Diagnosis and Management of Kearns-Sayre Syndrome Rely on Comprehensive Clinical Evaluation

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We appreciate the readers' interest and their comprehensive comments and advice about the article,[1] which mainly concerned details of the patients' information.

In this paper, we reported 19 Kearns-Sayre syndrome (KSS) patients whose diagnoses were in accordance with the current clinical diagnostic criteria of KSS, i.e., the triad of progressive external ophthalmoplegia, pigmentary retinopathy, and onset before 20 years of age, plus at least one of the followings: heart block, cerebellar symptoms, or cerebrospinal fluid protein levels above 1000 mg/L.[2] The diagnostic criteria have been widely used.[3] Apart from clinical features, muscle pathology and molecular genetic analysis can play a great role in the diagnostic workup. Muscle pathology showed ragged-red fibers (RRF), ragged-blue fibers (RBF), or cytochrome c-oxidase (COX)-negative fibers in almost all patients.[4] Southern blot or long-range polymerase chain reaction can detect single large-scale deletion in about 90% of KSS patients,[5] while mitochondrial DNA (mtDNA) point mutations or nuclear gene mutations have been reported in other KSS patients.[6] In general, single large-scale deletion can be detected only from the muscle, but not from blood cells of KSS patients.[7] Among the 19 patients reported by us, 15 patients underwent muscle biopsy in our hospital which showed RRF, RBF, and COX-negative fibers in all of them; however, mtDNA mutation detection was available in 11 of them because muscle tissue of the other four (patients 8, 10, 17, and 18) were not enough for further gene analyses; one patient (patient 12) had muscle biopsy in another hospital, and we got a little muscle tissue to do the mutation examination although RBF% cannot be counted. Three patients (patients 2, 5, and 7) refused to receive muscle biopsy, but all of them showed typical KSS features. We performed common mtDNA point mutations analysis (mtDNA A3243G, A8344G) in their blood, which were negative.

Biochemical investigations, especially activity assay of respiratory chain complexes in muscle tissues, can also help provide evidence for the diagnosis of mitochondrial disease.[8] Unfortunately, such a detecting platform has not been established in our laboratory.

There were several articles studying the exact nature of high signal lesions on diffusion-weighted imaging (DWI) in patients with mitochondrial diseases, especially mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes. However, the results were conflicting since some reported an increase in the apparent diffusion coefficient (ADC) values suggesting vasogenic edema while others described a decrease in the ADC values reflecting cytotoxic edema.[9] In our KSS patients, we also found the same interesting phenomena that the ADC values of the regions with high signal on DWI were not consistent. Some patients showed increased ADC values while the others showed decreased ADC values. We proposed that the discrepancy might be due to the different disease stages in different individual patients although further studies are needed to elucidate the underlying pathophysiological mechanism.

The results of Moraes *et al*.[2] showed cognitive decline in 31% of KSS patients, which was associated with the presence of disability. In our research, the present study was mainly focused on the electrocardiogram and brain magnetic resonance imaging changes of the patients. Cognitive function was only evaluated in one patient, which also showed a moderate decline of cognitive function.

In our research, all the patients underwent Holter monitoring, and as we reported in the article, none of them developed ventricular arrhythmias, which was also a big difference from previous reports. Therefore, the cardiologists did not suggest implantable cardioverter defibrillator implantation in these patients.

According to the height and weight standardized growth charts for Chinese children and adolescents aged 0–18 years,[10] we only found the heights of three patients more than two standard deviations below the mean for age and gender. The heights of other six patients were below the mean height for age and gender but did not reach the definition for short stature.

Again, we show our greatest thanks for the comments and advices,

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and hope that we can learn more about the disease to bring more effective treatment for the patients in the near future, by our efforts together.

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