SWISS SOCIETY OF NEONATOLOGY

“Here’s looking at you, kid”

May 2020

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Title figure:
Humphrey Bogart and Ingrid Bergman in Casablanca (1942): "Here's looking at you, kid" – "Ich schau Dir in die Augen, Kleines."
(Source: https://www.wypr.org/post/after-75-years-heres-looking-you-casablanca)

Apart from taking a good clinical history, a thorough physical examination is extremely important in medicine and this should remain so. However, there are widespread concerns about doctors' declining bedside skills and clinical aptitude (1). McMahon and colleagues reported that teaching of physical examination skills had become less frequent. As a result, they argued, physical examination skills had fallen into disuse among both trainees and attending physicians, leading to a spiral of decreased familiarity with signs, a decreasing sense of the utility of examination skills, and an increased reliance on laboratory and imaging tests.

In this context, quotes by Sir William Osler (Canadian physician, 1849 – 1919) deserve to be mentioned (2): "Medicine is learned by the bedside and not in the classroom. Let not your conceptions of disease come from the words heard in the lecture room or read from the book. See and then reason and compare and control. But see first." Osler, renowned for his pithy, memorable and defining quotations, also recommended: "Get the patient in a good light. Use your five senses. We miss more by not seeing than we do by not knowing. Always examine the back. Observe, record, tabulate, communicate."

CASE REPORT

This female infant was born at 36 3/7 weeks after an uneventful pregnancy to a healthy 39-year-old G1/P1. She adapted well with Apgar scores of 9, 10, and 10 at 1, 5, and 10 minutes, respectively. Arterial umbilical cord pH value was 7.28. Her birth weight was 2885 g (P45), length 48 cm (P25) and head circumference 35 cm (P75).

On initial physical examination, a number of clinical stigmata were noted: generalized muscular hypotonia, ocular hypertelorism with upslanting eye lids and medial epicanthal folds, a flat nasal bridge, macroglossia, a single transverse palmar crease on the left hand, as well as bilateral sandal-gap toes. These findings raised the suspicion of Down syndrome.

The attending physician agreed with the initial assessment. On further examination, a third fontanel and Brushfield spots (Fig. 1, 2) were also recognized. During later discussions, it became obvious that many junior (and some of the more senior) colleagues were not familiar with these findings.

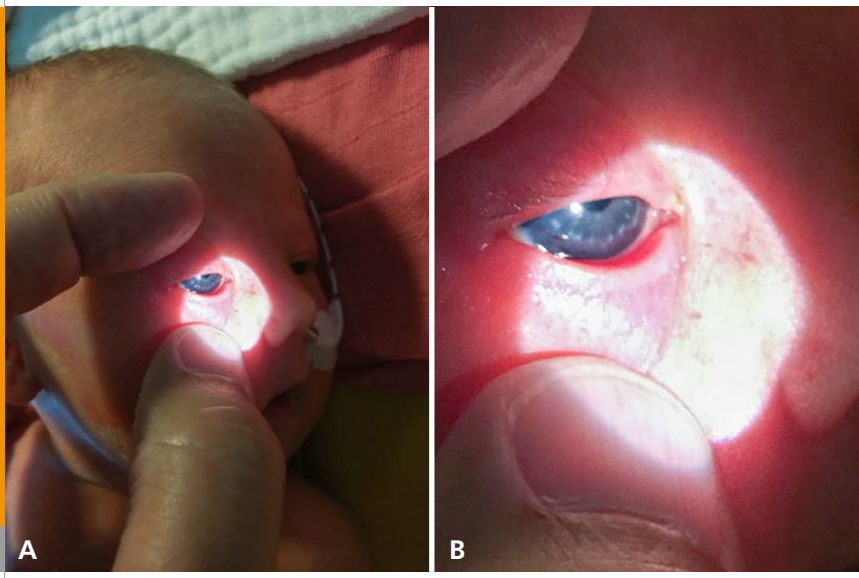

Fig. 1

Patient's right eye with a blueish iris: Brushfield spots can easily be detected with a normal ophthalmoscope (A: normal view; B: close-up view).

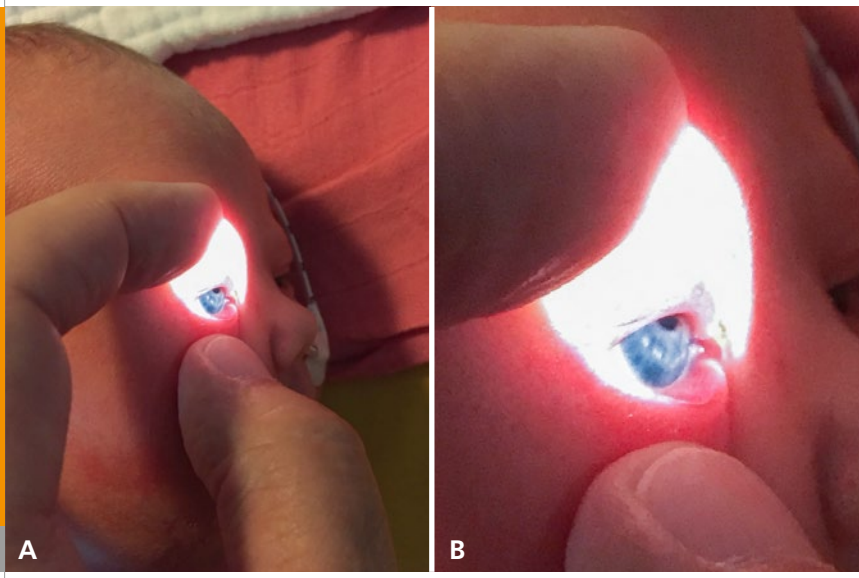

Fig. 2

Patient's right eye: Brushfield spots are typically located among the demarcation line between the apparently normal and hypoplastic iris (7) (A: normal view; B: close-up view).

A rapid test (QF-PCR) was positive for trisomy 21. Later on, the diagnosis was confirmed by conventional karyotyping (47, XY, +21). On echocardiography, a large atrial septal defect (ASD) with moderate left-to-right shunt and a patent ductus arteriosus (PDA) were demonstrated. Hypothyroidism was excluded.

DISCUSSION

Down's report of 1866 on the ethnic classification of idiots stated that a "large number of congenital idiots are typical mongols" (3). In this short essay, Down set forth the clinical description of the syndrome which still carries his name. It is noteworthy that the publication was later described by Philip Ferguson, Associate Editor of the journal Mental Retardation, as an example of 19th century scientific racism (4).

In 1966, Hall described ten principal features of Down syndrome in neonates (Table 1). He found at least four of these abnormalities in all of the 48 neonates with Down syndrome and six in more than 89 % of the them (5). Nevertheless, the specificity and sensitivity of individual findings are far from perfect. For example, a single transverse palmar crease is present in 45 % of patients with trisomy 21, but it also occurs in at least one hand in 1.5 % of the general population.

Physical abnormality	Prevalence
Hypotonia	80 %
Poor Moro reflex	85 %
Hyperflexibility of joints	80 %
Excess of skin on back of neck	80 %
Flat facial profile	90 %
Slanted palpebral fissures	80 %
Anomalous auricles	60 %
Dysplasia of pelvis	70 %
Dysplasia of midphalanx of fifth finger	60 %
Simian crease	45 %

Table 1
Prevalence of physical findings in 48 neonates with Down syndrome described by Hall in 1966 (5).

In 1924, the English psychiatrist Thomas Brushfield described white spots of varying sizes encircling the mid-periphery of only lightly colored irides in children with Down syndrome. The easily visible iris nodules quickly became known as "Brushfield spots" and were appreciated as a diagnostic indicator for the anomaly then called mongolism, now referred to as trisomy 21 (6, 7). Prior to the advent of karyotyping, Brushfield spots were widely discussed and taught in medical schools as an aid in the diagnosis of Down syndrome. Today, it appears, the clinical role has effectively diminished to the point of being of mostly historical interest (7).

Thinning of the peripheral portion of the iris, present in a minority (less than 10 %) of the general population, can be noted in the majority of individuals with Down syndrome. Brushfield spots are often located among the demarcation line between apparently normal and hypoplastic iris; they consist of a condensation of collagen tissue (7).

Until recently, Brushfield spots were described essentially in light colored irides. The specific iris features are less conspicuous in darker eyes because they are likely hidden by the higher density and number of melanin granules in the anterior border layer of darker colored irides. In 1961, using a special flash illumination and high magnification system, Donaldson was able to detect Brushfield spots and/or iris speckling in

77 % of individuals with Down syndrome with brown irides (8). In a recent study, Postolache and Parsa examined the prevalence of Brushfield spots in patients with dark irides using near-infrared light (Fig. 3). Using this technique, the overall percentage of children with Down syndrome presenting with Brushfield spots tripled, from 21 % under standard white light conditions, to 67 % using near-infrared illumination (7). It appears that the visibility of Brushfield spots in eyes of different color can be attributed in part to a "camouflaging" effect of overlying melanocytes.

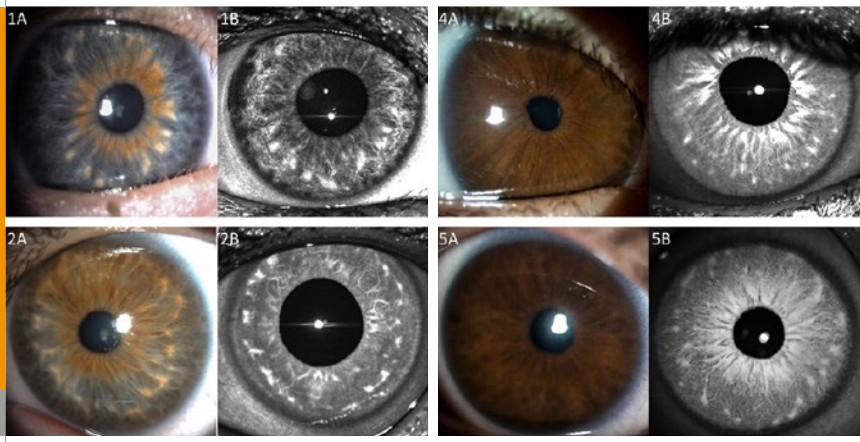

Fig. 3

Brushfield spots are readily visualized in lightly colored irides (1A, 2B: white light; 1B, 2B: 820 nm near-infrared light); in contrast, Brushfield spots in brown-eyed children with Down syndrome are not visible in white light (4A, 5A) but can be detected with near-infrared photography (4B, 5B); reproduced from Postolache et al. (7).

A small third fontanel interior to the posterior fontanel is occasionally found and is associated with Down syndrome and hypothyroidism.

In 1969, Chemke and Robinson noted that the frequency of third fontanels in an unselected population of 1020 newborn infants was 6.3 % but observed in all 10 successive infants with Down syndrome (9).

CONCLUSION

Clinical signs of trisomy 21 are neither highly sensitive nor specific. Nevertheless, the diagnosis becomes more likely the more signs are simultaneously present in a particular patient. Both Brushfield spots and a third fontanel are important clinical signs of trisomy 21. Unless actively looked for, they may easily be missed. Remember the quote by William Osler: "Get the patient in a good light. Use your five senses. We miss more by not seeing than we do by not knowing. Always examine the back. Observe, record, tabulate, communicate."

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