# A CASE OF BEAUVIEUX'S SYNDROME AND ITS EVOLUTION

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*The Authors report the evolution of a case of congenital pigmentation of the optic discs (Beauvieux's syndrome-like).*
*There was no evidence or history of hereditary or metabolic diseases, but it is important to point out the unusual age of the mother, who was 14 years old.*

In 1926 Beauvieux described, in three newborn babies, a bilateral ocular disease characterized by:

1) Lack of direct and consensual pupillary reflexes with moderate mydriasis;
2) Complete bilateral amaurosis since birth;
3) Motor incoordination with tendency to conjugated spasmodic contractions of the eye muscles and nystagmoid movements;
4) Slate-grey colour of the optic disc;
5) Chorioretinal hypopigmentation.

In the first case Beauvieux diagnosed a congenital optic atrophy probably of heredosyphilitic origin (even in absence of a positive serology). However, after a few months, the same author with surprise observed improvement of the vision. This picture seemed to be characteristic of premature babies.

In 1947 Beauvieux, who had observed in the meantime 6 or 7 new cases of the disease, distinguished two clinical pictures:

1) Cases without other ocular or general findings, where a complete functional recovery takes place;
2) Cases with a more complicated picture, where other abnormalities, such as eleveted myopia, squint, partial cataract, epicanthus, Little's disease, phychological disorders, are present.

In the second group the prognosis regarding the recovery of the vision, is less favourable even though the colour of the optic disc may become normal.

It seems that the recovery in the cases of prematures is better than in full-term infants.

A delayed myelination was supposed by Beauvieux to be the etiological factor involved. This hypothesis was based on his observation that, in one of these patients, « Little's disease » was present and this condition was then believed to be secondary to altered myelination of the pyramidal tract. This led him to study the myelination of the optic pathways in fetuses in various stages of intrauterine life (from two months to the end of gestation, including a 7-months premature baby who died after 15 days, and a full-term baby who died after a month).

His findings show that the first sign of myelination appears at the age of 5½ months only

Proc. 4th Int. Congr. Neurogenet. Neuroophthalmol. (1973)
*Acta Genet. Med. Gemellol.* (*Roma*), 23: 337-343

TABLE
ANALYSIS OF THE CASES OF BEAUVIEUX'S SYNDROME

| | Beauvieux 1923 | Beauvieux 1924 | Beauvieux 1925 | Halbertsma 1937 | Offret 1942 | Viallefont 1943 |
|---|---|---|---|---|---|---|
| Consanguinity | ? | ? | ? | no | ? | ? |
| Heredo-familial defects | deaf-mute harelip | no | no | no | ? | ? |
| Age of parents | ? | ? | ? | ? | ? | ? |
| First pregnancy | yes | yes | no, 2nd | yes | ? | ? |
| Type of pregnancy | difficult | difficult | normal | normal | ? | ? |
| Type of birth | 8th month, normal | 8th month, hydramnios | normal | normal | ? | full-term |
| Teratogenic agent | ? | ? | ? | ? | ? | ? |
| Sex | F | F | F | F | M | M |
| Age at first observation | 4 m. | 3 m. | 2 m. | 2 m. | 4 m. | 4 m. |
| Beginning of recovery | 7 m. | 4 m. | 3½ m. | 3 m. | ? | ? |
| Length of observation | 12 m. | 14 m. | 4 m. | 3 m. | ? | ? |
| Result | improved | recovery | recovery | recovery | ? | ? |
| Pupillary reflexes | no | no | signs | no | ? | ? |
| Fundus | hypopigment. | — | — | — | | |
| Nystagm | yes | yes | no | no | | |
| Refraction | myopia | — | — | — | | |
| Incoordinated movements | yes | yes | yes | no | | |
| Optic disc | slate-grey | slate | slate | slate | | |
| Final colour | slightly modified | normal | normal | normal | | |
| Other malformations | polar cataract | epicanthus | no | no | | |
| Nervous affection | no | Little's disease | no | no | | |
| Other defects | no | no | no | no | | |
| Mental development | — | delayed | — | — | | |
| ERG | — | — | — | — | | |
| EEG | — | — | — | — | — | — |
| Caryogram | — | — | — | — | — | — |
| Metabolic errors | — | — | — | — | ? | ? |

at the level of the upper visual tracts. At the age of 6½ months the myelin can be found on the level of the chiasma and the intracranial part of the optic nerve, but it is still irregularly distributed. At the age of 7 months it reaches the foramen opticum; in the 8th and 9th month it has progressed to the site of the central vessels, and only between the 9th month and the first 3-4 weeks of life it attains to the lamina cribrosa. There are individual variations at the same fetal stages.

According to Beauvieux, there is no doubt that light stimuli favour myelination. This observation was based on the examination of two 7-months old fetuses: the myelination was more marked in the premature who had lived longer.

In 1935 Karelitz and Vogel, after having observed some genetically grey discs (cases 1, 5, and 6 might be included in this syndrome), examined about 150 babies selected at random and in 87% cases (this applies only to the white race) the fundus was paler than in the adults and the optic disc was of a variable grey colour. In prematures the colour was darker, and during the first weeks of life the appearance became progressively normal.

Other authors have also described cases similar to those of Beauvieux: Halbertsma (one case, 1937), Hoefnagel (3 cases, 1937, cited by Beauvieux), Offret (one case, 1942, cited by

Table. *Contd.*

| Keiner 1951 (1st case) | Esente 1956 | Santino 1962 | François 1968 | Personal observation 1973 |
|---|---|---|---|---|
| ? | no | no | no | no |
| ? | no | no | no | deaf-mute, ptosis, squint |
| ? | ? | father 23 | young | mother 14, father 18 |
| ? | yes | yes | yes | yes |
| normal | normal | — | — | difficult |
| full-term | full-term, normal | full-term, normal | full-term | full-term |
| ? | no | antibiotics 5th month | no | yes |
| M | F | M | F | M |
| 2 m. | 8 m. | 1 m. | 7 w. | 4 m. |
| 8 m. | 12-14 m. | 1½ m. | 3-4 m. | 8 m. |
| ? | 6 m. | ? | 1 y. | under observation |
| recovery | slight improvement | ? | slight improvement | under observation |
| no | ? | no | yes | no |
| hypopigment. | hypopigment. | — | — | hypopigment. |
| | | | yes | yes |
| hyperm. | myopia | — | — | — |
| yes | no | yes | yes | yes |
| black-grey | slate | slate | grey | slate-grey |
| normal | modified | modified | normal 3rd m. | modified |
| squint | no | no | no | no |
| no | hypotonia, cerebropathy | — | hypotonia, encephalopatia | |
| no | no | malformed right hand | — | no |
| — | delayed | — | — | delayed |
| — | — | — | — | normal |
| — | — | normal | — | epylepsy |
| — | — | | | normal |
| ? | ? | ? | leucinosis | absent |

Beauvieux), Viallefont (1 case, 1943, cited by Beauvieux), Van der Hoeve (one unpublished case, cited by Beauvieux). In 1951 Keiner, in one of his studies on the origin of squint dealing with the delayed myelination, describes 12 personal cases which he includes in Beauvieux's syndrome. However, it seems to us that, except for cases 1, 5, and 9, the given data are not sufficient to support this identity because in some of them the examination of the optic disc was not possible and in the others it was normal. (Keiner says that the appearance of the optic disc is not fundamental for the diagnosis.) Two more cases have been observed by Esente and D'Aprile (1956) and by Santino (1962).

An interesting case has been recently reported by P. François et al. (1968). This concerns a little girl, 7 weeks old, who had a branched-chain ketonuria (maple syrup urine disease). This inborn error of metabolism is transmitted as an autosomal recessive character and the biochemical defect is characterized by a block of the oxidative decarboxylation of three branched-chain ketoacids with accumulation of their respective aminoacids, leucine, isoleucine, and valine, in the blood. A decrease in the content of glycolipids in the brain, due to a disorder in the synthesis of the myelin lipids can, according to the authors, cause a defect in the myelination. This might confirm Beauvieux's first opinion.

https://doi.org/10.1017/S1120962300024045 Published online by Cambridge University Press

## CLINICAL CASE

G.M., a 4-months-old boy, was hospitalized at the Department of Pediatrics and then at the Eye Clinic of this University because the parents, in the first period of life, had observed that the child did not react to light stimuli and that he had wandering eye-movements. He has never had spasms, convulsions, or myoclonic spells.

The baby was born at full term. The labour was medically induced. Birth weight was 3800 g. The father was 18 years old at the moment of conception, the mother only 14. Between the end of the 2nd and the 3rd month an interruption of the pregnancy was attempted, first by mechanical means, then with a hormone (doses unknown). The mother at the 7th month was treated for kidney colic and had a threatened abortion. A paternal aunt has a slight emiptosis, a paternal cousin has a squint, and another cousin is deafmute (according to the relatives this was noted after smallpox vaccination). There is no consanguinity among the ancestors.

*General Physical Examination*: Unremarkable.

*Neurological Examination*: The baby did not follow objects that were moved in front of his eyes, but reacted well to sound stimuli and smiled in response to familiar voices. Deep tendon reflexes were normal and symmetrical. The patient was able to control his head and to grasp objects placed in his hands.

*Eye Examination* (28-2-1973):

Pupils were moderately mydriatics with absence of light reflex. Ocular fundi were examined under narcosis: optic discs of a slate-grey colour with normal vascularisation and chorioretinal hypopigmentation (Figs. 1 and 2).

ERG was normal (wave b 250 μV). Radiological examination of the chest and skull were normal. There was no difference in the X-ray findings of the foramen opticum, compared bilaterally.

Laboratory examinations included complete urinalysis, blood count, ESR. Blood glucose, calcium ad phosphorus and nitrogen, total plasma protein, electrophoresis and immunoelectrophoresis, blood ammonia and uric acid, dye test for toxoplasmosis, chromosome analysis from peripheral leucocytes after phytohaemagglutinin stimulation, and blood serology for syphilis, were all negative. Also normal was the chromatogram of the plasma aminoacids, the Berry's test for mucopolysaccharides. The plasma aminoacid concentration was also measured with an automated analyzer and was found within normal limits; urinary aminoacids excretion was also normal.

The EEG showed irregular basic frequencies when awake. During spontaneous sleep, irregular spike and wave discharges were noted on the left parieto-occipital region.

On account of the above-mentioned findings, the possibility of a Beauvieux's syndrome was considered. In view of the possibility that this situation might be related to a delayed myelination and considering the presence of convulsive activity demostrated by the EEG, the patient was treated with 12 units of Synacthen Depot for 10 days, followed by another cycle of the same dosage of corticotropin three time a week for another 15 days, and a preparation of $B_{12}$ and $B_1$ vitamin until the 3rd admission. At the end of this period the patient was readmitted to the Clinic. There were no changes in the behaviour and the ocular findings were substantially those previously reported. The EEG was normal. The patient was again hospitalized at the age of 8 months for further evaluation. Neurological examination was substantially as previously reported, but psychomotor evaluation showed that the patient was able to sit without support, and sometimes stand on his feet if sustained by the hands. He also smiled.

*Eye Examination* (3-7-1973, age 8 months): During spontaneous sleep there was myosis without anisochoria. Under ethrane narcosis at fundoscopic examination there was the impression of a whitish nuance at the emergence of the retinal vessels from the optic disc; this finding was perhaps more marked in the left eye, where the disc was more grey. The EEG was also normal.

*At the last control* (at 10 months) the slate grey colour was further diminished (Figs. 3 and 4).

Fig. 1. R.E. 1°

Fig. 2. R.E. 2°

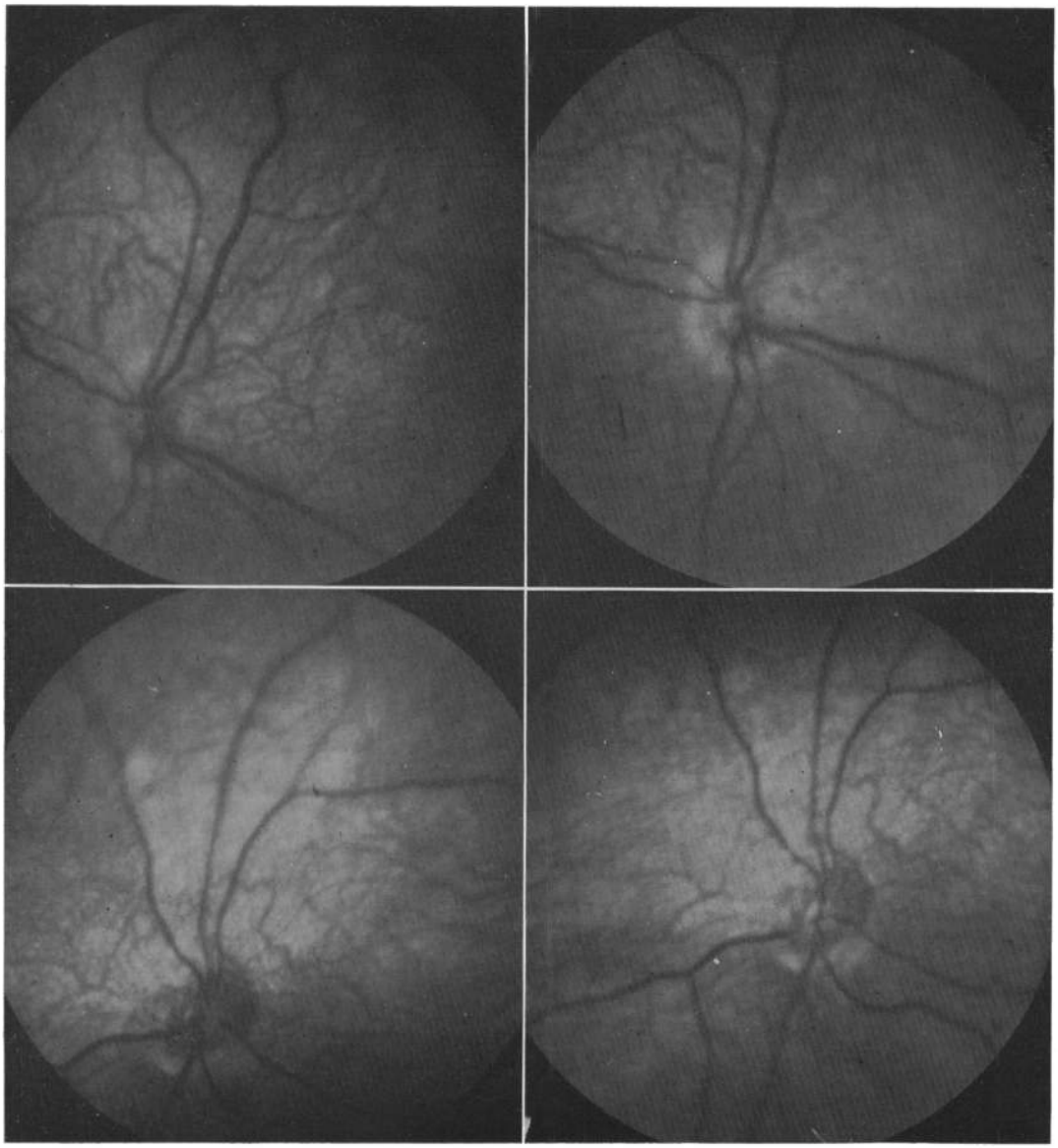

Fig. 3. L.E. 1°

Fig. 4. L.E. 2°

https://doi.org/10.1017/S1120962300024045 Published online by Cambridge University Press

## DISCUSSION

Total bilateral blindness, slate-grey colour of the optic disc, chorioretinal hypopigmentation, complete lack of pupillary reflexes with moderate mydriasis, and incoordinated nistagmoid eye-movements, as presented by our patient, can be considered typical of Beauvieux's syndrome.

However, the important element of the progressive ocular improvement of the visual function, in our case, up to the present time is lacking. Only a feeble tendency of the pupils to react to light is present at the age of 8 months. In the cases previously reported, the recovery was more precocious, except for the first of Beauvieux cases, in which the first sign of pupillary reactivity was noted between the 7th and 8th month and the first optic-disc changes between the 11th and 12th month. In Esente's case the first improvement was observed at the age of 11 months.

The differential diagnosis must be considered in regard to a primary optic atrophy and congenital pigmentations of the optic disc. The former can easily be excluded because the colour of the optic disc is light grey or frankly white and the aspect of the retinal vessels is normal in Beauvieux's syndrome, while they are threadlike in the optic atrophy.

Many papers regarding congenital pigmentation of the disc are reported in the literature: Hirschberg (1881), Förster (1881), Hilbert (1882), Pick (1900), Dijckmeester (1903), Ogawa (1905), Menacho (1917), Kraupa (1917), Scheerer (1922: histological preparations, pigmented cells of the optic nerve), Reese (1933), Sobanski (1939), Halbron and Genet (1946), Auw-Yang-Sien (1946), Cimbal (1949), Bischler and Franceschetti (1956). De Vincentiis and Gaipa (1960).

Walsh and Hoyt (1969) distinguish four principal forms of pigmentation of the optic disc (eliminating those where the pigment is of choroidal origin and is generally situated at the margins of the disc): (1) occasional flecks lying upon the nerve head on the lamina cribrosa; (2) dense plaques lying on the disc or extending out of it; (3) linear stripes of pigment; and (4) a slate-grey colour of the entire disc.

After having seen the cases published, we share Bregeat and Bonamour's opinion of accepting only photography as a valid document for the interpretation of the ophthalmoscopic pictures.

Regarding the congenital pigmentations of the optic disc, according to our opinion, the papers are not entirely reliable, because in most of them photographic documentation and drawings of any type are lacking.

In any case, important diagnostic criteria are: (1) the unilaterality of the pigmentation, often associated with severe ocular malformations, and (2) the normality of the vision in cases where other abnormalities are lacking.

It is interesting to note that in our case the ERG was normal. This investigation had not been previously performed in the other cases reported. This finding speaks against any abnormality of the retina.

Another point of interest is the absence of metabolic errors, particularly as regards branched-chain ketonuria, and the existence of epileptiform discharges which disappeared after ACTH administration. We can only speculate on these findings, which, if observed in other cases, could contribute to clarify the pathogenesis of the syndrome.

We do not know what bearing on the situation the attempted abortion and the very young age of the mother have had.

The further evolution of our case will probably add new data for the understanding of this syndrome.

## REFERENCES


Auw-Yang-Sien 1946. Papille noire. Ophthalmologica, 119: 184-188.

Beauvieux J. 1926. La pseudo-atrophie optique des nouveau-nés (Dysgénésie myélinique des voies optiques). Ann. Ocul. (Paris), 163: 881-921.

Beauvieux J. 1947. La cécité apparente chez le nouveau-né, la pseudoatrophie grise du nerf optique. Arch. Ophtalmol. (Paris), 7: 241-249.

Bischler V., Franceschetti A. 1956. Bull. et Mem. S.F.O., 69: 408.

Cimbal 1949. Ein Fall von sogenannt schwarzer Papille. Klin. Monatsbl. Augenheilk., 114: 183.

De Vincentiis M., Gaipa M. 1960. Su di un caso di disco ottico nero. Arch. Ottal., 27-29.

Dijckmeester H. 1903. Ein Fall von pigmentierter Sehnervenpapille. Arch. Augenheilk., 48: 55-61.

Esente I., D'Aprile V. 1956. Pseudo-atrofia ottica dei neonati. G. Ital. Oftal., 9: 493-497.

Förster R. Von 1881. Ueber Albinismus (schwarze Papille). Klin. Monatsbl. Augenheilk., 19.

François P., Fontaine G., Farriaux J. P., Masingue P., Masingue M., Hache J. C. 1968. Syndrome de Beauvieux (papille grise) au cours d'une aminoacidopathie rare: la leucinose. Bull. Soc. Ophtalmol. Fr., 68: 584-589.

Halbertsma K. T. A. 1937. Pseudoatrophie der papil bij jonggeborenen (dysgénésie myélinique des voies optiques, Beauvieux). Ned. Tydschr. Geneeskd., 81: 2990-2991.

Halbron P., Genet M. 1946. Un cas de mélanose de la papille optique. Arch. Ophtalmol., 6: 314.

Hilbert R. 1882. Eine eigenthüliche Pigmentanomalie des Augenhintergrundes. Klin. Monatsbl. Augenheilk., 276-278.

Hirchberg J. 1881. Ein schwarzer Sehnerv. Z. Augenheilk., 389-393.

Karelitz S., Vogel P. 1935. Ophthalmoscopic appearance of the nerve head in the new-born and in the young infant. Am. J. Dis. Child., 50: 872-878.

Keiner G. B. J. 1951. New viewpoints on the origin of squint. A clinical and statistical study on its nature, cause and therapy. Thesis, Leiden.

Kraupa E. 1917. Studien über die Melanosis des Augapfels. Arch. Augenheilk., 82: 67-93.

Menacho M. 1917. La pigmentation congénitale du nerf optique. Ann. Ocul. (Paris), 54: 296-299.

Ogawa G. 1905. Ueber Pigmentierung des Sehnerven. Arch. Augenheilk., 52: 437-454.

Pick L. 1900. Schwarzer Sehnerv. Arch. Augenheilk., 41: 96-99.

Reese A. B. 1933. Pigmentation of the optic nerve. Arch. Ophthalmol., 9: 560-570.

Santino D. 1962. Su di un caso di sindrome di Beauvieux. G. It. Oftal., 15: 179-189.

Scheerer R. 1922. Pigmentzellenbefunde im Sehnerven. Klin. Monatsbl. Augenheilk., 69: 583-591.

Sobanski J. 1939. Eine schiefergraue Sehnervenpapille. Klin. Monatsbl. Augenheilk., 102: 704-706.

Walsh F., Hoyt W. 1969. Clinical Neuro-Ophthalmology. 3rd ed., Vol. I. Baltimore: Williams-Wilkins.


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