Interestingly, the majority of cases reported involved a right-sided ectopic pregnancy[3,6,7]. Periappendicitis was the predominant feature on histological examination of the appendix, probably as a result of contact with the ectopic or free blood[3,5,7]. This may well progress to transmural inflammation. An interesting feature of our case is that histological examination of the appendix revealed a predominantly mucosal inflammatory process with minimal serosal inflammation (Fig. 1). Furthermore, this was a left sided ectopic pregnancy with the appendix situated at the right pelvic brim. Therefore, this is a unique case of two unrelated pathological processes occurring in the same individual.

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Supernumerary chromosomes in mosaic Turner Syndrome

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Summary

The finding of a supernumerary or marker chromosome in a karyotype poses difficulty in genetic counselling. The true incidence and significance of this chromosomal aberration is unknown in Malaysia. We report two patients who presented with supernumerary chromosomes in mosaic Turner syndrome.

Key Words: Mosaicism, Supernumerary chromosome, Turner syndrome, Medical genetics

Introduction

Supernumerary chromosome refers to any unidentifiable marker chromosome, usually found in addition to the normal chromosome complement[1]. These very small "pieces" of marker chromosome are occasionally found in chromosome cultures, usually in a mosaic state.

Supernumerary chromosomes pose considerable difficulties in genetic counselling and prenatal diagnosis. They may represent familial markers which may be passed on from one generation to another or they may represent new mutations or "de novo" marker chromosomes[2]. Supernumerary chromosomes usually consist of insignificant centric heterochromatin although larger pieces are most certain to contain extra chromosomal materials, thus causing an imbalance chromosome complement resulting in an abnormal phenotype.

In addition, these supernumerary chromosomes are usually so small that it may be difficult to characterise specifically by standard banding methods. Newer methods of molecular cytogenetics involving specific DNA probes and fluorescent in-situ hybridisation may permit better identification[3]. In this review, chromosome analysis was performed from peripheral blood lymphocytes. Following standard tissue culture technique, G-banding was employed on the aged slides. When necessary, C-banding was performed. At least 30 metaphase spreads were screened and 10 were photographed. In the case of mosaicism, at least 50 cells were observed. For a very low presence of mosaicism, 100 cells were studied.

We report two patients with supernumerary chromosomes in mosaic Turner Syndrome.

Case 1

A 14-month-old Chinese girl was referred to the University Hospital Kuala Lumpur for further investigation of dysmorphic features and short stature. She had a normal full term delivery. Her birthweight was 2.4 kg with an uneventful perinatal period. The parents were non consanguinous and they have 3 previous healthy children. There is no significant past or family history. Her dietary history was satisfactory.

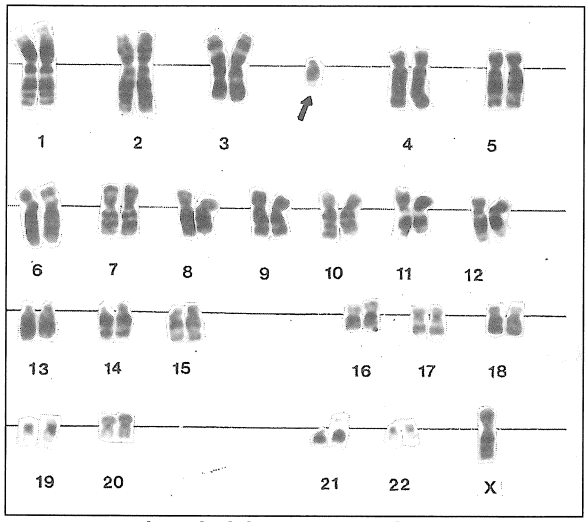

Fig. 1: G-banded karyotype of patient case 1 showing 45, X

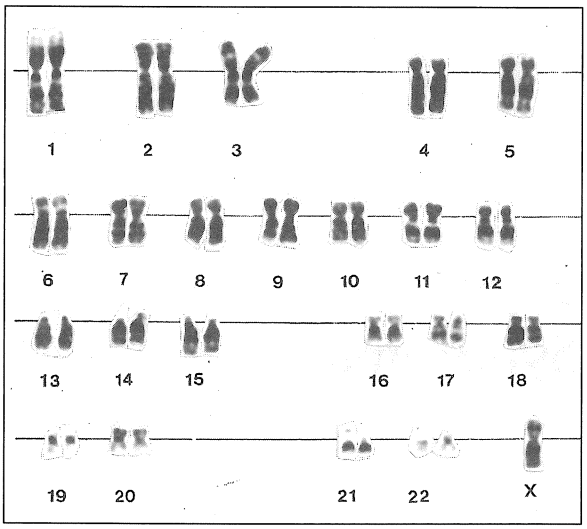

Fig. 2: G-banded karyotype showing 46, X0, + mar; arrow points to supernumerary chromosome

Developmentally, she rolled over at 5 months and only managed to sit unsupported at 1 year of age. She babbles with no meaningful words although she interacts socially.

Physical examination revealed a small but active child. Her length of 69 cm, weight of 6.7 kg and occipitofrontal circumference of 42 cm corresponded

to less than the third percentile on the growth charts. She had dysmorphic features consisting of low set ears, hypertelorism, prominent epicanthic folds, webbed neck and bilateral single transverse palmar creases. Her vital signs were stable with normal cardio-respiratory findings. There was no significant abdominal findings with normal female genitalia. Apart from mild hypotonia there was no other neurological deficits.

In view of the short stature and dysmorphic features, a diagnosis of Turner Syndrome was made. Chromosome analysis from the peripheral blood lymphocyte culture confirmed the diagnosis of mosaic Turner Syndrome with 2 cell line populations being demonstrated with conventional G banding – 45, X were seen in 11 spreads (22%) (Fig. 1) and 46, X0, + mar in 39 spreads (78%) (Fig. 2). C-banding did not confirm the marker chromosome as a Y chromosome. Karyotyping of parents' chromosomes was not done.

Case 2

A 32-month-old Chinese girl was referred to the University Hospital, Kuala Lumpur for further assessment of her developmental delay and short stature. She was delivered term at a private maternity clinic. Her birthweight was 3 kg with an occipitofrontal circumference (OFC) of 32 cm. Apart from mild neonatal jaundice, her perinatal period was uneventful. The parents were non-consanguinous and they had an older boy who was normal. Developmentally, she smiled at 1 month of life and was able to support herself on her forearms in the prone position at 4 months. She sat with support at 7 months and held her own bottle at 8 months. However, she only managed to stand with support at 15 months and walked unsupported at 2 years. She is just beginning to learn to say a few words with meanings.

Physical examination showed a small girl, with a weight of 9.8 kg, height 86 cm and an OFC of 43.5 cm which corresponded to the third percentile. There was no dysmorphic features with normal visual and hearing on gross assessment. The cardio-respiratory system and abdomen were normal. She had generalised mild hypotonia and hyporeflexia. There was no focal neurological deficits. Her fundi were normal.

Initial investigations which included full blood counts, biochemical screening and electrolytes were normal. TORCHES screening for congenital infections was negative. The levels of uric acid and creatine kinase were not elevated. Urine chromotography for amino acid and organic acid were negative. Computerised tomography of the brain was normal. Chromosomal analysis of the lymphocyte culture showed 2 cell lines population, consisting of 45, X in 98 spreads (98%) and 46, X0, + mar in 2 spreads (2%).

Discussion

We reported two female children with short stature, consistent with the diagnosis of Turner Syndrome. Both children had developmental delay and chromosome analysis indicated mosaic Turner Syndrome with supernumerary or marker chromosomes. Turner's Syndrome is one of the commonest sex chromosome aneuploidies occurring in approximately 1 in 1850 live female births[4]. About 50% of cases have a 45, X karyotype with the remainder having mosaic karyotypes with one 45, X cell line and another different cell line being present[4]. The chromosome constitution is clinically important; for example patients with an iso Xq are like classic 45, X patients, whereas those with a deletion of Xq often have only gonadal dysfunction.

In our 2 patients we are confronted with the problem of marker or supernumerary chromosomes, which are usually found in less than 8% of Turner's karyotypes. On the whole, supernumerary chromosomes are found in about 0.06% to 0.1% of amniocentesis and occurring in about 0.05% of livebirths[1,3]. Approximately 50% of these supernumerary chromosomes are familial with little risk of abnormal phenotype. However the de novo marker chromosome may present with phenotypic, behavioural and cognitive abnormalities. Extreme variability in the phenotype spectrum is well known.

Another peculiar feature of supernumerary chromosomes is the high incidence of mosaicism. The reason for this is unclear although it is speculated that there is a greater tendency for these chromosomes to be lost at a higher rate than in other forms of aneuploidies. Some patients have the extra chromosomes in every cell while in certain mosaics, these may be found only in a proportion of their cells.

Hence the importance of repeating cell cultures for karyotyping using different tissues.

Nevertheless it is still difficult to identify the origin of specific supernumerary chromosome even with the use of conventional chromosomal G-banding supplemented with high resolution karyotyping due to their small physical size. The majority of supernumerary chromosomes are satellited or bisatellited and some of these appear to have transcriptionally active ribosomal deoxyribose nucleic acid sequences[2]. Recent reports suggest that these extra chromosomes usually have one of the more common trisomies such as trisomy 13, 18, 21 or an extra X or Y chromosome[3]. These chromosomal fragments need chromosome specific probes used in tandem with fluorescent in-situ hybridisation (FISH) to delineate the exact chromosomal origin.

The finding of a supernumerary chromosome in any patient, especially during prenatal diagnosis poses significant difficulties in genetic counselling if the origin of these extra chromosomes cannot be positively identified. This is important as prognosis and outcome depended upon the amount and origin of the extra chromosomal material. Long term epidemiological studies indicated an abnormal outcome in 15% of de novo events[2]. More studies are needed in our local population in this area of chromosomal abnormality.

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