ELECTROPHYSIOLOGICAL EVALUATION AND SURGICAL TREATMENT RESULTS OF A SCOLIOSIS PATIENT WITH FRIEDREICH ATAXIA

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SUMMARY:

A fourteen years old boy with a former diagnosis of idiopathic scoliosis was examined at Neurology Department of Hacettepe University Faculty of Medicine after development of an ataxic gait, weakness and dispnea after a posterior instrumentation and fusion operation at 1st Department of Orthopaedics and Traumatology of Ankara Social Security Hospital in April 1994. Transcranial magnetic stimulated motor evoked potential and nerve conduction study of the patient were performed. This patient also had bilateral mild pes-cavus. The electrophysiological findings correlated with a demyelopathy and polyneuropathy. Myocardial dysfunction was determined with echocardiography. The final diagnosis was Friedreich Ataxia. Preoperative Cobb angle which was 95° was brought to physiological limits (40°). Lateral trunk shift was significantly corrected from 2.6 vertebral units (VU) to 0.9 VU. However, after a follow-up of 18 months a severe correction loss was recorded at the frontal plane. This case is presented to emphasize the importance of a meticulous neurological examination as it can also effect the future therapy planning.

Key Words: *electrophysiology, Scoliosis, Friedreich ataxia.*

INTRODUCTION

In Friedreich's ataxia, the most common form of the hereditary cerebellar ataxias, both the cerebellar and the spinal cord pathways are involved. In the spinal cord there are degenerative changes of the dorsal and ventral spinocerebellar tracts, the corticospinal tracts and posterior column. There may be loss of anterior horn cells. In the cerebellum there is atrophy of the Purkinje cells and the dentate nuclei; changes in the brain stem may occur. Degeneration of the corticospinal tract may occasionally extend above the level of the medulla. Certain characteristic musculoskeletal deformities are observed. A slowly progressive scoliosis usually in the thoracic region is most common and is present in approximately 80-90 per cent of patients (1, 23).

In this study, we report a patient who had had a diagnosis of idiopathic scoliosis initially and had been fused and instrumented posteriorly, but after developing an ataxic gait and progressive loss of correction during postoperative follow up had been diagnosed as Friedreich's ataxia with electrophysiological evaluation.

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CASE REPORT:

In January 1994, a fourteen years old male patient was admitted to the 1st Department of Orthopaedics and Traumatology. Ankara Social Security Hospital with a complaint of hump in his back. It had been first noticed when he was 9 years old and had progressed in the following 5 years. The patient was hospitalized with the diagnosis of idiopathic scoliosis. Cobb angle of thoracic curve in the frontal plane was 95° and angle of thoracic kyphosis was 66° (Figure 1). In April 1994, his flexible curvature was instrumented with Texas Scotish Rite Hospital (TSRH) System and fused with autologous graft posteriorly. In the early postoperative period no complication and neurologic deficit was observed. After a month he developed an ataxic gait with weakness in his legs and also numbness in his legs and hands. The patient was evaluated for neurologic disability with clinical examination and electrophysiological methods.

In the neurological re-examination, bilateral gaze - evoked horizontal nystagmus was found. He was quadriparetic and had stocking - glowe hypoesthesia. There was a prominent loss of proprioception below T-2 level. Deep tendon reflexes were hypoactive in the upper extremities but were completely lost in the lower extremities. Plantar reflex was abolished bilaterally and aschilles clonus was positive bilaterally.

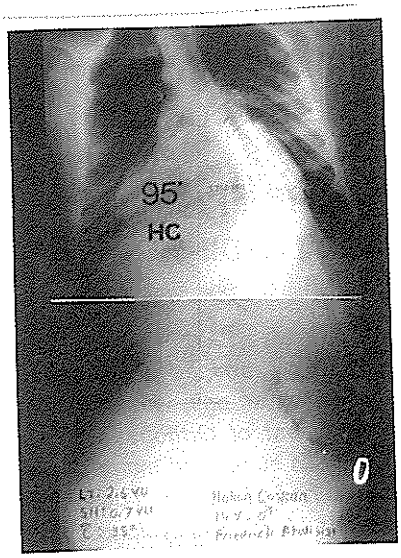


Figure 1a

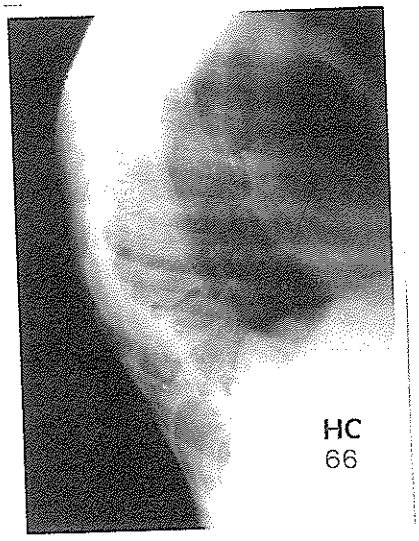
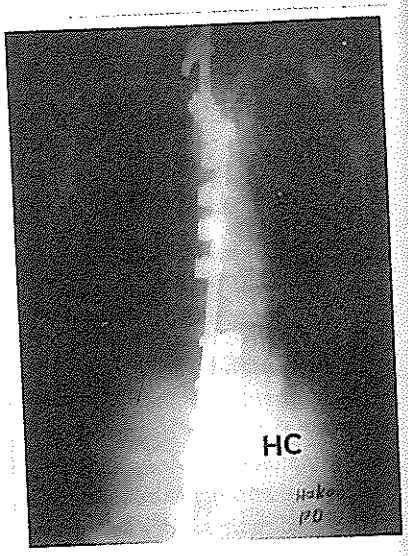


Figure 1b



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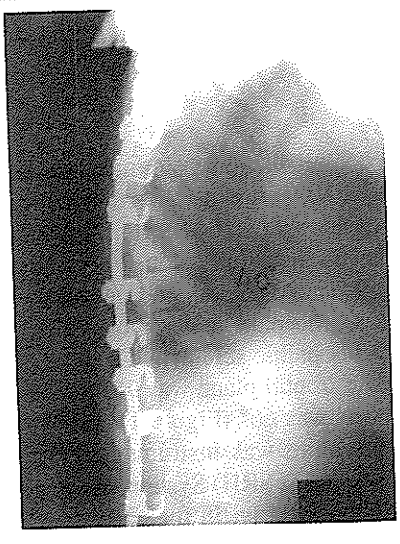

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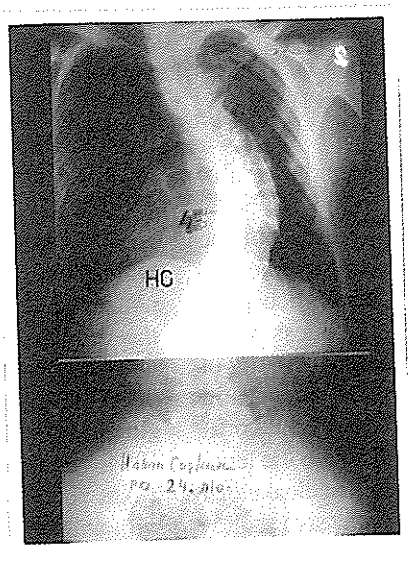

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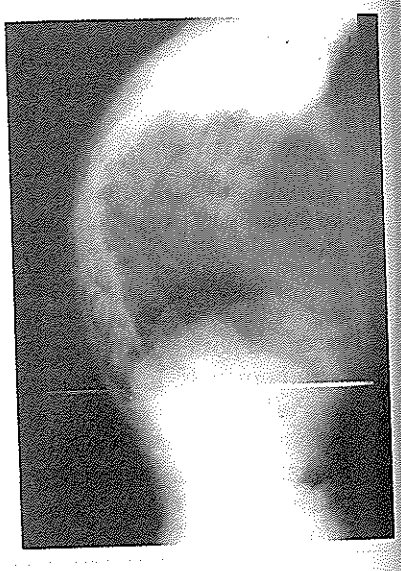

Figure 1f

Figure 1. Preoperative (a, b), postoperative (c, d) and last (e, f) antaroposterior and lateral radiograms of the patient.

Cerebellar tests were abnormal. Shoulder girdle, hypothenar and interosseous muscles were atrophic bilaterally.

In the orthopaedic examination, moderate pes cavus and hammer toe deformities were observed bilaterally.

Cranial, cervical and thoracal MR imaging were normal (Figure 2). For instrumentation, titanium TSRH implants were used. There was no artefact in MR imaging because titanium is MR compatible. There was also no syrinx or medullary atrophy in MRI.

From his anamnesis it is learned that his uncle had bilateral pes cavus, and his mother and father were relative (son and daughter of each others uncle).

Nerve conduction study and transcranially magnetic stimulated motor evoked potentials were

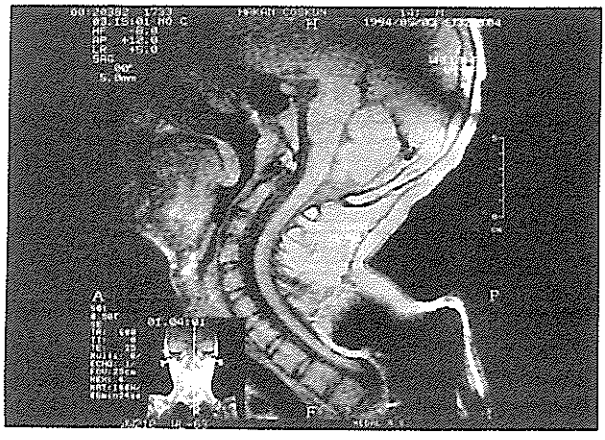

Figure 2a

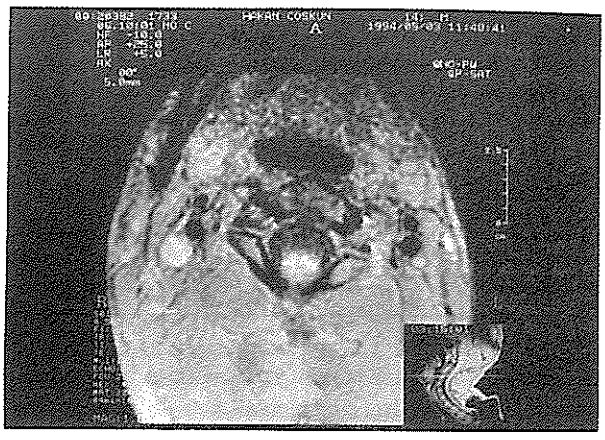

Figure 2b

Figure 2. Cervical axial and sagittal MRI of the patient were normal.

performed, and the results are shown in Table 1 and 2. In motor evoked potential study with transcranially magnetic stimulation there was no muscle response in the lower extremities and bilateral prolongation of both central motor conduction time and peripheral motor conduction time of the cervical spinal cord. In nerve conduction study of the patient peripheral motor and sensory nerve conduction velocities were found to be markedly decreased in consistence with a mixed type of demyelinating polyneuropathy. There was no answer in sural nerve conduction bilaterally. In his echocardiography and electrocardiography there were myocardial dysfunction and myocardiopathy. With clinical and electrophysiologic findings it was thought to be Friedreich ataxia.

Table 1. The findings of the motor examination of the patients (According to Modified Medical Research Council (MRC) Scale).

	Right	Left
Deltoid Muscle	4 - / 5	4 + / 5
Biceps Muscle	4 - /5	4 + / 5
Triceps Muscle	4 - /5	4 + / 5
Distal hand Muscles	4 + / 5	5 / 5
Iliopsoas Muscle	3 / 5	4 - / 5
Quadriceps Muscle	4 - / 5	4 + / 5
Hamstring Muscle	4 - / 5	4 - / 5
Dorsif lexor Muscle	3 / 5	3 / 5

4 - Resistance to gravity and mild resistance
4 + Cannot overcome

In the preoperative period his frontal Cobb angle was 95° degrees. In the postoperative period it was 24° with a correction rate of 74.7%. His thoracal kyposis angle was 66° preoperatively and was corrected to normal physiological limits. Lateral trunk shift was 2,6 VU in the preoperative period and was broght to 0.9 VU in the postoperative period. In his last control in postoperative 18th month, there was 45% loss of correction and because of the protuberance of implants, all the implants were removed (Figure 1). Because the cardiac problems were great potential risk for anesthesia, revision was not considered.

He is still in our follow-up. His ataxia and peripheric hypoesthesia got worse and his functional capasity is lowered (Figure 3).

DISCUSSION

The German neurologist Nikolaus Friedreich (1863) described an inherited degenerative disease with sclerosis of the dorsal and lateral columns of the spinal cord. The disorders is accompanied by ataxia, speech impairment, lateral curvature of the spinal column and muscle weakness, particularly involving the lower extremities (3). Males and females are effected equally (1, 23). The prevalence of Friedreich ataxia is approximatelly one in 50.000 (14).

It is definitely hereditary and is commonly transmitted by an autosomal resessive gene. Often it can be traced through a number of generations. In some members of the family, it may occur only in mild and incomplete forms (1, 22). Because his uncle has a mild form of disease and because his mother and father are

Table 2. MEP findings of the patients (ms: milliseconds, Amp: amplitude, mV: milivolt, CCT: Central conduction time).

	Right		Left	
	Latency (ms)	Amp. (mV)	Latency (ms)	Amp. (mV)
Verteks-ADM	47.2	1.7	55.4	0.2
C7-ADM	26.6	0.3	43.5	0.1
CCT	20.6	–	11.9	–

healthy relatives our patient is thought to have an autosomal recessive transmission.

Friedreich ataxia and ataxia with selective vitamin E deficiency (AVED) share very similar clinical phenotypes. Ben Hamida et al. mapped the AVED locus to proximal 8q in the three large consequinous Tunisian families (4). But, the abnormal gene is located on cromosome 9 in the patient with Friedreich ataxia. Otherwise the biochemical disorders that cause the disease has not yet been identified (11). The Friedrich's ataxia locus is tightly linked to markers D9S5 and D9S15 located in 9q13-q21 (9, 14, 23). Duclos et al. found eight polymorphic DNA changes but no causative mutations were found. The discovery of a simple sequence repeat polymorphism in the most centromeric gene allowed the localization in a Friedreich ataxia family,

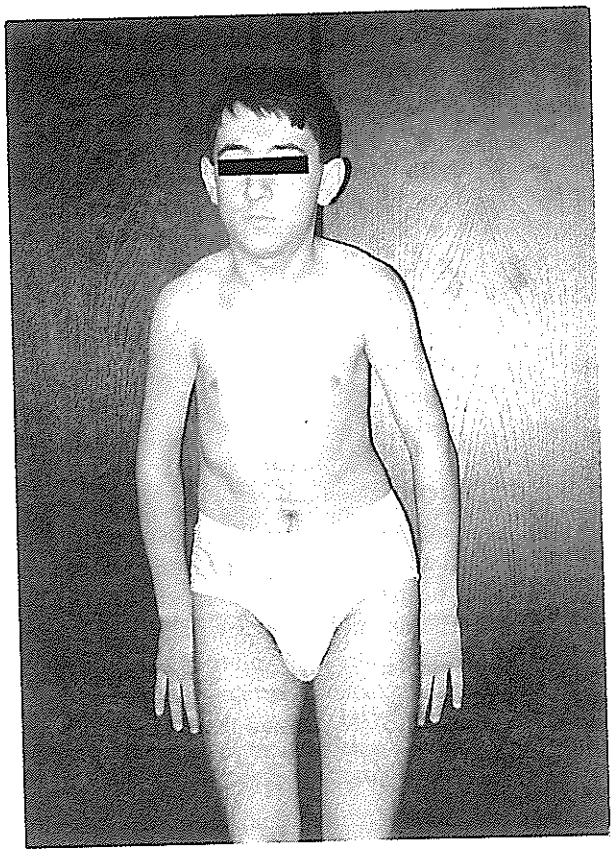

Figure 3a

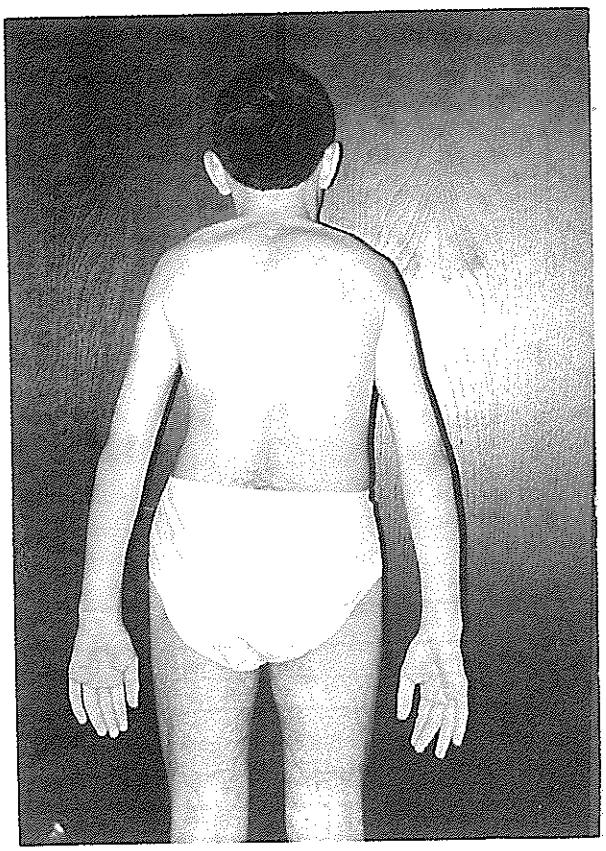

Figure 3b

Figure 3. Pictures of the patient at the last control. His ataxia and peripheric hypoesthesia got worse and his functional capasity is lowered.

Table 3. The results of nerve conduction studies of ulnar nerves and peroneal nerves in the patient
(ms: milliseconds, mV: millivolt).

	Latency (ms)	Velocity (wrist/leg) (m/sn)	Amplitude (mV)
Right Ulnar Nerve	8.5	25	2.4
Left Ulnar Nerve	11.1	31	1.4
Peroneal Nerve	6.7	20	1.5

therefore excluding the two distal genes from the FRDA region (19, 21). The condition appears to be a single - gene disorder with variation in characteristics such as the age at onset and rate of progression, due to different mutation at the same locus (14, 22).

The onset of symptoms is usually in childhood, between the ages of seven and fifteen years: the mean age at onset in two large studies was eleven and twelve years, but often is so insidious and difficult to determine when the condition was first present (1, 13, 22). An unsteady gait is almost always the first symptom to attract attention. Over a period of years, these symptoms progress and ataxia of the upper limbs develops (1). In our patient, probably, the symptoms began in same ages but by chance, progressed in the postoperative period and his ataxic gait became evident.

Geoffroy et al. identified strict criteria for the clinical diagnosis of Friedreich ataxia. These criteria include the primary symptoms and signs required to make the diagnosis, and the secondary symptoms and signs that are present in most patients are not essential for the diagnosis. The primary symptoms and signs include onset before the age of 20 years, ataxic gait, documented progression of the ataxia, dysartria, decreased proprioception and/or vibratory sense, muscle weakness and absent deep tendon reflexes. The secondary symptoms and signs include pes cavus, scoliosis, a Babinski sign and cardiomyopathy (3).

The ataxia is both spinal and cerebellar in type. The feet, as a rule, show symmetrical cavus deformity with marked elevation of the longitudinal arch and hammer toes. Pes cavus may be the initial deformity prior to the development of any neurologic signs (22, 24). Our patient also had moderate degree of bilateral pes cavus and hammer toe.

Cranial nerves are normal, eventually, however, a horizontal or rotatory nystagmus develops (3, 20). And in our patient there was bilateral horizontal end point nystagmus.

The deep tendon reflexes- the knee and ankle jerks- in two lower limbs usually became absent very early in the course of the disease. Subsequently the biceps and triceps jerks in the arms disappear. The plantar response is extensor. On sensory examination, position and vibration senses, two-point discrimination are lost, initially in the feet and later in the hand (1, 3, 17, 20, 22). In our patient DTR were weak in upper extremities and absent in lower extremities. He had extreme loss in his position and vibration senses.

Nerve conduction studies show slight decrease in motor fiber conduction velocity but marked decrease in sensory action potential. This finding distinguishes Friedreich's ataxia from hereditary motor sensory neuropathies -in the latter there is marked decrease in motor nerve conduction (1, 7, 12, 17, 20, 22). In his MEP examination there was increase in bilateral vertex-ADM latancies, and decrease in amplitudes, especially in left side. His ulnar nerve conduction velocity was decreased to 20 m/sec. Peroneal muscle weakness was the most common finding either in isolated form or in combination with paresis of the anterior tibial (12). Also our patient had same kind of muscle weakness.

A cardiomyopathy is seen in almost all patients, as diagnosed on the basis of abnormalities on electrocardiograms and echocardiograms, but it is rarely symptomatic in childhood, adolescence, or early adulthood (1, 5, 22). Cazassa et al. reported clinical, electrocardiographic and echocardiographic 5 -year follow- up results of 61 patients with Friedreich ataxia in their institution. They found that cardiac failure was evident in 5 % of the patients and was the most common cause of death. Cardiac arrhythmias were most commonly supraventricular in origin, usually occured together with the onset of cardiac failure. ST-T abnormalities were present in 91 % of the cases. Left ventricular hypertrophy was evident at the echocardiogram in 75 % of the cases (8). Our patient's echocardiographic examination showed cardiomyopathy and myocardial disfunction. He also had ST-T abnormalities in his electrocardiogram.

Recent studies have confirmed that scoliosis occurs essentially in all patients who have Friedreich ataxia (22). Cady and Bobechko reported on 42 patients with

Friedreich ataxia and identified 38 with scoliosis: a prevalance of 88 per cent (6).

Aranson et al. concluded that the incidence of scoliosis associated with Friedreich ataxia over the patient's entire life time approaches 100 per cent (3). The age at the occurance of the scoliosis was variable but it began and progressed while the patient was still able to walk. The natural history of scoliotic deformity has been characterized as showing a statistically significant correlation between the progression and severity of the scoliosis and both the onset of the disease before the age of ten years and the recognition of the scoliosis before the age of fifteen years. After 16 years of age, the curves were usually stable (2, 15). Our patient was a fourteen years old boy and his Cobb angle 95° preoperatively.

Labelle et al. reported on the natural history of scoliosis associated with Friedreich's ataxia in 56 patients. 36 had been followed up for at least 10 years, and two distinct groups were identified. Group 1 contained 20 patients whose scoliotic curves were greater than 60°, and all curves progressed. Group 2 contained 16 patients whose curves were less than 40°, and all curves stabilized that did not progress. They concluded that not all scoliosis curves in Friedreich's ataxia undergo relentless progression as has been reported in the literature, and recommended that curves less than 40° should be observed. They hypothesized that the scoliosis associated with Friedreich's ataxia was not secondary to muscle weakness, but probably related to ataxia which caused difficulty with equilibrium and postural reflex (18). Shapiro et al. concluded that although structural scoliosis always occured in Friedreich ataxia, the pattern was more like that seen in idiopatic scoliosis than in a neuromuscular disorder (22). We also thought the curvature of our patient had been idiopathic. After occurance of ataxia, we determined structural scoliosis with Friedreich ataxia was like idiopathic pattern. Thoracic hyperkyphosis beyond 40 degrees was associated with scoliosis in two-thirds of patients (18). Thoracic kyphosis of our patient was 66° preoperatively.

Daher et al. reported on their experience in 19 patients with Friedreich ataxia and scoliosis, and also found that non-operative treatment with a brace was unsuccessfull (10). Shapiro et al. also found similar results (22).

Cady and Bobechko recommended the curves reaching 40° to 50° should have a long posterior spinal fusion with Harrington instrumentation (6). Based on their study, Labelle et al. proposed the following protocol of the treatment: curves less than 40 degrees should be kept under observation; curves more than 60 degrees should be treated surgically; and curves of between 40 and 60 degrees should be observed or treated surgically, depending on the age of the patient at the onset of the disease and such characteristics of the scoliosis at the age when it is recognized, evidence of progression of the curve, and so on (18). So that we operated our patient posteriorly and stabilized the curve with TSRH instrumentation. Preoperative Cobb angle which was 95° was brought to 24° and corrected by 74.7%. Thoracic kyphosis which was 66° preoperatively was also brought to physiological limits (40°). Lateral trunk shift was significantly corrected from 2.6 vertebral units (VU) to 0.9 VU.

More vertebrae should be included in the arthrodesis (and the instrumentation) than for corresponding idiopathic curves, and the arthrodesis should extend from the upper region of the thoracic spine to the lower region of the lumbar spine (22). For this reason, we performed the long fusion from T2 to L4. However, after 18 months' of follow-up a severe correction loss was recorded at the frontal plane and because of the protuberance of implants all were removed.

Good results have been reported with several posterior-arthrodesis techniques involving Harrington rod instrumentation and Luque instrumentation (6, 10, 18). Reports have documented solid fusion with multiple techniques, in each of twelve patients who were operated on at an average age of eighteen years, preoperatively. Scoliosis of 49 degrees that improved to 26 degrees postoperatively, with a correction rate of 47 per cent and average value of 33 degrees postoperatively with a correction rate of 41 per cent. The more recently described posterior instrumentation techniques, such as the Cotrel-Dubousset instrumentation system should be effective, although result of their use in this disorder have not yet been reported (22). So, this case report is the first report about this subject. There was a 45% loss of correction, but he still has good correction and fusion. In our study, we provided a correction rate of 72.7% in the frontal plane and hyperkyphosis was brought in to physiological limits with single rod technique using TSRH system.

The course of classic Friedreich's ataxia is steadily progressive to complete disability. Remissions are uncommon in Friedreich's ataxia. An early onset is a

poor prognostic sign. Death usually occurs in fourth or fifth decade of life due to the progressive hypertrophic cardiomyopathy, pneumonia or aspiration. The range is wide, with one investigation reporting death at a mean age of 38±14.4 years (16, 22). Although neurologic findings of our patient had progressed during the follow-up, he was able to walk and do his daily activities, perhaps because of the later onset of the disease than usual. This case is reported to review Friedreich ataxia and to indicate the importance of neurologic and electrophysiologic studies to eliminate the neurological diseases manifested with scoliosis.

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