Abdalla Saad Abdalla Al-Zawi, Kingsely Osayi, Marina Barron, Turhan Comez
Basildon & Thurrock University Hospital, Nethermayne, Basildon, United Kingdom

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

Zespół Rubinsteina-Taybiego związany z nowotworem piersi — opis przypadku

Abstract

A number of cases of Rubinstein-Taybi Syndrome associated with different neoplastic lesions have been reported since this syndrome was first named in 1963. This paper reports a case of Rubinstein-Taybi Syndrome associated with breast cancer. Our aim is to share this finding and to emphasize how this case discussion allowed us to improve the management pathway in the future.

Medycyna Paliatywna w Praktyce 2017; 11, 3: 122–125

Key words: diagnosis, Rubinstein-Taybi syndrome, breast cancer

Streszczenie

Od 1963 roku odnotowano szereg przypadków zespołu Rubinsteina-Taybiego związanych z różnymi zmianami nowotworowymi. W poniższej pracy przedstawiono opis przypadku zespołu Rubinsteina-Taybiego związanego z nowotworem piersi. Celem pracy jest prezentacja wyników badań oraz ulepszenie zasad postępowania w podobnych przypadkach.

Medycyna Paliatywna w Praktyce 2017; 11, 3: 122–125

Słowa kluczowe: rak piersi, rozpoznanie, zespół Rubinstein-Taybi

Introduction

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.

Adres do korespondencji: Abdalla Saad Abdalla Al-Zawi
Basildon & Thurrock University Hospital,
Nethermayne, SS16 5NL, Basildon, United Kingdom
e-mail: abdalasaad@gmail.com

Medycyna Paliatywna w Praktyce 2017; 11, 3, 122–125

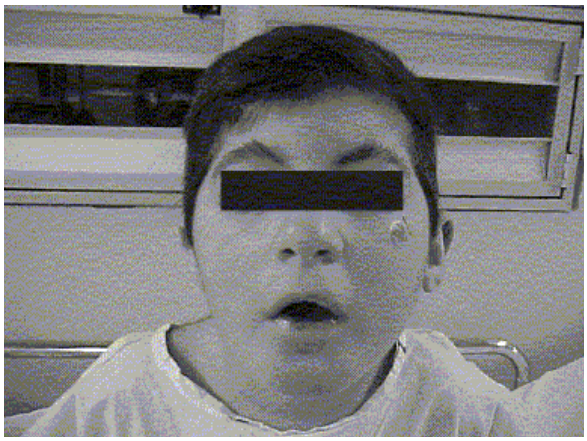

Figure 1. Typical facial features of Rubinstein-Taybi syndrome (Oliveria 2005)

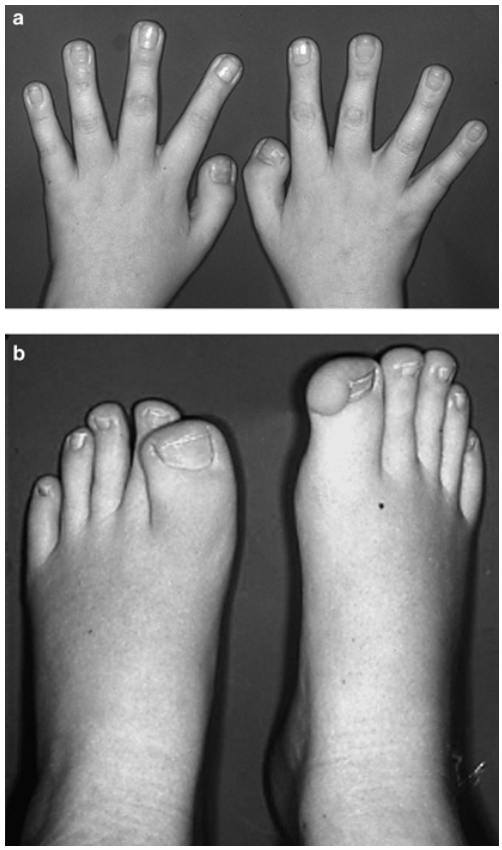

Figure 2. (a, b) Hands and feet in RSTS, Broad thumbs, broadened terminal phalanges, mild cutaneous syndactyly between 3rd and 4th on the right and broad halluces (Hennekam 2006)

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 × 30 × 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).

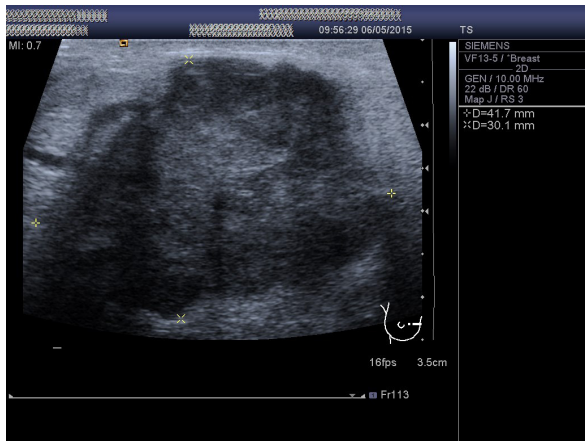

Figure 3. Right breast US revealing the pre-treatment tumour size of 42 mm

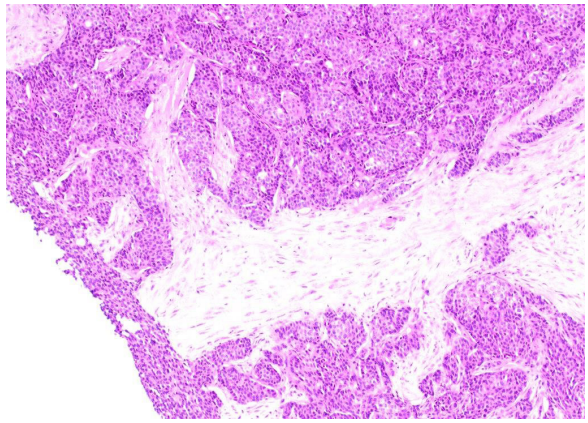

Figure 4. Grade 2 invasive ductal carcinoma

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 meningeoma [9], neuroblastoma [10, 11], pheaochromocytoma [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 compromisation [15]. There are some events during peri-operative period related to the anaesthesia as, intra-operative self-limiting de-saturation, copious secretions causing airway compromise, arrhythmias and delayed recovery. All theses 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.

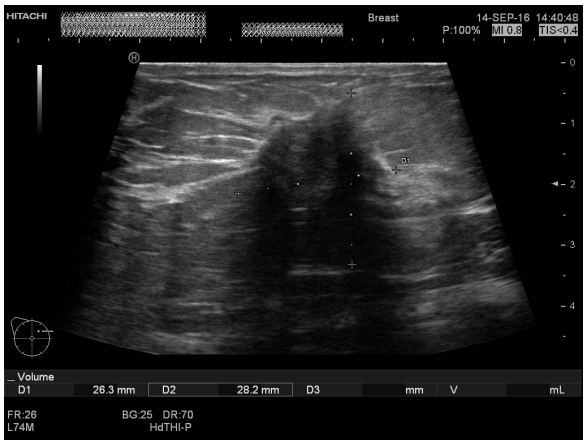

Figure 5. Right Breast US after six months of hormonal manipulation , showing tumour size reduction up to 26 mm

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

1. Hallam TM, Bourtchouladze R. Rubinstein-Taybi syndrome: molecular findings and therapeutic approaches to improve cognitive dysfunction. Cell Mol Life Sci. 2006; 63(15): 1725–1735, doi: 10.1007/s00018-005-5555-8, indexed in Pubmed: 16786226.
2. Michail J, Theodorou S. Arched, clubbed thumb in strong abduction-extension & other concomitant symptoms. Rev Chir Orthop Reparatriuce Appar Mot. 1957; 43(2): 142–6.
3. S Mishra, S K Agarwalla, D R Potpalle, N N Dash. RSTS with corpus callosum agenesis. Journal of Pediatric Neurosciences • April 2015;Vol. ; 10: 175–176.
4. Hennekam RC, Van Doorne JM. Oral aspects of Rubinstein-Taybi syndrome. Am J Med Genet Suppl. 1990; 6: 42–47, indexed in Pubmed: 2118777.
5. RUBINSTEIN JH, TAYBI H. Broad thumbs and toes and facial abnormalities. A possible mental retardation syndrome. Am J Dis Child. 1963; 105: 588–608, doi: 10.1001/archpedi.1963.02080040590010, indexed in Pubmed: 13983033.
6. Cassidy S, Allanson J. Management of Genetic Syndromes. 3rd Edition 2010.
7. D Milani, F Manzoni, L Pizzani, P Ajmoni, C Gervasini, F Menni, F Esposito. Rubinstein-Taybi Syndrome: Clinical features, genetic bases, diagnosis, and management. Italian Journal of Pediatrics. 2015; 41: 4.

8. Imaizumi K, Kuroki Y. Rubinstein-Taybi syndrome with de novo reciprocal translocation t(2;16)(p13.3;p13.3). Am J Med Genet. 1991; 38(4): 636–639, doi: 10.1002/ajmg.1320380430, indexed in Pubmed: 2063911.
9. Hennekam RCM. Rubinstein-Taybi syndrome. Eur J Hum Genet. 2006; 14(9): 981–985, doi: 10.1038/sj.ejhg.5201594, indexed in Pubmed: 16868563.
10. Ihara K, Kuromaru R, Takemoto M, et al. Rubinstein-Taybi syndrome: a girl with a history of neuroblastoma and premature thelarche. Am J Med Genet. 1999; 83(5): 365–366, doi: 10.1002/(sici)1096-8628(19990423)83:5<365::aid-ajmg4>3.3.co;2-g, indexed in Pubmed: 10232744.
11. Jang YJ, Hee-Hwang S, Hwang YS, et al. Case of Medulloblastoma Associated with Rubinstein-Tybi Syndrome. The Seoul Journal of Medicine. June 1991; Vol 32,No. ; 2: 91–95.
12. Bonioli E, Bellini C. Rubinstein-Taybi syndrome and pheochromocytoma. Am J Med Genet. 1992; 44(3): 386, doi: 10.1002/ajmg.1320440325, indexed in Pubmed: 1488992.
13. Miller RW, Rubinstein JH. Tumors in Rubinstein-Taybi syndrome. Am J Med Genet. 1995; 56(1): 112–115, doi: 10.1002/ajmg.1320560125, indexed in Pubmed: 7747773.
14. Siraganian PA, Rubinstein JH, Miller RW. Keloids and neoplasms in the Rubinstein-Taybi syndrome. Med Pediatr Oncol. 1989; 17(6): 485–491, indexed in Pubmed: 2586363.
15. Agarwal S, Ahmad YH. Talpesh, ARIA Zestos . Anasthetic anagement of Children with Rubinstein-Taybi Syndrome. M E J Anesth. 2011; 21(2): 309–314.
16. Patel S, Hakim M, Krishna S, et al. Anesthetic Implications in Rubinstein-Taybi Syndrome. Journal of Medical Cases. 2015; 6(11): 534–536, doi: 10.14740/jmc2344w.