Norcia:

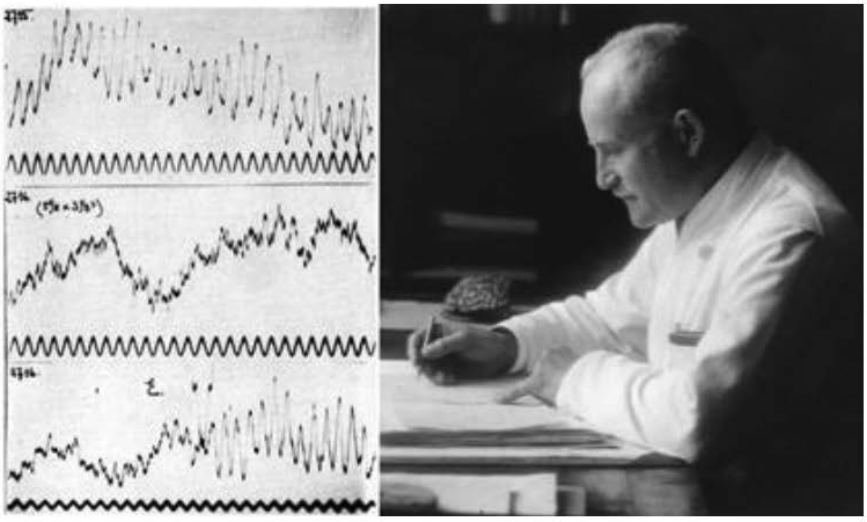


Figure 8. *Hans Berger (1873-1941) in 1927, with the 'Elektrenkephalogramm' of his daughter Ilse. Upper trace: Ilse in rest (alpha waves), middle trace: Ilse in calculating a sum (beta waves), and lower trace: Ilse in giving the outcome of the sum (mixes waves).*

Beres:

"A fallacious similarity between the elevation of the optic disc caused by buried drusen and optic disc edema caused by increased intracranial pressure presents a problem of differential diagnosis, expressly in younger children"

- H. Erkkila (1975)

Malmqvist et al. 2017; 2020

Petrushkin et al. 2011, Spencer et al. 2004, Hoover et al. 1988, Miller N. 1986

Santavuori & Erkkila, 1976

[1]Vahlgren et al., 2020.

[2]Pilat et al., 2014.

[3]Flores-Rodriguez, et al, 2012.

[4]Erkkila H., 1975.

[5]Edwards et. Al, 1996.

[6]Weng CY., Barnett D., 2018

[7]Plaza et al., 2017.

[8]Paun et al., 2012.

[9]Lee et al., 2015.

[10]Birnbaum et al., 2016.

[11] Komur et al. 2012

[12]Rossiter et al., 2005.

[13]Petrushkin et al., 2011

[14]Antcliff R, Spalton D, 1999

[15]Grover et al. 1997

Taylor & Hoyt's Pediatric Ophthalmology and Strabismus, 5th Ed

Rimmer S, et al., AM J Ophthalmol 1993

Park S, et al., Sci Rep 2019.

Kim, et al. Ophthalmology, 2018.

Spencer et al. 2004; Frisen 2008; Lee et al. 2013

Malmqvist, 2017

Malmqvist et al., 2018

Lee et al. 2011, Floyd et al. 2005

Lee et al.,2013

Ghassibi et al. 2017

Malmqvist et al.,2018

Teixeira, 2019

Floyd et al. 2005

[1]Vahlgren et al., 2020.

[2]Pilat et al., 2014.

[3]Flores-Rodriguez, et al, 2012.

[4]Erkkila H., 1975.

[5]Edwards et. Al, 1996.

[6]Weng CY., Barnett D., 2018.

[7]Plaza et al., 2017.

[8]Paun et al., 2012.

[9]Lee et al., 2015.

[10]Birnbaum et al., 2016.

[12]Rossiter et al., 2005.

[13]Petrushkin et al., 2011.

[14]Antcliff R, Spalton D, 1999.

[15]Grover et al. 1997.

[16]Larsen JS, Acta Ophthalmol 1971.

[17]Rimmer S, et al. 1993.

[18]Evans K, Wishart PK, Ophthalmic Physiol Opt. (1992).

[19]Malmqvist et al., 2018.

[20]Floyd et al., 2005.

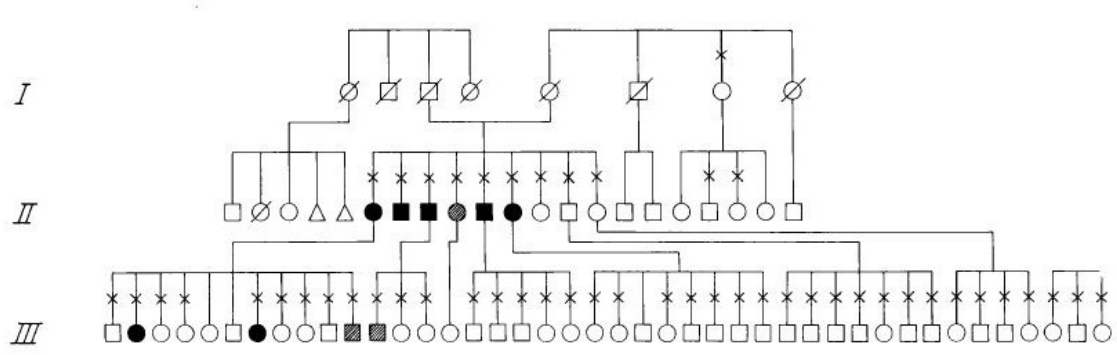
Moss:

Moss et al, IOVS 2015

Gowrisankaran, Doc Ophthal 2013

Moss, 2016

Hamann:



Leimgruber (1936). Stammbaum I.

Fig. 6.

Case Reports › Mol Vis. 2006 Dec 4;12:1483-9.

A New Autosomal Recessive Syndrome Consisting of Posterior Microphthalmos, Retinitis Pigmentosa, Foveoschisis, and Optic Disc Drusen Is Caused by a MFRP Gene Mutation

Raul Ayala-Ramirez [1], Federico Graue-Wiechers, Violeta Robredo, Monica Amato-Almanza, Iliana Horta-Diez, Juan Carlos Zenteno

Affiliations + expand

PMID: 17167404

Ocular Ultrasound in Alagille Syndrome

A New Sign

Ken K. Nischal, FRCOphth,[1] Melanie Hingorani, FRCOphth,[2] Christopher R. Bentley, FRCOphth,[2] Anthony J. Vivian, FRCS, FRCOphth,[3] Alan C. Bird, MD, FRCS, FRCOphth,[3] Alistair J. Baker, MRCP,[4] Alex P. Mowat, FRCP,[4] Georgina Mieli-Vergani, MD, PhD, FRCP,[4] Wagih A. Aclimandos, FRCS, FRCOphth[2]

Background: Alagille syndrome (AS) is one of six forms of familial intrahepatic cholestasis, all of which present with neonatal jaundice and paucity of intrahepatic bile ducts. Differentiation of these individual syndromes is crucial as their treatments and prognoses vary. It is the ophthalmic features, posterior embryotoxon on particular, that distinguish AS.

Methods: The authors performed full ocular examination, including A- and B-scan ultrasound, refraction, and, where possible, fluorescein angiography in 20 unrelated children with AS and 8 with non-AS-related cholestasis.

Results: There was ultrasound evidence of optic disc drusen in at least one eye in 95% and bilateral disc drusen in 80% of patients with AS but in none of the patients who were non-AS at the time of examination. Independent review of hard-copy scans suggested drusen in at least one eye in 90% of the cases and bilateral drusen in 50%, although this latter figure rose to 65% on review of the angiograms. This is markedly higher than the incidence in the normal population (0.3%–2%). Axial lengths were shorter than expected for the older age group (older than 10 years of age), but this was not associated with gross ametropia.

Conclusion: This strong association of AS and optic disc drusen has not been reported previously and represents not only the first significant association between a systemic condition and disc drusen but also a possibly useful tool in the diagnosis of AS, especially in young children. *Ophthalmology 1997;104:79–85*

Journal français d'ophtalmologie (2019) 42, 262–268

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

ORIGINAL ARTICLE

A study of optic nerve head drusen in 38 pseudoxanthoma elasticum (PXE) patients (64 eyes). Location of optic nerve head drusen in PXE

Étude des drusen du nerf optique dans le pseudoxanthome élastique chez 38 patients (PXE). Localisation des drusen du nerf optique dans le PXE

V. Pipelart[a,*], B. Leroux[a], S. Leruez[a], S. Henni[b,c], N. Navasiolava[c], L. Martin[c,d], J.-M. Ebran[a,c]

[a] *Department of Ophthalmology, Angers University Hospital, 2, rue Larrey, 49933 Angers cedex 9, France*
[b] *Department of Vascular Function Investigation, Angers University Hospital, 49933 Angers, France*
[c] *Pseudoxanthoma Elasticum Referral Centre, Angers University Hospital, 49933 Angers, France*
[d] *Department of Dermatology, Angers University Hospital, 49933 Angers, France*

Received 5 July 2018; accepted 22 August 2018
Available online 15 March 2019

KEYWORDS
Pseudoxanthoma elasticum;
Calcification;
Bruch's membrane;
Retinal pigment epithelium atrophy;
Optic nerve head drusen

Summary
Purpose. — To investigate the prevalence and location of optic nerve head drusen and their potential association with other PXE-related ophthalmic abnormalities.
Materials and methods. — Thirty-eight of the 155 patients (57 male and 98 female aged 49 ± 17 years) included in this retrospective study had optic nerve head drusen. All of the patients underwent a comprehensive ophthalmic examination, including color images using red-free, blue and red filters, autofluorescence imaging and late-phase ICG frames. Comparative analysis of both groups (optic nerve head drusen or not) was conducted using R statistical software.
Results. — The prevalence of optic nerve head drusen in our cohort was 24.5%. In this study, no evidence of a significant link between optic nerve head drusen and other fundus abnormalities was detected. They were more commonly located in the nasal sector than in the temporal sector of the optic disc ($P < 0.001$). They were more frequently situated superonasally than inferonasally ($P < 0.004$), superotemporally ($P < 0.001$) or inferotemporally ($P < 0.03$). No central visual field defect was observed in OND+ patients who were unaffected by macular disorders.

* Corresponding author. Service d'ophtalmologie, CHU, 2, rue Larrey, 49933 Angers cedex 9, France.
E-mail address: valentinpipelart@yahoo.fr (V. Pipelart).

https://doi.org/10.1016/j.jfo.2018.08.007

Original Paper · Travail original · Originalarbeit

Ophthalmologica 1994;208:239–242

L. Pierro
R. Brancato
M. Minicucci
A. Pece

Department of Ophthalmology and Visual Sciences, University of Milan, Scientific Institute H.S. Raffaele, Via Olgettina 60, Milan, Italy

Echographic Diagnosis of Drusen of the Optic Nerve Head in Patients with Angioid Streaks

Key Words
Angioid streaks
Drusen of the optic nerve head
Pseudoxanthoma elasticum
Echography
Fluorescein angiography

Abstract
A total of 58 patients (116 eyes) with angioid streaks, referred to this department over 2 years (1990–1992), underwent a thorough ophthalmic examination, retinal fluorescein angiography, dermatological visit with skin biopsy, and a series of other examinations (blood and biochemistry, skull X-ray, vascular echo Doppler, abdominal ultrasound) and eye ultrasonography. Fifty patients (100 eyes, 86.2%) had pseudoxanthoma elasticum (PXE). In the whole caselist, 21.6% had drusen compared with 21.0% in the group with PXE. Both these findings are higher than those published elsewhere. Drusen of the optic nerve head were also found in 25% of the 16 eyes (8 patients) with angioid streaks but no PXE. We believe we found a higher prevalence of drusen of the optic nerve head in these patients with angioid streaks because we systematically employed ultrasound.

Introduction

The association of drusen of the optic nerve head (ONH) and angioid streaks has only been described in patients with pseudoxanthoma elasticum (PXE) [1–3]. More than 90% of these patients present streaks [4, 5], but the prevalence of drusen is reported as ranging from only 6% [6] to 16% [7]. However, angioid streaks with drusen have recently been described in a patient with Waldenström's macroglobulinemia and it is conceivable that the two clinical signs may occur together in other diseases too [8].

To our knowledge, echography has never been used systematically to check for drusen of the ONH in patients with angioid streaks, although we believe this diagnostic technique lends itself better to identifying calcified matter. In the present study ocular echography was employed to check the prevalence of ONH drusen together with angioid streaks.

Patients and Methods

Fifty-eight patients (116 eyes) with angioid streaks, who were referred to us in the 2-year period 1990–1992, underwent an ophthalmic examination, retinal fluorescein angiography, dermatological visit with skin biopsy, and a series of other examinations (blood and biochemistry, skull X-ray, vascular echo-Doppler, abdominal ultrasound) and ocular echography. Of these, 25 were male (43.1%) and 33 female (56.9%); their mean age was 53.1 years (range 36–74, SD 8.49 years).

Autofluorescence of the ONH was checked before fluorescein angiography, using the angiograph excitation filter alone. An Ophtascan S (Biophysic Medical) echograph was employed in the A-B scan mode. A skin biopsy for histological testing (immunochemistry and ultrastructure) was taken from the arm pit or side of the neck, wherever there were any visible alterations attributable to PXE. The person responsible for each method did not know the results of the other test.

Received: February 7, 1994
Accepted: April 19, 1994

Department of Ophthalmology and Visual Sciences
University of Milan
Scientific Institute H.S. Raffaele
Via Olgettina 60
I-20132 Milano (Italy)

0030–3755/94/2085–0239
$ 8.00/0

Frequency of Optic Disc or Parapapillary Nerve Fiber Layer Drusen in Retinitis Pigmentosa

Sandeep Grover, MD,[1] Gerald A. Fishman, MD,[1] Jeremiah Brown, Jr., MD[2]

Purpose: To determine the frequency and characteristics of optic disc and parapapillary nerve fiber layer drusen in patients with retinitis pigmentosa and to attempt to document any differences in the frequency within different genetic subtypes of retinitis pigmentosa.

Methods: This retrospective case series reviewed 117 patients with autosomal-dominant, 84 with autosomal-recessive, and 61 with X-linked recessive forms of retinitis pigmentosa. Color fundus photographs were reviewed independently by three investigators. The presence of optic disc or parapapillary nerve fiber layer drusen was documented only when all three observers concurred as to their presence. The number (isolated or multiple), site (disc, parapapillary, or both), and bilaterality (unilateral or bilateral) were noted in each patient.

Results: Optic disc or parapapillary nerve fiber layer drusen or both were observed in 11 patients (9.4%) with autosomal-dominant, 6 patients (7.1%) with autosomal-recessive, and 7 patients (11.5%) with X-linked recessive types of retinitis pigmentosa. The differences in the observed frequencies were not statistically significant ($P = 0.67$). Overall, the frequency of optic nerve head or parapapillary drusen or both in 262 patients with retinitis pigmentosa was 9.2%.

Conclusion: In a large population of patients with retinitis pigmentosa, our findings suggest that approximately 10% are likely to show optic nerve fiber layer drusen involving the optic disc or parapapillary regions or both. The frequency does not vary significantly between different genetic subtypes. *Ophthalmology 1997;104:295–298*

Müller (1858) The first to give a histologic description of ODD found together with RP in both eyes of an almost blind man, aged 75

Nieden (1878) First ophthalmological description of ODD seen in a 14-year-old girl with RP

Ancke (1885) Described ODD in 3 members of a sibship of 5 and in 2 members of sibship of 5. The ODD were in all 5 cases associated with RP

ACTA OPHTHALMOLOGICA VOL. 39 1961

From the University Eye Clinic, Århus
(Chief: Professor Viggo A. Jensen, M. D.)

DRUSEN OF THE OPTIC DISK, AN IRREGULARLY DOMINANT HEREDITARY AFFECTION

BY

S. E. Lorentzen

- Braun (1935): 2 families, 3 relatives affected out of 22 examined in one family and none affected in 26 relatives in the other family

- Leimgruber (1936): 8 families, 4 families with 13 relatives affected out of 72 examined, although in the other 4 families no relatives were affected

Selected References
Grover et al 1997
Pierro et al 1994 Pipelart et al 2019
Nischal et al 1997 Kim & Fulton 2007
Ayala-Ramirez et al 2006 Morillo Sánchez et al 2019

*Müller'*s drawing attending the first histologic description of optic disc drusen (1858)

*De Wecker & Jäger'*s (1870) drawing of optic disc drusen after *Iwanoff'*s histological specimen

*Stood'*s (1883) illustration of the ophthalmoscopic image of optic disc drusen

de Schweinitz' (1892) photomicrograph of optic disc drusen (x about 200)

Svend Erik Lorentzen (1966)

Trans. ophthal. Soc. U.K. (1975) **95,** 4

Drusen of the optic disc—
A histopathological study

A. H. FRIEDMAN, P. HENKIND, AND S. GARTNER

From the Department of Ophthalmology, Albert Einstein College of Medicine/Montefiore Hospital and Medical Center, New York.

FIG. 6 *Superficial disc haemorrhage delineated by arrow. Haematoxylin and eosin.* ×125

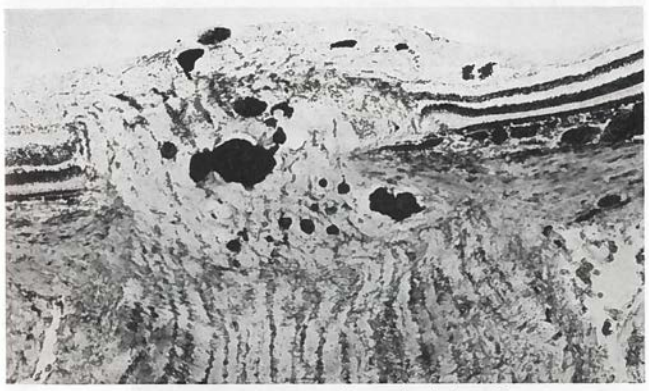


FIG. 2 *Photomicrograph showing elevated optic disc with multiple drusen anterior to lamina cribrosa. Haematoxylin and eosin.* ×50

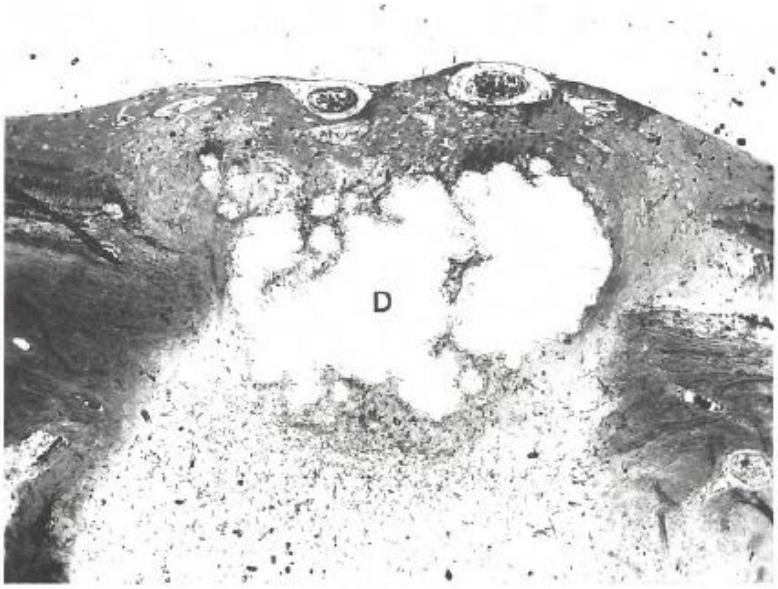


Fig 1. Multilobulated drusen (D) occupy most of the optic nervehead, so that the optic cup is filled and the peripapillary retina is displaced laterally. Considerable glial and axonal tissues lie anterior to the drusen. The calcified material of the drusen is shattered during the sectioning process with a glass knife (×40).

Pathology and Pathogenesis of Drusen of the Optic Nervehead

MARK O. M. TSO, MD

Lasse Malmqvist phd on ODD (2017)

Optic Disc Drusen Studies Consortium (2016)

Roh et al., Ophthalmology 1998

Malmqvist et al., JNO 2018

Malmqvist et al., Ophthalmology 2018

Skougaard et al., Acta Ophthalmol 2019

Girard et al., ARVO 2020

American Journal of Ophthalmology
Available online 13 April 2020
In Press, Journal Pre-proof

Original Articles

Young Adults with Anterior Ischemic Optic Neuropathy: A Multicenter Optic Disc Drusen Study

Steffen Hamann [1], Lasse Malmqvist [1], Marianne Wegener [1], Valérie Biousse [2], Lulu Bursztyn [3], Gülsenay Citirak [1], Fiona Costello [4], Alison V. Crum [5], Kathleen Digre [5], Masoud Aghsaei Fard [6], J Alexander Fraser [3, 7], Ruth Huna-Baron [8, 9], Bradley Katz [5], Mitchell Lawlor [10], Nancy J. Newman [2], Jason H. Peragallo [2], Axel Petzold [11, 12], Patrick A. Sibony [13], Prem S. Subramanian [14], Judith EA. Warner [5], Sui H. Wong [15], Clare L. Fraser [10] for the Optic Disc Drusen Studies Consortium

[1] Department of Ophthalmology, Rigshospitalet, University of Copenhagen, Denmark
[2] Departments of Ophthalmology and Neurology, Emory University School of Medicine, Atlanta, USA
[3] Department of Ophthalmology, Western University, Canada
[4] Departments of Clinical Neurosciences and Surgery, University of Calgary, Canada
[5] Department of Ophthalmology and Visual Sciences, John A. Moran Eye Center, Department of Neurology, University of Utah, USA
[6] Farabi Eye Hospital, Tehran University of Medical Science, Iran
[7] Department of Clinical Neurological Sciences, Western University, Canada
[8] Goldschleger Eye Institute, Sheba Medical Center, Israel
[9] Sackler Faculty of Medicine, Tel Aviv University, Israel
[10] Save Sight Institute, Faculty of Health and Medicine, The University of Sydney, Australia
[11] Moorfields Eye Hospital, The National Hospital for Neurology and Neurosurgery, Queen Square Institute of Neurology UCL
[12] Neuro-ophthalmology Expertise Centre, Amsterdam UMC (locatie VUmc), The Netherlands
[13] Department of Ophthalmology, State University of New York at Stony Brook, USA
[14] Departments of Ophthalmology, Neurology, and Neurosurgery, Sue Anschutz-Rodgers UCHealth Eye Center, University of Colorado School of Medicine, USA
[15] Department of Neuro-ophthalmology, Moorfields Eye Hospital, United Kingdom

Mahajan:

Velez G, Tsang SH, Tsai Y-T, Hsu CW, Gore A, Abdelhakim AH, et al. Gene Therapy Restores Mfrp and Corrects Axial Eye Length. Nature Publishing Group. Springer US; 2017 Nov 16;7(1):1–8. PMCID: PMC5701072

Chekuri, A. et al. (2019) 'Long-Term Effects of Gene Therapy in a Novel Mouse Model of Human MFRP-Associated Retinopathy', Human Gene Therapy, 30(5), pp. 632–650. doi: 10.1089/hum.2018.192.

Li, Y. et al. (2014) 'Gene Therapy in Patient-specific Stem Cell Lines and a Preclinical Model of Retinitis Pigmentosa With Membrane Frizzled-related Protein Defects', Molecular Therapy, 22(9), pp. 1688–1697. doi: 10.1038/mt.2014.100