Family Practice Grand Rounds

Multiple Sclerosis

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DR. ERICH BRUESCHKE *(Residency Director, Professor and Chairman of the Department of Family Practice)*: Today's Family Practice Grand Rounds conference will be presented by Dr. Vasireddy Bhoopal, second year family practice resident who is the patient's family physician. Although I would like generalized questions and comments from all residents present, I would particularly like to have Dr. Gerald Sutton (second year family practice resident), Dr. Edward Shanik (third year family practice resident), and Dr. Carolyn Lopez (first year family practice resident) bring out any areas relevant to family practice or the patient that may not be evident in Dr. Bhoopal's presentation.

The Rush-Christ Residency's family practice center is at Christ Hospital. The service area of the family practice center, within a three-mile radius, encompasses a population of almost 100,000 people consisting of young and old working class and middle class families of predominately white ethnic background, as well as increasing numbers of blacks and other minorities, many of whom are poor, unskilled, and unemployed. Most of these families contain at least two children, the majority of them in their preteens. The community also contains a large number of older residents who suffer from the major chronic diseases that are associated with the aging process. These individuals, many of whom are members of large extended families living in the community, need continuous health care. As a population base, they also provide a particularly good opportunity for the practice of preventive medicine. This population is in need of comprehensive, quality primary health care and is an ideal site for the family practice training center.

The family practice center has been in operation for four years. At the present time there are 7,400 registered patients in the family practice center with 15,000 patient visits per year. Continuity of experience is assured for both the patient and the resident who serves as the patient's primary physician before admission, during hospitalization, and for follow-up.

The patient was self-referred, living with her parents about two miles from the family practice center. This case especially illustrates that while the presenting complaint may be substantiated by the physical findings, other significant problems may be identified through careful history and physical examination.

DR. VASIREDDY BHOOPAL *(Second year family practice resident)*: Miss S. A. is a 23-year-old white woman who registered with us upon the suggestion of her mother who had heard favorable comments about the family practice center from neighbors who are center patients. She

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0094-3509/80/010131-05$01.25

was seen by me in August 1978 with a chief complaint of chest pains on and off for the past six months which progressed gradually and subsequently remained unchanged in severity. This was described as a vise-like tightness in the left side of the chest anteriorly, aggravated by exercise and emotional stress. It was not associated with shortness of breath or perspiration. She admitted to having had palpitations on and off, much worse when emotionally upset or when tired. She also complained of dizziness which was first noted ten months prior to her first visit and which had improved in two months but recurred at this time. She denied true vertigo, nausea, flashing lights, or colored halos. She denied any spots in her vision but admitted to some buzzing noises in both ears which were worse on the left side. These were the only symptoms originally presented. Upon completion of the initial outpatient physical examination and returning to the history, the patient admitted to mild weakness in both legs and easy fatigability with loss of balance at times mostly to the left. She equated this to her generalized weakness and did not attach much importance to these symptoms. She also admitted seeing double in the left eye on looking to the left. She did not like hot baths as they made her feel dizzy. She had experienced frequency of urination and mild dysuria on two different occasions in the past. Occasional retro-orbital ocular pain was relieved by aspirin.

Personal History

The patient was divorced in 1976, has two children aged two and four years who live with her, is a housewife who has been infrequently employed, and is currently supported by public aid. She graduated from high school in 1968. She lives with her parents and one brother aged 24, and she frequently gets upset at home over simple arguments with them. Her father retired from the post office two months prior to her first visit to the center. They live in a simple family home in a blue-collar suburb where her mother works as a clerk in a grocery store. There is no significant family history of diabetes, hypertension, carcinoma, or neurological problems. She smokes one pack of cigarettes a day and denies using any drugs or alcohol. Her menstrual history is normal and she is not taking medications.

Past History

She had rheumatic fever at the age of nine and was hospitalized for three weeks in Chicago. Subsequently, she was on prophylactic sulfadiazine for five years (as she was allergic to penicillin), but stopped because she did not go to any physician for follow-up. She had the usual childhood diseases, no history of significant traumatic injury, no surgical operations or additional hospitalizations.

DR. BRUESCHKE: Would you like to ask further questions pertaining to history at this point?

DR. GERALD SUTTON *(Second year family practice resident)*: Did she ever complain of arthralgia or rash at any time?

DR. BHOOPAL: No, she did not.

Physical Examination

The patient is a thinly built 23-year-old white woman, anxious looking, not in distress. The blood pressure in both arms was 90/50 mmHg; pulse rate was 90 per minute and regular; no alopecia, no lymphadenopathy, and no rash were noted. The cardiovascular examination revealed a normal S-1 but a sharp and accentuated S-2 with midsystolic click which was best heard in the fourth and fifth left intercostal space and which increased in intensity on standing. There was also a soft, grade II/VI, late systolic murmur best heard at the apex. The lungs were clear, the abdomen was within normal limits with no organomegaly. Examination of the central nervous system revealed very important signs. Both pupils were equal and reacting briskly but when the light was kept focused on the pupils they dilated showing the Marcus-Gunn phenomenon. There was bilateral coarse nystagmus in horizontal, vertical, and rotatory directions which became worse on lateral gaze. There was also diplopia in the left eye on lateral gaze. Eye pressure was normal, fundi showed pallor of the temporal aspect of the disc and distention of the venules with a picture resembling early papilledema. Visual acuity was normal and color vision testing by Ishara charts showed mild blindness to red and green. Examination of the cranial nerves from 1 to 12 were within normal limits except the left fourth nerve showed mild paresis. Examination of the ears was

within normal limits. Sensory examination for light touch, 2 point discrimination, temperature, and pain were all within normal limits. Vibration sense in the lower limbs was diminished and she made mistakes at times during testing of joint sense. Examination of motor power revealed definite weakness in hip flexors. The muscle tone in the lower limbs was increased. Deep tendon reflexes were exaggerated in the lower limbs with patellar and ankle clonus. She had bilateral Babinski sign. Gait was ataxic and she could not perform tandem gait. The Romberg test was negative. Toe-heel walk was fairly good and coordination was basically intact. Repetitive movements were done without difficulty. Examination of the spine did not reveal any local tenderness and movement of the spine was within normal limits. The superficial abdominal reflexes were absent. Her speech seemed to be slurred at times. Pelvic examination was within normal limits as was rectal sphincter tone.

DR. BRUESCHKE: At this point what are the differential diagnoses you have in mind?

DR. BHOOPAL: This is a 23-year-old white woman with chief complaint of anginal-type chest pain, diplopia, and dizziness at intervals, and retro-orbital pain. The pertinent physical signs were a loud sharp midsystolic click and grade II/VI, late systolic ejection murmur. Moderate hypotension was evident on repeated blood pressure readings. Neurological signs showed an early picture of papilledema or optic neuritis, paresis of the left fourth cranial nerve, absent abdominal reflexes, ataxia and pyramidal symptoms with spasticity, mild proximal weakness of lower limbs, and questionable disordered posterior column sensations.

Taking these into consideration I think that two different entities account for this patient's symptomatology. The chest pains and palpitations are most probably due to a prolapsed mitral valve with typical click and murmur. The neurological picture of symptoms-signs involves various levels of the central nervous system without continuity, with a pattern of remission and exacerbations mainly involving white matter. This makes me think of a demyelinating disease. Other possibilities such as migraine, cerebellopontine angle tumor, slowly growing gliomas, neurosyphilis, heavy metal poisoning, spinal cord compression, transverse myelitis, and systemic lupus erythematosus involving the central nervous system must be kept in mind.

DR. EDWARD SHANIK *(Third year family practice resident)*: Was there a history of convulsions, or history of recent vaccination or infections?

DR. BHOOPAL: No. This is a very pertinent question as post-vaccinal syndromes and even the Guillain-Barré syndrome may have certain features in common.

DR. BRUESCHKE: What was your working diagnosis, how did you propose to do the work-up, and what were the laboratory findings?

DR. BHOOPAL: My working diagnosis was "diffuse demyelinating disease," possibly multiple sclerosis, and I decided to admit the patient on an elective basis, explaining to the patient and the family the various possibilities.

Laboratory Data on Admission

CBC, electrolytes, BUN, SMA-12, sedimentation rate, and rapid plasma reagin (RPR) were all within normal limits. The urinalysis showed a moderate number of red blood cells, but on history, the patient admitted to having her period. A repeat urinalysis later was normal. The electrocardiogram (ECG) was reported as normal but, as she was complaining of palpitations, a 24-hour Holter monitoring was done which showed multiple PVCs during the day which disappeared in sleep. An echocardiogram clearly demonstrated a prolapsed mitral valve. Isotopic brain scan and EEG were within normal limits. X-ray films of the chest, lumbosacral region, and skull, and tomograms of the petrous pyramids were all within normal limits. A CAT scan of the head with and without infusion study were within normal limits. The electrophoretic pattern of serum proteins was within normal limits. The immune profile showed positive ANA 1:160 titre with homogenous pattern. Anti DNA and ENA were negative. LE prep was negative. IgG, IgA, and IgM levels were within normal limits.

As all the above tests were normal and inconclusive for specific neurological disease, my suspicion of multiple sclerosis (MS) strengthened, and we decided to perform visual evoked response (VER) tests at Rush-Presbyterian-St. Luke's Medical Center. The results were very abnormal and further suggested MS. Thus, the picture, resem-

bling papilledema of her fundi with some visual acuity deficit and color blindness, was instead optic neuritis from MS. A lumbar puncture was also done and showed normal pressure, color, cell count, sugar, chlorides, LE prep, and compliment levels. The spinal fluid, VDRL, culture for bacteria-fungi, counter-immuno-electrophoresis, and limulus were negative. The IgG/albumin index was increased at 0.56, the upper limit being 0.44. The oligoclonal IgG band was positive on agar gel electrophoresis.

DR. BRUESCHKE: Did the patient have any euphoria?

DR. BHOOPAL: I am glad you asked this question as I overlooked it. After I disclosed the most probable diagnosis and its implications and prognosis to her as well as the possibility of being disabled, she was not terribly upset or depressed but conveyed to me the impression that as long as it was not lethal it did not bother her. This lack of concern suggests a significant degree of euphoria.

DR. CAROLYN LOPEZ *(First year family practice resident)*: How do you explain her hypotension and retro-orbital pain?

DR. BHOOPAL: In patients with MS it is not unusual to have some autonomic disturbances, and hypotension could be due to autonomic imbalance; retro-orbital pain was possibly from edema around the optic nerves as it disappeared after treatment with steroids.

DR. SHANIK: How would you suspect MS and what are the pathognomonic features and laboratory tests for this disease?

DR. BHOOPAL: There is no single feature or laboratory test which is pathognomonic of multiple sclerosis. However, the following criteria are useful as a guideline. MS is a disease "scattered in time and space" and several features weigh heavily in the diagnosis:

1. Evidence of fluctuations in the course of the disease with well-defined remissions and exacerbations against a background of slow progression.
2. Elicitation of signs and symptoms indicating scattered lesions of white matter in the central nervous system.
3. Abnormal VER, high IgG/albumin index, and oligoclonal bands support the diagnosis.
4. If there is evidence of involvement of basal ganglia or central nervous nuclei or anterior horn cells of the spinal cord, MS can be ruled out most of the time as MS is a disease of white matter.[1] An almost pathognomonic sign resulting from plaque formation in the posterior columns of the cervical cord is the occurrence of tingling or electric-like paresthesias extending into limbs or trunk on flexion of neck; this is known as Lhermitte sign.

DR. SUTTON: How do you plan to treat this patient, and what is the prognosis?

DR. BHOOPAL: Steroids have been the main therapeutic tools in acute attacks only and do not seem to inhibit or stop the process.[2] Both ACTH and prednisone have been used. Some benefit for acute episodes has been shown by Miller et al[3] by using ACTH at doses of 40 units twice a day for 7 days, 20 units twice a day for 4 days, and 20 units daily for 30 days. However, the study done by Rose et al[4] showed no evidence of improvement in symptoms and signs, and the ultimate result was no greater than placebo. So there appears to be little basis for using ACTH. Others have advised use of immunosuppressant therapy with azathioprine (Imuran), and favorable results have been reported by Tucker et al.[5] These modalities have yet to be accepted and have not been proven by controlled therapeutic trials. Spasticity, a major drawback in patient daily activities, could be minimized by use of dantrolene (Dantrium), diazepam (Valium), or lioresal (Beclofen). Physical therapy is of help in reducing flexor spasm and gaining functional improvement.

Before the therapy was started a neurological consultation was obtained and the neurologist examined the patient. Our work-up agreed with the diagnosis of a demyelinating disease. Steroid treatment was agreed upon. Before the steroids were started the usual precautions were taken. A barium study of the upper gastrointestinal tract was done to exclude any active peptic ulcer disease. A skin test with PPD (purified protein derivative), 5 units, was done and was negative. There were no other contraindications for steroids in this patient. Our patient was treated with prednisone in the following regimen: 60 mg a day for 10 days, 40 mg a day for 10 days, 20 mg a day for 10 days, and gradually tapered over another 3 weeks time. After starting the steroids, she was discharged after about ten days and improved dramatically in most symptoms and signs. Her retro-orbital pain completely disappeared. The ataxia was still present but to a considerably lessened degree. There was no improvement in her nystagmus. Diplopia persisted but was not bother-

some to the patient. She has been followed in the Rush-Christ family practice center and is doing well. She was also started on propranolol 40 mg three times a day, after an initial dose had been well tolerated. The pulse rate came down to 60 beats per minute with no great rise after mild exercise indicating adequate beta blockade. The chest pain subsided and there were no complaints of palpitations. She was restarted on sulfadiazine, 1 gm a day, as prophylaxis for rheumatic fever.

The prognosis in MS is not altogether as bleak as one initially might think. One third of the patients live a comfortable life with no assistance needed, one third of the patients are restricted to a wheelchair but still can function usefully, and only one third become totally crippled and bedridden, needing assistance in their daily care. Longevity is probably equal to that in the general population or at least 25 to 30 years. Death is usually due to secondary complications such as urinary tract infection and pneumonia.[6]

DR. BRUESCHKE: Our time is up. Thank you, Dr. Bhoopal, for your presentation of this interesting case. This once again points up the variety of problems we see in our unselected patient population in family practice and the necessity to remain alert to various possibilities in the patient.

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