Rubinstein-Taybi syndrome associated with breast cancer — a case report

Rubinstein-Taybi syndrome (RSTS) is a rare congenital disease with mental disability and multiple physical anomalies. These include growth deficiency, abnormal morphology of thumbs and big toes [1]. Cardinal diagnostic signs include short stature, distinctive Craniofacial features as highly arched eyebrows, long eyelashes, down-slanting palpebral fissures, broad nasal bridge, beaked nose with the nasal septum extending well below the alae, highly arched palate, and mild micrognathia (fig.1). Also there is broad and duplicated distal phalanges of thumbs and halluces, and behavioural problems as moderate to severe intellectual disability (fig. 2. a, b).

RSTS was initially reported by Greek orthopaedic surgeons Michail, Matsoukas and Theodorou from Athens, in 1957 [2–4], however, syndrome has been named after Jack Rubinstein, a paediatrician from Cincinnati (USA) & Hooshang Taybi, a paediatric radiologist from Oklahoma (USA) who reported six RSTS cases in 1963 [5]. The name of Rubinstein-Taybi syndrome was definitively chosen by Warkany in 1974 [6].

It is known to be associated with some neoplasms, in this paper we report a female patient of RSTS associated with breast cancer.
disability, congestive cardiac failure, scoliosis, spina bifida, osteopenia and significant osteoporosis. Also she had a premature menopause.

Clinically in addition to classical features of RSTS as short stature, typical facial appearance, abnormally broad thumbs, significant mental retardation, hypertelorism (widely spaced eyes), a "beak-shaped" nose, broad nasal bridge and micrognathia (small lower jaw) with a small mouth opening and numerous carious lesions. There is large suspicious mass right breast ILQ (inner lower quadrant) of the right breast. Right breast ultrasound scan showed in the large irregular shaped hypoechoic solid lesion in ILQ, which has ill defined margins and which shows increased vascularity. The lesion measures $42 \times 30 \times 36$ mm ($24.4$ cm$^3$ volume). The appearance is of a malignancy and the finding graded as U5 using BIRADS [Breast Imaging-Reporting and Data System] (fig. 3). Ultrasound guided core biopsy from the lesion revealed, Grade 2 invasive ductal carcinoma of the right breast, PR 8, ER 8, HER2 negative Ki67-55% (fig. 4).

Case report

A 52-years old lady presented with a recent history of right breast lump, noticed by the mother, who is the carer of this patient. She is a known case of Rubenstein-Taybi syndrome with sever psychomotor disability, congestive cardiac failure, scoliosis, spina bifida, osteopenia and significant osteoporosis. Also she had a premature menopause.

Clinically in addition to classical features of RSTS as short stature, typical facial appearance, abnormally broad thumbs, significant mental retardation, hypertelorism (widely spaced eyes), a "beak-shaped" nose, broad nasal bridge and micrognathia (small lower jaw) with a small mouth opening and numerous carious lesions. There is large suspicious mass right breast ILQ (inner lower quadrant) of the right breast. Right breast ultrasound scan showed in the large irregular shaped hypoechoic solid lesion in ILQ, which has ill defined margins and which shows increased vascularity. The lesion measures $42 \times 30 \times 36$ mm ($24.4$ cm$^3$ volume). The appearance is of a malignancy and the finding graded as U5 using BIRADS [Breast Imaging-Reporting and Data System] (fig. 3). Ultrasound guided core biopsy from the lesion revealed, Grade 2 invasive ductal carcinoma of the right breast, PR 8, ER 8, HER2 negative Ki67-55% (fig. 4).
Discussion

RSTS is also known as broad thumb-hallux syndrome. It is an extremely rare condition, with a prevalence of one case per 125,000 live births [7].

It is inherited as an autosomal dominant pattern or sometimes as fresh sporadic genetic mutations. This is due to micro-deletion in the chromosomal region 16p13.3 [8].

It is a genomic region encoding cyclic AMP response element binding protein (CREB) binding protein (CBP). CBP is a transcriptional co-activator that binds to CREB when the latter is phosphorylated and promotes gene transcription [1].

Also can be caused by mutation in gene E1A-binding protein (p300) [9].

RSTS is a multiple congenital anomaly syndrome. Cardinal diagnostic signs include short stature, distinctive Craniofacial features, broad and duplicated distal phalanges of thumbs and halluces, and behavioural problems as well as moderate to severe intellectual disability.

As mentioned earlier, the pathway of inheritance usually autosomal dominant, however, the patients with RSTS rarely reproduce [3].

This condition is associated with an increased risk of developing some neoplastic diseases as meningioma [9], neuroblastoma [10, 11], pheochromocytoma [12], Rhabdomyosarcoma, leiomyosarcoma, seminoma, embryonal carcinoma [13] and leukemia [14].

As RSTS patients are prone to craniofacial developmental abnormalities, this will increase the risk of gastro-oesophageal reflux disease, (GERD) and congenital tracheal stenosis. This predisposed them to difficult intubation and airway compromise [15]. All these factors should be considered and thorough risk assessment should be performed to ensure the optimum care decision and choice [16].

This case has been discussed in the Breast Multidisciplinary Team Meeting. In an ideal world she should have surgical excision of her tumour, however, due to high risks associated with general anaesthesia, the patient is treated with hormonal manipulation of tamoxifen only. A 12 months follow-up breast USG, showed a good response to the tamoxifen (fig. 5).

To our knowledge, no case of RSTS associated with breast cancer has been reported before.

Most women with a family history of breast cancer have alterations in particular genes, mainly BRCA1 and BRCA2, but also CHK2, ATM, STK11 and others. There are previous reports related to the genetic mutations seen in RSTS having an association with breast cancer.

Conclusion

RSTS association with breast cancer has not been reported before. Continuous observation and research is essential to explore this subject. Careful assessment needed with RSTS patients if general anaesthesia considered, this should cover craniofacial anomalies, airway anatomy, pulmonary function as well as cardiopulmonary status. If the patient is a high risk, then less invasive options should be considered.

References

Abdalla Saad Abdalla, Al-Zawi et al., Rubinstein-Taybi syndrome associated with breast cancer


