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LETTERS TO THE EDITOR

Dear Editor,

EXPANDED NEWBORN SCREENING PROGRAMME IN SAUDI ARABIA: ARE WE READY?

We read with interest the article by Alfadhel *et al.* on Saudi newborn screening.[1] We would like to highlight the following:

1 The reported incidence was 1:043[2]; the incidence of the screened metabolic disorders was 1:1443, which is comparable to other gulf countries but still underestimated.[3,4] The incidence reported in previous pilot studies in Saudi Arabia for the period 1995–1998 was 1:1381,[1] and for the year 2000, the incidence was 1:690 (personal experience).
2 It is important to implement a good legislative system and education for public, medical professionals and legislators, with the establishment of an integrated infrastructure with policies and guidelines and financial and legislative support prior to establishing nationwide newborn screening (NBS).
3 Homocystinuria must be included as it meets NBS committee selection criteria, with the establishment of a rapid method for detecting the total homocysteine in dried blood spots by MS/MS.[3] Other common disorders to be included are tyrosinemia type 1, very long chain acylcoA dehydrogenase deficiency and 3 methyl glutaconic aciduria.
4 The time for the second recall sample and time lag from the first suspicion till implementation of specific therapy is not stated clearly, which is, in my experience, between 1 week and a month, which is too long to pre-symptomatically treat cases. We encounter these cases in our emergency department before the results. This has ethical and prognostic implications.
5 The false positive results were 0.56%; however, no false negative results were reported, which is important to assess the efficacy of the testing system and the measures taken to identify these cases.
6 Although a good proficient specimen work flow has been put in place, it is not linked to the clinical management of the patients.
7 Only 51% of the positive cases were retested, which could be related to poor legislative recall system and the wide geographical area of Saudi Arabia.
8 It is important to report how many proven positive cases have been managed and what is the long-term follow-up and prognosis.
9 It is useful to know what second-tier testing was used to confirm positive cases like molecular testing and what further management and family counselling measures are used for further preventive reproductive options.

Finally, we want to stress that NBS as a population-based screening must function as a system[2,3] with the pre-analytic, analytical and post-analytical phases, with continuous system audit and improvement.

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Dear Editor,

INFANTILE POMPE DISEASE AND ENZYME REPLACEMENT THERAPY

We describe an interesting case of infantile Pompe disease and the effect of enzyme replacement therapy. A 1-week-old female, born at term, was brought to the emergency room with marked respiratory distress. A chest X-ray obtained in the emergency room revealed severe cardiomegaly. An electrocardiogram (ECG) was performed, which showed short PR interval and biventricular hypertrophy with strain pattern. Subsequent echocardiogram revealed severe left ventricular hypertrophy and moderately depressed left ventricular function. Acid α-glucosidase (GAA) activity on dried blood spot was found to be reduced, and urine hexose tetrasaccharide level was found to be markedly elevated, suggestive of Pompe disease. Molecular analysis of the *GAA* gene by sequencing revealed two mutations (c.1210G > A and c.2227C > T), thus confirming the diagnosis of Pompe disease. A skin biopsy was performed to determine cross-reacting immunological material (CRIM) status in order to assess her ability to respond to enzyme replacement therapy. She was CRIM positive. Subsequently, she underwent recombinant human GAA replacement at biweekly intervals. After 2.5 years of treatment, there is

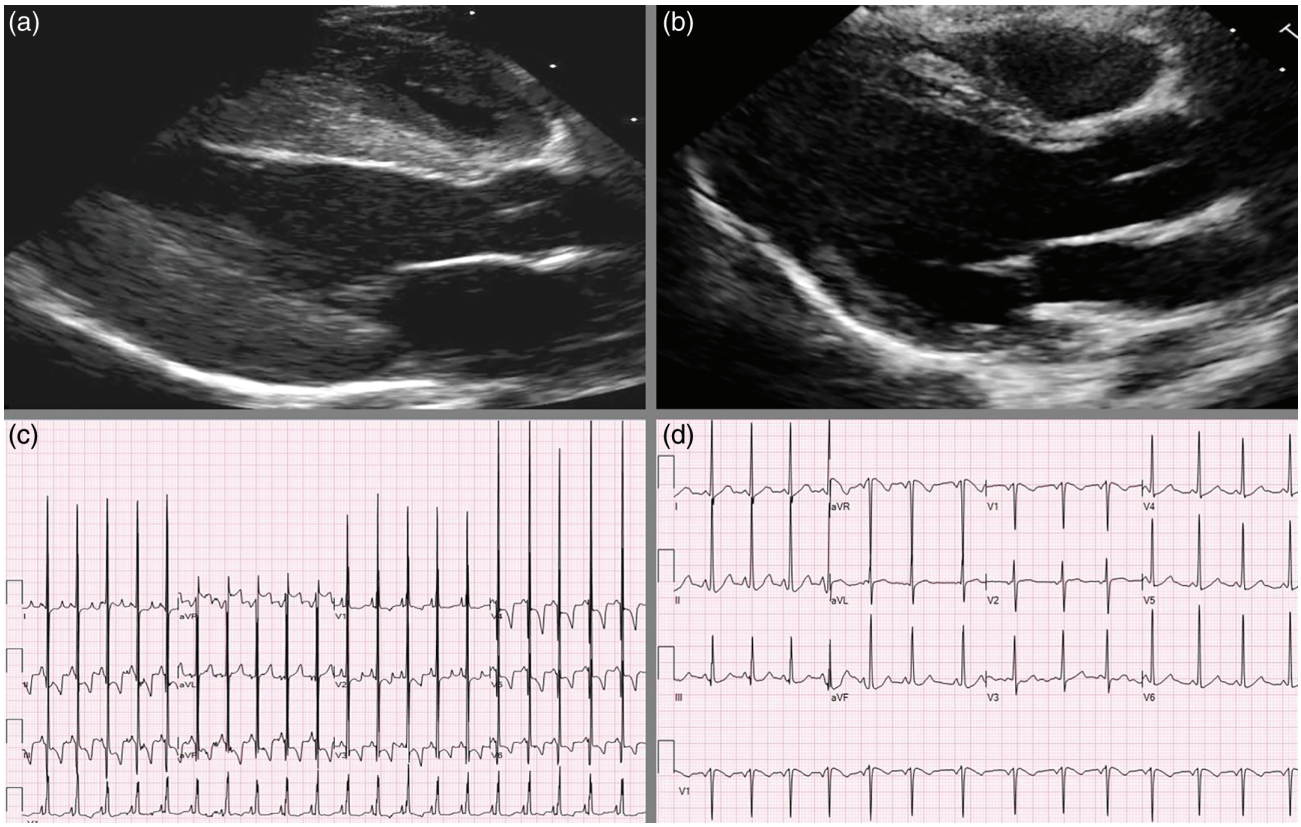

Fig. 1 Echocardiogram: Parasternal long axis view (a) pre- and (b) post-enzyme replacement therapy showing complete resolution of left ventricular hypertrophy. Electrocardiogram: (c) Pre- and (d) post-enzyme replacement therapy showing improvement in biventricular hypertrophy (decreased voltages).

near complete resolution of the abnormalities seen on her initial ECG and echocardiogram, along with normalisation of left ventricular function (Fig. 1). Pompe disease (glycogen storage disease type II) is an autosomal recessive disorder caused by deficiency of the lysosomal enzyme GAA, leading to generalised accumulation of lysosomal glycogen in the heart, skeletal and smooth muscle and the nervous system. This disease was first identified in the 1930s by Dr Pompe.[1] Infants with infantile (classic) Pompe disease typically present during the first few months of life with hypotonia, macroglossia, feeding difficulties, respiratory distress and cardiomegaly. Lysosomal glycogen deposition in heart results in hypertrophic cardiomyopathy and conduction abnormalities. If untreated, it results in death mostly from cardiorespiratory failure by 1 year of life.[2,3] Enzyme replacement therapy by recombinant human GAA decreases left ventricular mass, improves skeletal muscle function and prolongs overall survival.[4] It also improves left ventricular voltages, QT dispersion and PR intervals on ECG.[5] Our case is a visual illustration of near complete resolution of electrocardiographic (short PR interval, biventricular hypertrophy) and echocardiographic (severe left ventricular hypertrophy, depressed left ventricular function) abnormalities in a case of infantile Pompe disease through the use of biweekly recombinant human GAA replacement.

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