CASE REPORT

Fatty liver in a two days old neonate

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SUMMARY
Neonatal death due to inborn error of metabolism (IEM) is rare in Malaysia. We report a sudden neonate death just a few hours after being discharged from the hospital. The deceased was a two-day-old baby boy and was asymptomatic until his demise. He was fed with expressed breast milk and formula milk. Autopsy revealed fatty changes of the liver and an enlarged heart. Laboratory investigation confirmed very long chain Acyl-CoA dehydrogenase deficiency which resulted in his death. Autopsy of sudden unexpected death in neonate should include investigation for inborn error of metabolism. Fatty liver and enlarged heart could give a clue for the diagnosis.

INTRODUCTION
Inborn Errors of Metabolism (IEM) comprises a group of genetic defects that affects the metabolic pathways in our body. The lack of a particular enzyme can cause a block in a biochemical reaction, which may lead to accumulation of toxic substances and also reduced ability in production of essential compounds, thereby interfering in the normal function of the organ, such as the brain, nerve, liver, heart, eye, muscle, bone, or other organs. The true incidence of IEM in Malaysia is still not known. This is mainly due to inadequate diagnostic facilities and the condition is often misdiagnosed as septicemia or cerebral palsy. From 1998 to 2008, a total of 191 patients with amino acid disorders and 255 patients with various organic acids disorders were diagnosed. The three commonest IEM in Malaysia were maple syrup urine disease (MSUD), urea cycle disorders (UCD) and methylmalonic acidemia.

The first factual diagnosis of an inborn error of metabolism in an infant death was made in 1984. This was a case of 14-month-old infant who died suddenly after history of nonspecific malaise. Autopsy findings revealed fatty changes of the internal organs and the laboratory investigation confirmed medium-chain acyl-CoA dehydrogenase deficiency. Since then, more cases of medium-chain acyl-CoA dehydrogenase deficiency was recognised.

Here, we report a 2-day-old male neonate who died shortly after being discharged from the hospital. His death was attributed to very long chain acyl CoA dehydrogenase deficiency.

CASE REPORT
The child was a product of a consanguineous marriage. His mother has a medical history of perimembranous ventricle septal defect with severe mitral valve regurgitation secondary to infective endocarditis. This is the third pregnancy for the mother. The first child is was five years old and healthy. The second pregnancy was terminated due to worsening heart condition.

He was delivered via spontaneous vaginal delivery in Hospital Kuala Lumpur. The delivery was uneventful. The Apgar score was 9 for 1 minute and 10 for 5 minutes. Throughout the stay in the hospital, the child was fed with expressed breast milk and formula milk. Upon discharge, the parents took the deceased back home in their car. The child was breastfed 30 minutes before he became unresponsive in the car.

Post mortem was carried out on the next day and revealed term baby with body weight of 3380grams. The external examination and anthropometric measurement were consistent with a term baby. The post mortem baby weight was 3380grams and There was no obvious dysmorphic features noted. On the internal examination, the heart weighed 20grams and grossly was unremarkable. The liver weighed 138grams and showed fatty changes on sectioning. Further examination of other organs was unremarkable grossly. Histology examination of heart showed evidence of cardiomyopathy with fatty infiltration of the myocardium and section of the liver showed microvesicular steatosis with mild periporal chronic inflammatory cells infiltration. Section of other organs showed nonspecific congestion.

Blood on spot paper was sent for IEM studies. Most of long chain of acylcarnitines is elevated. Marked elevation seen in C14, C14:1 and moderate elevation seen in C16 and C16:1. Also elevated are methionine and citrulline. The profile was suggestive of fatty acid oxidation disorder, specifically very long chain acyl CoA dehydrogenase deficiency.

DISCUSSION
Individuals with a fatty-acid metabolism disorder are unable to metabolise fat source for energy. The fats are broken down to fatty acids in the liver. The fatty acids are then transported to the target cells but are unable to be broken down, resulting in a build-up of fatty acids in the liver and other internal organs. This is clearly evident in our case. We found fatty...
infiltration in the liver and heart at the post mortem examination.

The affected individual of very long chain acyl-CoA dehydrogenase deficiency commonly presents with growth failure, hypoglycemia and reduced fasting tolerance. The signs depend on the degrees of involvement of liver, skeletal, and cardiac muscle. All currently known conditions are inherited as autosomal-recessive traits. There are at least 25 enzymes and specific transport proteins in the pathway of β-oxidation and 16 have been associated with human disease. Laboratory investigation is essential in the diagnosis. Blood and bile could be conveniently collected on the same filter paper card, the one identical to those used for G6PD screening, stored at room temperature, and submitted for analysis once dried. Both specimens should be collected to provide a better chance of detecting and independently confirming the largest possible number of disorders. Some reports recommends to collect a frozen specimen of liver and a skin biopsy in addition to the blood and bile especially in the presence of diffuse fatty infiltration of the liver.

In addition to the current tests, there has been new development in the metabolic analysis. A new platform for untargeted metabolomic analysis has been developed. A single metabolomic analysis can provide information that currently would require multiple different clinical tests, including targeted panel assays for amino acids, acylcarnitines, organic acids, purines, pyrimidines, acylglycines, bile acids, and carnitine biosynthesis intermediates. In this current platform, it is possible to use one test to screen for dozens of IEMs that might otherwise require ordering multiple unique biochemical tests. Despite that, future research in laboratory diagnosis should also focus on the rapidity and accuracy of the results. This would help to improve the detection and thus, prevent further deaths.

CONCLUSION

We now recognise that most of the disorders of mitochondrial fatty acid b-oxidation can present with sudden unexpected childhood death. Families were provided a plausible reason for the unexpected demise of their children and an opportunity to prevent morbidity and mortality in asymptomatic but affected siblings, to receive genetic counselling, and to seek prenatal diagnosis. Post mortem screening of paediatric cases of sudden and unexpected death has received only limited attention despite the frequency of metabolic disease among unexpected death cases is about 5%. This unfortunate case is an important example why metabolic disorder investigation should be included in investigating sudden unexpected infant death and perhaps as a screening in the high risk living newborn. Features of fatty infiltration in liver and heart could give a clue for the diagnosis.

REFERENCES