocrine Fellows Foundation (EFF). In each issue, we seek to provide practical clinical information on a variety of topics.

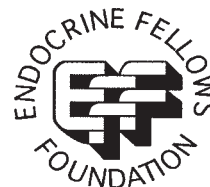
The Endocrine Fellows Foundation realizes that, as dedicated medical practitioners, our mentors and peers are our best resource for growth and education. Endocrine Fellows are encouraged to submit ideas and/or articles for publication and will receive a \$300 honorarium for accepted material.

Articles should range from 800–1000 words or two to four typewritten pages. Exceptions for longer or shorter articles may be made based on content. Submissions should include an original manuscript (including all applicable bibliographic references), a diskette containing the article (Word 6.0 preferred, ACSII format also accepted), plus any accompanying photographs, charts, or graphs (graphic accompaniment to submitted articles is highly encouraged).

Figures should be submitted as TIFF or EPS files. Photoshop files are also acceptable. Please submit artwork at the size it should be printed. See <http://cjs.cadmus.com/da> for additional information. Please provide a good quality hard copy for each figure submitted. Please send figures on CD or disk rather than e-mail.

Please note: EFF reserves the right to edit the material as necessary to accommodate the available space. **Your Mentor must review, approve, and sign off on your articles before you submit them to our office.**

If you have a topic that you think would be of interest to our readers, please forward your submission to Marilyn Fishman, Executive Director, The Endocrine Fellows Foundation, 5959 W. Century Boulevard, Suite 550, Los Angeles, CA 90045. For questions, please call (877) 877-6515.



To All Program Directors:

Please help us update our database so that

ALL of your Fellows will receive our valuable information, such as:

- *EndoTrends* – A quarterly publication published by EFF to disseminate clinical and research findings of interest to Fellows
- Research Grants – Grants awarded annually during two award cycles, Spring and Fall.
- Scientific Forums – Travel grants are offered to one Fellow from each accredited training program.
- Preceptorship – The EFF offers two-week preceptorial programs designed to provide fellows the opportunity to work with mentors in specific areas of endocrinology and metabolism.

Incoming and Current Fellows as of July 2008:

Name: _____ Phone: _____ Fax: _____

Fellowship Year: 1st 2nd 3rd– Completion date of Fellowship: _____ E-Mail _____

Name: _____ Phone: _____ Fax : _____

Fellowship Year: 1st 2nd 3rd– Completion date of Fellowship: _____ E-Mail _____

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