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Lacrimal caruncle nevus associated with Rubinstein–Taybi syndrome

Znamię barwnikowe mięska łzowego u chorego z zespołem Rubinsteina–Taybiego

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Summary: We present a 28-year old man with diagnosed Rubinstein–Taybi syndrome (RSTS), known as „Broad thumb – Hallux syndrome" with co-existing lacrimal caruncle tumor. Because of the documented enlargement of the lacrimal caruncle mass and known increased risk to develop malignancies in RSTS patients we decided to perform excisional biopsy, which revealed caruncle nevus. To our knowledge this is the first description of such an association.

Słowa kluczowe: zespół Rubinsteina–Taybiego, znamię barwnikowe spojówki, znamię mięska łzowego, zez rozbieżny, goniodysgeneza, hiperteloryzm.
Key words: Rubinstein–Taybi syndrome, conjunctival nevus, lacrimal caruncle nevus, exotropia, goniodysgenesis, hypertelorism.

The Rubinstein–Taybi syndrome (RSTS) known also as „Broad thumb – Hallux syndrome" is a well known mental retardation syndrome associated with multiple congenital anomalies. It was first described by Rubinstein and Taybi in 1963 (1).

The incidence of the syndrome is estimated to be 1:100 000 newborns (2). The molecular genetic studies showed that RSTS is in part caused by microdeletions at chromosome 16p13.3 or mutations of CREB-binding protein (CREBBP), a nuclear protein participating as a co-activator in cAMP-regulated gene expression (3,4). We present a patient with RSTS and an enlarging lacrimal caruncle nevus. The patient and his parents gave the informed consent to participate in the study.

Case report

28-year old Caucasian male with diagnosed RSTS presented in January 2006 at the Department of Ophthalmology and Ocular Oncology of Jagiellonian University in Krakow with an enlarging, brownish-reddish mass in lacrimal caruncle in his left eye (Fig. 1a) noted by his parents 6 months ago. The family history regarding RSTS or malignancies was negative. Snellen visual acuity (VA) test results were not fully adequate because of patient's mental retardation and aphasia. In preferential looking test (Teller Acuity Charts, Richmond Products Inc., USA) the right eye (RE) VA was 4.8 cy/cm (Snellen equivalent 0.2) and the left eye (LE) VA was 6.5 cy/cm (Snellen equivalent 0.3). The patient did not present any color vision disturbances in „Color Vision Testing Made Easy" by Terrace L. Waggoner (Bernell Corp., USA). The direct and consensual pupil reactions were normal and anisocoria was visible – the pupil diameter in the RE was 2 mm bigger than in the LE. The patient showed diminished growth, broad and medially deviated thumbs, (Fig. 1b) big toes, posterior rotated ears, hypertelorism, antimongoloid slant of the palpebral fissures, beaked nose, (Fig. 1c, Fig. 1d) high-arched palate, and dental abnormalities. We diagnosed alternating exotropia 9Δ, V-syndrome, and lack of convergence. Slit-lamp examination showed in LE a pigmented lacrimal caruncle tumor, which measured 7 mm in diameter and 1 mm in thickness, ocular melanosis in both eyes and partial iris atrophy. Gonioscopy disclosed mild signs of goniodysgenesis in form of hypoplasia of peripheral part of iris, basal iris processes associated with delicate membranaceous structures and marked angle hyperpigmentation, especially in RE. The intraocular pressure was 18 mmHg in RE and 17 mmHg in LE. The refractive error after cycloplegia was in RE -0.25 sphD +1.25 cyl D ax 43 and in LE + 0.75 cyl D ax 154. Axial length measured in RE was 23.36 mm and in LE 22.76 mm. Funduscopy revealed normal optic nerve head and mild macular abnormalities in form of absent foveal reflex and unusual distribution of pigment (Fig 1e). The fluorescein angiography showed corresponding window defects in both macular regions (Fig 1f). The performed Jones test and irrigation of lacrimal drainage system did not reveal any sings of stenosis. Because of the documented, worrisome for the patient's parents enlargement of the lacrimal caruncle mass and known increased risk to develop malignancies in RSTS patients we decided to perform excisional biopsy in general anesthesia. The histopathology revealed a pigmented nevus of lacrimal caruncle.

Discussion

RSTS is a rare genetically determined disease (3) Petrij et al. showed that the breakpoints at chromosome 16p13.3 are all restricted to a region that contains CREBBP (4). Genetic heterogeneity in RSTS is shown by the demonstration of mutations in the EP300 gene as a cause of the disease. (OMIM Online Mendelian Inheritance in Man #180849) The variety of different abnormalities (including ocular) is undoubtedly caused by disfunction of mutated CREBBP (5) or chromosomal lesions mentioned above.

The ocular findings in RSTS include among others hypertelorism, antimongoloid slant of the palpebral fissures, epicanthal folds, ptosis, congenital obstruction of the lacrimal drainage system, strabismus, latent nystagmus, ametropia, macrocornea, microphthalmos, iris and optic nerve head colobomas, congenital cataract and

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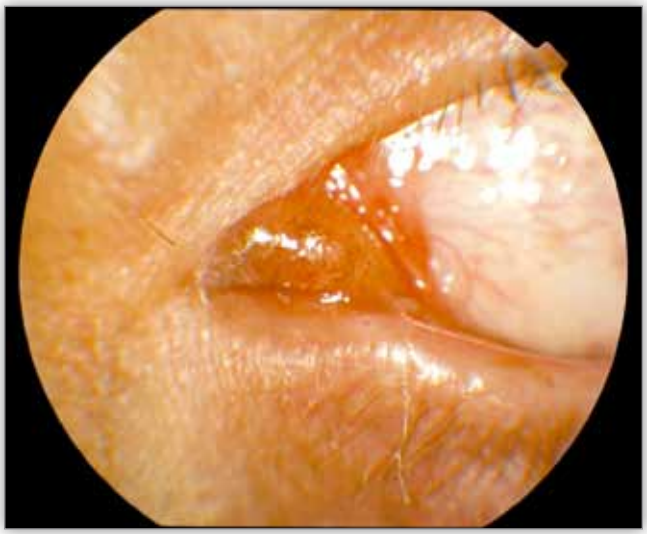

Fig. 1a. Enlarging, brownish-reddish mass in the left caruncle.
Ryc. 1a. Powiększone, brązowawo-czerwone masy na lewym mięsku łzowym.

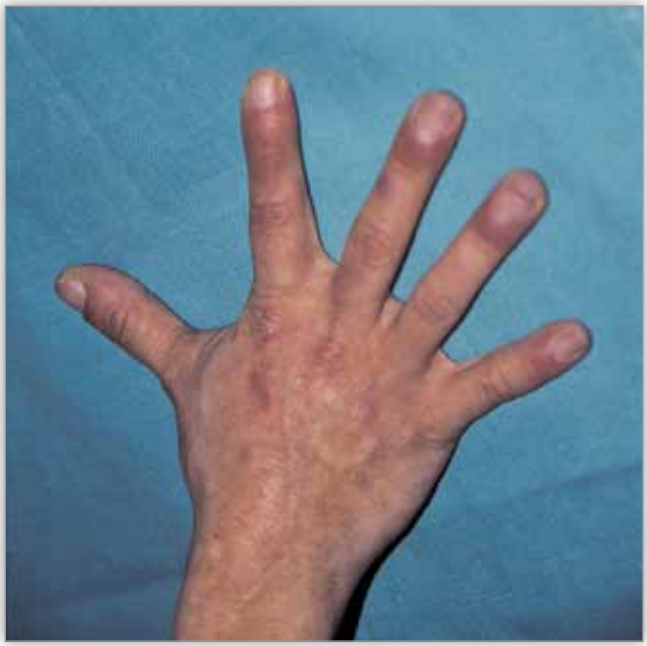

Fig. 1b. Broad and medially deviated thumbs.
Ryc. 1b. Szerokie i przyśrodkowo odchylone kciuki.

glaucoma, optic nerve atrophy and retinal changes (5,6). Van Genderen et al. analyzed 24 patients with ocular abnormalities in RSTS patients and found strabismus in 67% (17/24), high myopia in 25% (6/24), lacrimal duct abnormalities in 25% (6/24) patients, congenital or presenile cataract in 25% (6/24), retinal abnormalities in 75% (18/24), and in few cases congenital glaucoma and colobomata (5). The lacrimal duct abnormalities are very common in RSTS patients (7,8) van Genderen et al. found nasolacrimal duct obstruction in 25% of patients (5). Rubinstein et al. described it in 37% of patients (9). However our patient did not show any abnormalities of the lacrimal drainage system (6). Our patient had alternating exotropia, similarly to the findings of van Genderen et al. who found this abnormality in 15 among 17 patients with RSTS and strabismus (5). Rubinstein et al. published results of the analysis of 571 patients with RSTS and discovered different forms of strabismus in 71% of patients, and

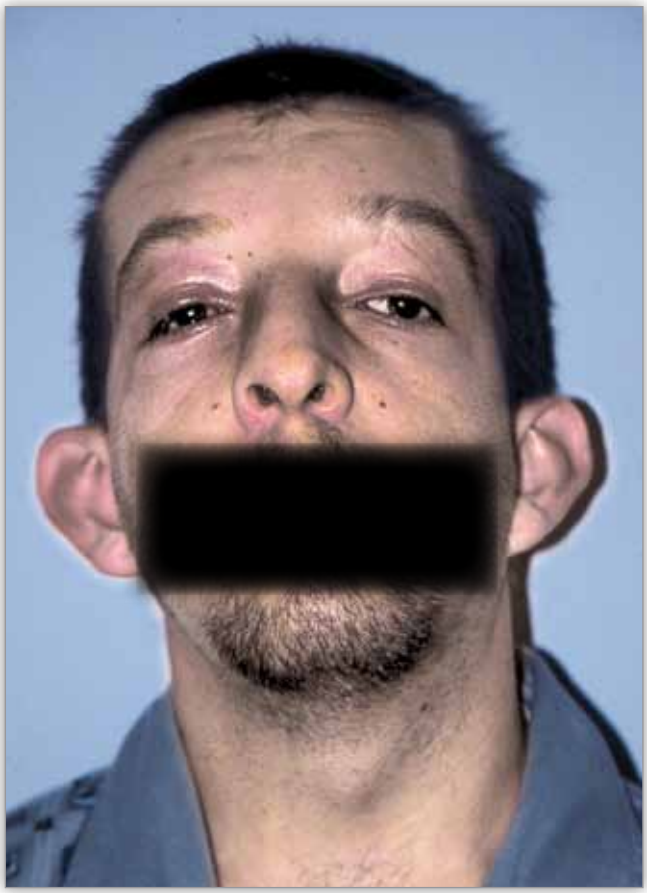

Fig. 1c. Diminished growth, hypertelorism, antimongoloid slant of the palpebral fissures, and beaked nose.
Ryc. 1c. Niewielki wzrost, hiperteloryzm, zmarszczka nakątna w szparze powiekowej, haczykowaty nos.

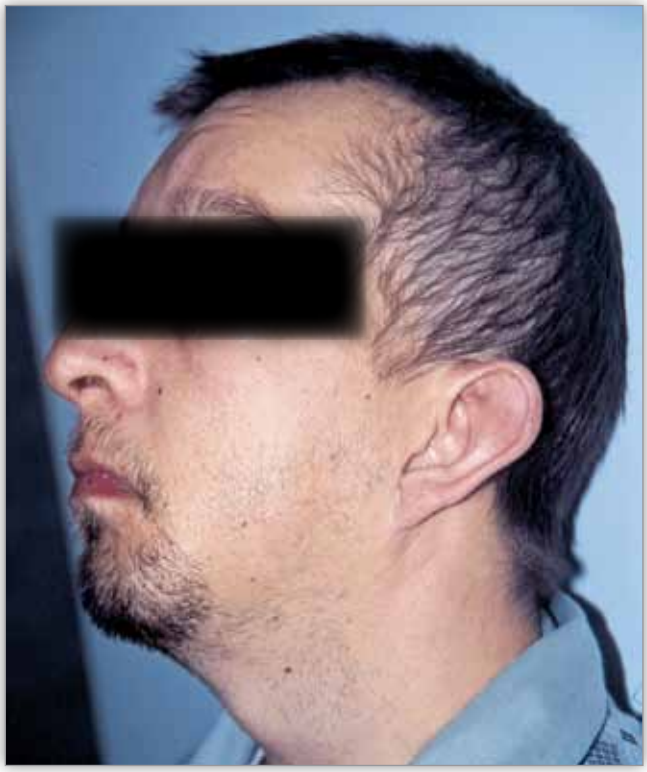

Fig. 1d. Posterior rotated ears.
Ryc. 1d. Uszy skręcone do tyłu.

Fig. 1e. Mild macular abnormalities in form of absent foveal reflex and unusual distribution of pigment.

Ryc. 1e. Łagodne zmiany w plamkach w postaci braku refleksu i niezwykłym ułożeniu barwnika.

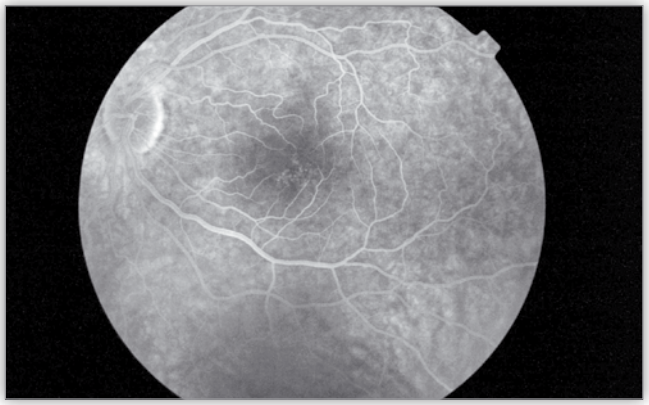

Fig. 1f. Fluorescein angiography showing window defects in macular region.

Ryc. 1f. Angiografia fluoresceinowa – widoczny ubytek w okolicy plamki.

refractive errors in 56% of patients (9). Congenital cataract or congenital glaucoma is common in RTST patients. Our patient did not demonstrate them; however he had mild degree goniodysgenesis. Besides signs of goniodysgenesis described above we did not find other signs described by Wajda et. al. like irregular Schwalbe's line, invisible Schlemm's channel, hypoplastic scleral spur, or abnormal vessels in the angle (7,10). Some authors describe unilateral ptosis in RSTS patients, which we did not notice in our case (11). Van Genderen et al. describe macular abnormalities in 75% of patients in their series with RSTS (5). In our case we were able not only to observe them during funduscopy, but also to see window defects in macular region during fluorescein angiography.

Miller and Rubinstein noted that patients with RSTS have an increased risk of malignant and benign tumors formation, especially in the nervous system (12). These authors analyzed over 700 patients with RSTS and found 17 with malignant tumors and 19 with benign tumors. Twelve of 36 tumors were located in the nervous system and included meningioma, oligodendroglioma, medulloblastoma, and neuroblastoma. Other tumor types included rhabdomyosarcoma and leukemias (12). Sammartino et al. describe spontaneous formation of multiple keloids in patient with RSTS (11). Petrij et al. suggested that the unusual incidence of neoplasms in RSTS, as well as propensity to form keloids, may be explained by the role proposed for CREBBP in cAMP-regulated cell immortalization. (OMIM) Our patient had a benign pigmented nevus of lacrimal caruncle. Schepis et al. described RSTS patient with epidermal nevus (13). To our knowledge it is the first report of an association of RSTS and lacrimal caruncle nevus.

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