Ex- and Enophthalmos: General Aspects

7

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Learning Objectives
- Exophthalmos and enophthalmos are cardinal features of orbital pathology.
- The most common cause of both bilateral and unilateral exophthalmos is Graves' orbitopathy, whereas an orbital fracture is the most common cause of unilateral enophthalmos.
- Exophthalmos and enophthalmos are clinically assessed with an exophthalmometer.

Fig. 7.1 Measuring AGP with a Hertel exophthalmometer

Introduction: The (Axial) Globe Position

The Axial Globe Position (AGP) is defined as the distance between the apex of the cornea and the lateral rim of the orbit in the sagittal plane and it is measured with an instrument called an exophthalmometer (Fig. 7.1). One of the first exophthalmometers was designed by the German ophthalmologist Ernst Hertel (1870–1943) [1], who became so famous that the term 'Hertel value' has become a synonym for AGP.

AGP differs between ethnic groups and between females and males, but within these groups it shows a normal distribution. In Caucasians, AGP varies between 10 and 17 mm in women and between 10 and 20 mm in men. African people tend to have a slightly higher, Asian people a slightly lower AGP. A difference of up to 2 mm in AGP between both globes is generally considered normal. Thus, a difference between both eyes of >2 mm should raise suspicion for a pathological process. Generally, an AGP less than 10 mm is called enophthalmos; AGP >20 mm is called exophthalmos.

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We measured the AGP in 160 healthy Caucasian men and women and compared the results with those of a group of patients with Graves' orbitopathy (GO), and assessed the accuracy of the measurements [2]. We concluded that:

1. Exophthalmometry using a Hertel exophthalmometer is reliable and reproducible.
2. AGP shows a normal distribution in both healthy individuals and patients with GO and is gender dependent.
3. Regression analysis revealed an upper limit of normalcy of 16 mm in females and 20 mm in males.

AGP distribution has been determined in different ethnic groups [3–6]. AGP can also be assessed—albeit less accurately—using digital photography, CT scans, or MRI scans [7]. Conventional exophthalmometers have a number of disadvantages. To overcome these, we developed a parallax-free exophthalmometer (Fig. 7.2) based on the concepts of Davanger [8, 9].

For patients, in whom the lateral wall is missing, i.e. in orbital fractures or after surgery, Naugle developed a superior and inferior orbital rim-based exophthalmometer [10]. Exophthalmos is also called proptosis or (eye)protrusion. Pseudoproptosis refers to a situation that seems to indicate proptosis, which cannot be confirmed by AGP measurement. This is often seen in patients with unilateral upper eyelid retraction (Fig. 7.3). Therefore, AGP should always be measured.

Besides forward displacement, the globe can be pushed downward (hypoglobus), upward

Fig. 7.2 Parallax-free exophthalmometer according to Mourits

Fig. 7.3 Patient with upper lid retraction, but normal AGP (pseudoproptosis)

Fig. 7.4 Patient with deep superior sulcus of the left orbit

(hyperglobus), sideward, or any combination. Hypoglobus and enophthalmos are typically seen in orbital floor fractures. A beginning negative discrepancy between the volume of the orbital cavity and the volume of the orbital soft tissues shows by a deep superior sulcus, i.e. the space between the upper lid and superior orbital margin (Fig. 7.4).

The direction of globe displacement gives an indication about the localization of the orbital disease process. For instance, downward displacement suggests an orbital floor fracture or a mucocele of the frontal sinus with a perforated orbital roof, whereas a medial plus downward displacement is

indicative for a disease process in the lacrimal gland fossa. Upward displacement with or without proptosis can be seen in diseases of the maxillary sinus, such as shown in Figs. 7.5 and 7.6. Retrobulbar lesions tend to push the globe in a forward direction (Fig.7.7), but often cause other symptoms, such as reduced color vision or a Relative Afferent Pupil Defect (RAPD) in an early stage of the disease due to compression of the optic nerve.

For a correct diagnosis of disorders with exophthalmos and enophthalmos, the following variables are of cardinal importance:

1. Age.
2. Gender.
3. Onset and duration of the complaints.

Figs. 7.5 Female patient with a cystic lesion of the left maxillary sinus resulting in orbital floor elevation. (Courtesy of Dr. P. Gooris)

Fig. 7.6 CT scan of the same patient as shown in Fig. 7.5 (Courtesy of Dr. P. Gooris)

4. Eyelid and conjunctiva abnormalities: swelling, redness, ptosis, retraction.
5. Eye motility.
6. Visual acuity, color vision, pupil reaction
7. MRI scans and/or CT scans.
8. Blood tests.

Some phenomena are strongly connected to a particular disease. Thus, an increase of exophthalmos with the Valsalva maneuver suggests an orbital varix and enlarged corkscrew epibulbar vessels are indicative for an arteriovenous fistula.

Diseases with Exophthalmos

The list of diseases and disorders causing exophthalmos is almost infinite. Here, we will shortly discuss the most frequent ones. By far, GO heads the list. It is estimated that >50% of all patients with proptosis suffer from GO [11]. GO will be discussed in Part 6.

Orbital Meningioma

Orbital meningioma is a relatively frequent orbital tumor, with an estimated incidence of approximately sixty cases per year in the Netherlands [12]. The most common presentation is that of an extension into the orbit from an intracranial meningioma located on the outer ridge of the sphenoid bone (Figs. 7.7 and 7.8), hence its name spheno-orbital meningioma (SOM). SOM typically causes hyperostotic changes of the sphenoid wing. These changes result in a reduction of orbital cavity volume and push the globe forward.

Less frequent are meningiomas that arise from the meninges (arachnoid mater) surrounding the optic nerve, the so-called optic nerve sheath meningioma (ONSM, (Fig. 7.9). Because of their localization and direct compression of the optic nerve, they cause visual impairment (reduced (color) vision, reduction of the visual field, RAPD) rather than proptosis in the early stages. Fundoscopy may reveal opticociliary shunt ves-

Fig. 7.7 Exophthalmos and hyperostosis (arrow) secondary to intracranial meningioma (which itself is not visible on this CTscan)

Fig. 7.8 Gadolinium-enhanced MRIscan showing intra-cranial meningioma (arrow)

Fig. 7.9 Optic nerve sheath meningioma in the right orbit. Notice the sparing of the optic nerve, a sign that is called the tram-track phenomenon which is present in circa 25% of patients with this kind of tumor
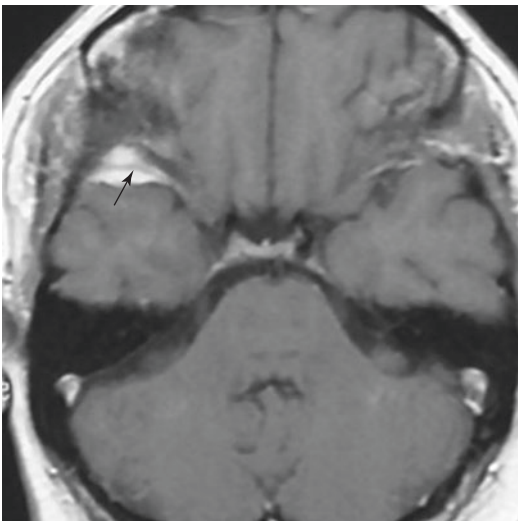
The diagnosis of SOM is usually straightforward using CT scans and gadolinium-enhanced MRI scans. The diagnosis of ONSM may be challenging, when no clear tram-track phenomenon (Fig. 7.9.) is seen. With a sensitivity of 100% and a specificity of 97% at a threshold uptake ratio of 5.9, somatostatin receptor scintigraphy is a useful additional tool in diagnosing ONSM [13]. The differential diagnosis of ONSM includes: metastasis, lymphoma, sarcoidosis, and other inflammatory diseases.

Meningiomas are managed by careful observation, radiotherapy, or surgery. SOMs with significant morbidity can be reduced in size by a multidisciplinary team consisting of a neurosurgeon and an orbital surgeon via pterional, fronto-temporal, or cranio-orbital approaches.

Optic Pathway Glioma (Pilocytic Astrocytoma)

Optic nerve gliomas or optic pathway gliomas (OPG; Fig. 7.10) occur along the entire length of the pre-cortical optic pathways and were usually considered hamartomas, but are now classified as pilocytic astrocytoma's. They arise frequently in association with neurofibromatosis type 1 and then have a better visual prognosis than solitary

sels, together with swelling or pallor (in a later stage) of the optic nerve head.

Orbital meningiomas are usually benign, well-vascularized, slow-growing tumors, that affect—at least in Caucasians—women more often than men. They arise from meningothelial cap cells of the arachnoid villi. They typically become apparent in the fourth to sixth decades. The assumption that hormonal changes play a role in the etiology of meningiomas has never been corroborated. Cranial irradiation, however, is a risk factor for the development of meningiomas.

Fig. 7.10 T1-weighted MRI scan showing an optic nerve glioma in a 6-year-old child (arrow)

OPGs [14]. They mostly affect children younger than 10 years of age and 60% of them will eventually have a visual acuity of finger counting or less. Exophthalmos is present in 95% of patients. OPGs will rarely progress to the optic chiasm or the contralateral side. Therefore, observation alone will often be sufficient. Disfiguring proptosis or orbital pain can be a reason for surgical excision. In advanced cases, chemotherapy with vincristine and carboplatin is considered treatment of first choice.

Orbital Cavernous Hemangioma (Orbital Cavernous Venous Malformation)

Orbital cavernous hemangioma (OCH) is a well-encapsulated vascular hamartoma with a spongy structure made up of interconnected vascular channels filled with blood. Cavernous hemangiomas can occur everywhere in the body, but are relatively frequent in the orbit in adults. They sometimes do not cause any complaint and are accidently found in individuals undergoing a screening total body scan. On CT scans, they appear as a well-defined, round to oval homogeneous mass; on T1-weighted MRI scans they produce a homogeneous signal iso-intense to muscle. On T2-weighted scans they are hyperintense to fat and brain.

We described two presentations (Fig. 7.11): [1] the apple-shaped anterior/mid-intraconal, and [2] the pear-shaped apical intraconal type [15]. The former causes a painless exophthalmos and can be easily 'delivered' with some traction of a cryoprobe via a lateral or anterior orbitotomy, as it lies freely in the orbit. The apically located OCH, even if its size is modest, causes reduction of visual acuity and visual field narrowing in the early stages of the disease, because of compression of the optic nerve. A RAPD is usually present. The capsule of this type fuses with adjacent vessels and nerves. Total removal is impeded by poor visualization, lack of maneuvering space, excessive bleeding and risk of damaging of the oculomotor nerves and the ciliary ganglion. Partial removal with or without bipolar cautery shrinkage has been suggested as an alternative procedure, as well as radiotherapy [16, 17].

Orbital Capillary or Infantile Hemangioma

Capillary or infantile hemangiomas are the most common benign vascular orbital neoplasms of childhood, most often located in the superior and anterior orbit or eyelid, and seen more often in girls. On CT scans they appear as a well-defined or infiltrating mass; on T1- and T2-weighted MRI scans they show a heterogeneous signal, hyperintense to muscle and hypo-intense to fat [18]. They typically enlarge during the 6th–12th month and then spontaneously regress until the end of the seventh year of life, when they often have disappeared almost completely. They, therefore, do not need treatment as long as there are no complications. If treatment is required, oral propranolol or topical timolol can be given. Prednisone is also effective, but can cause significant body growth retardation, even if given locally.

Orbital Rhabdomyosarcoma

Rhabdomyosarcoma is the most frequent orbital malignant neoplasm of the orbit in children, with a peak incidence at the age of 7 years and account-
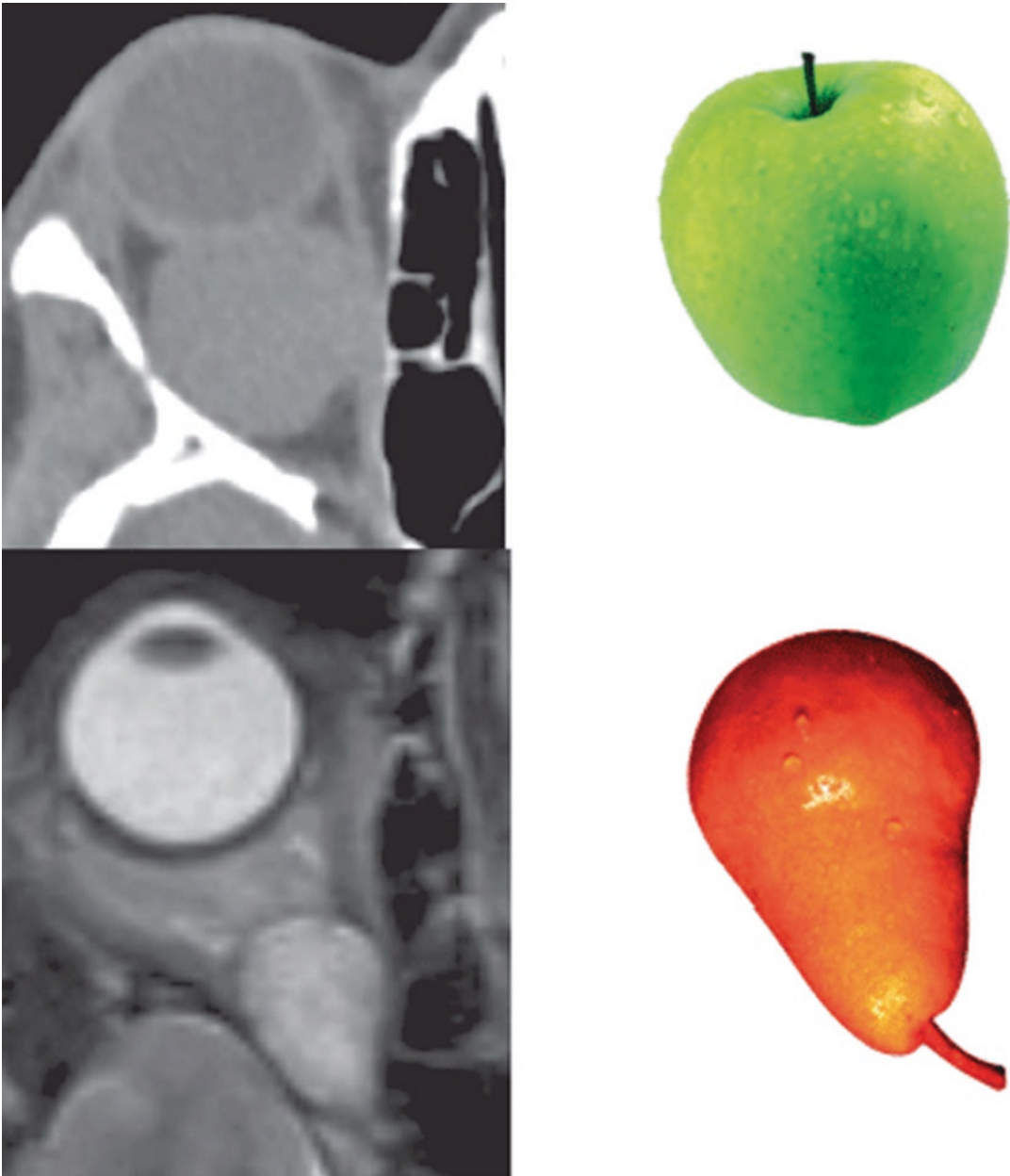
Fig. 7.11 CT scan and T2-weighted MRI scan showing apple- and pear-shaped orbital cavernous hemangiomas

ing for approximately 4–6 new cases per year in the Netherlands [19]. It grows so rapidly that it may mimic an orbital cellulitis or an insect bite (Fig. 7.12). CT scans show a moderately well-defined soft tissue mass. On MRI scans, it is a rather homogeneous irregular mass, more or less iso-intense to muscle tissue. The prognosis has improved over the last sixty years with a survival rate of 30% (after exenteration) around 1960 and a survival rate of 95%, at present, after treatment with vincristine and cyclophosphamide, with or without radiotherapy [20].
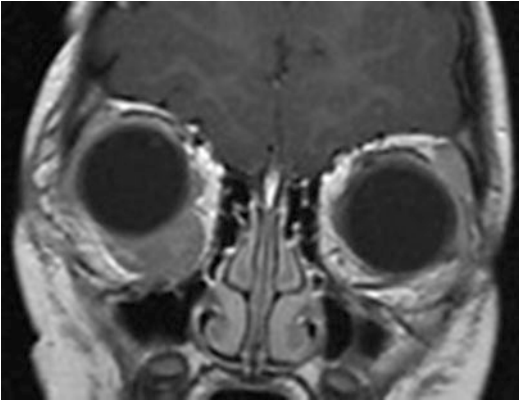
Fig. 7.12 MRI scan of rhabdomyosacoma in the lower medial quadrant of the right orbit in young female
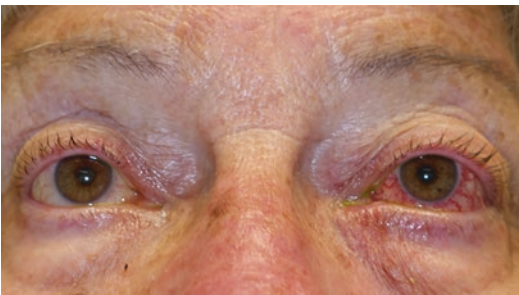

Fig. 7.13 Dilated epibulbar vessels and proptosis in a patient with a traumatic caroticocavernous fistula

Arteriovenous Shunts and Fistulas

A direct connection in the carotid-cavernous area between the arterial and venous systems can cause a pulsating exophthalmos and enlarged epibulbar 'corkscrew' vessels due to a reversal of blood flow in the orbit (Fig. 7.13). Because of an elevated outflow resistance, the intraocular pressure increases and the patient may complain of pain, nausea, and reduced vision. In these 'high-flow' lesions, a pulsating sound (bruit) synchronous to the heart beat may be heard over the orbit or skull. Arteriovenous (AV) fistulas as a result of head trauma arise in a few hours to days.

Slowly evolving proptosis as a result of 'spontaneous' dural AV fistula is seen in older patients with vasculopathy (DM, hypertension). Dural AV fistulas are frequently associated with a dilated superior ophthalmic vein or with supe-rior ophthalmic vein thrombosis [21]. The extra-ocular muscles are often swollen due to congestion, which may be mistaken for GO. AV shunts are best shown with arteriography. Up to 50% of them disappears spontaneously. As long as they exist, ocular hypertension is treated in the same way as glaucoma. When they do not close or cause significant complications, embolization by an interventional radiologist can be considered.

Orbital Non-Hodgkin Lymphoma

An insidious development of a painless exophthalmos, with a lesion most frequently anteriorly located in the orbit or on the globe, with little or no functional interference, is suggestive for an orbital non-Hodgkin lymphoma NHL [11]. On the globe it appears as a salmon-colored patch (Fig. 7.14). Orbital NHL is mostly seen in patients above 60 years of age, but it is not exceptional in younger patients. Orbital NHLs occur both unilateral and bilateral and compete with sarcoidosis for the second largest cause of bilateral exophthalmos after GO.

Neither CT scans nor MRI scans are conclusive for the diagnosis of NHL. Therefore, a tissue biopsy is always required. The next step is then staging of the disease. Almost 60% of orbital NHLs belong to the extranodal marginal zone B-cell lymphomas of the mucosa-associated lymphoid tissue (MALT) type [22]. These are usually relatively benign in nature. Treatment consists of
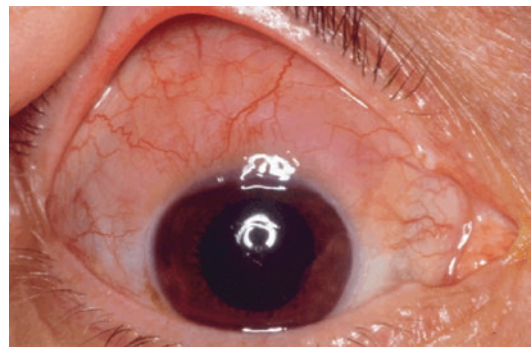

Fig. 7.14 Salmon-colored patch on the globe, suggestive for a non-Hodgkin lymphoma

low-dose radiotherapy, monoclonal antibodies directed to B-lymphocytes (rituximab), or chemotherapy in disseminated forms.

Lacrimal Fossa Lesions

Lesions in the lacrimal fossa tend to push the globe forward, downward, and in the medial direction. In addition, they often cause an S-shaped swelling of the upper eyelid. The most frequent lesions in this area are: dacryoadenitis, lacrimal gland pleiomorphic adenoma, and adenocystic carcinoma, but the lacrimal fossa also may contain NHLs as well as idiopathic orbital inflammatory lesions and many other lesions. The lacrimal gland fossa appears to be a true Pandora's box [23–25].

Dacryoadenitis

Dacryoadenitis shows as an enlarged, hyperdense lacrimal gland with well-demarcated borders on CT scans. The inflammation can be caused by bacteria and viruses, but mostly remains idiopathic. A trial of broad-spectrum antibiotics is recommended. Enlargement of the lacrimal gland is also seen in sarcoidosis.

Pleiomorphic Adenoma

Pleiomorphic adenoma of the lacrimal gland (Figs. 7.15 and 7.16) is a benign lesion, usually of the posterior lobe of the lacrimal gland. It occurs at all ages, but most frequently in adults around the age of 40 years, slightly more in males. On scans, it appears as a well-
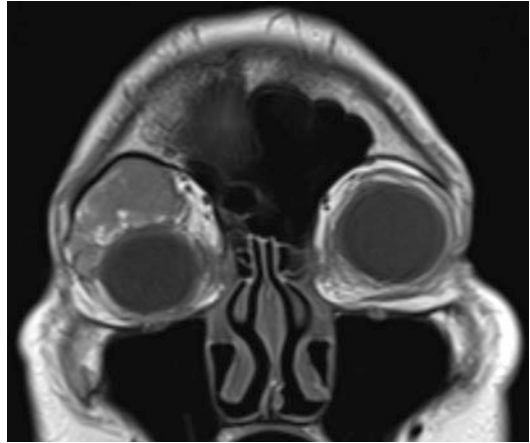

Fig. 7.16 Coronal T1 MRI scan of the same patient showing enlargement of the lacrimal gland

circumscribed round mass in the superolateral quadrant of the orbit. Pressure on the bony orbit may cause indentation, while compression on the globe may cause deformation and choroidal folds. Complete resection including the capsule is required, because recurrence or malignant transformation can otherwise pose significant therapeutical challenges. Consequently, tissue biopsy before removal is contraindicated.

Adenoid Cystic Carcinoma

Adenoid cystic carcinoma is a rarely encountered lesion, despite the fact that it is the most frequent malignant lacrimal gland tumor. It is feared for its bad prognosis. It appears most frequently in the fourth decade. CT scans show bony destruction as a result of its infiltrative growth pattern (Fig. 7.17).

Sarcoidosis

Sarcoidosis is a disease of unknown etiology that may affect multiple organs in the body. In the orbital region, it is most frequently seen in the lacrimal gland. Sarcoidosis is commonly seen in people of African or Scandinavian descent. Similar to GO and orbital NHL, it may present with unilateral or bilateral exophthalmos (Figs. 7.18 and 7.19). Sarcoidosis around the optic nerve causes visual impairment and may be

Fig. 7.15 Adult with a pleiomorphic adenoma of the right lacrimal gland

Fig. 7.17 CT scan showing bony destruction in a patient with an adenoid cystic carcinoma of the lacrimal gland

Fig. 7.18 64-year-old patient with bilateral orbital sarcoidosis

Fig. 7.19 T1 MRIscan of the same patient as shown in Fig. 7.18, showing an indistinct mass around the globe

confused with other forms of optic neuritis. Sarcoidosis can also occur within the globe (uveitis). The diagnosis (increased serum levels of lysozyme and angiotensin-converting enzyme (ACE), gallium scan, biopsy) can be difficult. Treatment consists of prednisone.

Orbital Noninfectious Inflammatory Diseases

To the more common noninfectious inflammatory diseases of the orbit next to sarcoidosis belong granulomatosis with polyangiitis (GPA; formerly called Wegener's granulomatosis), non-specific idiopathic orbital inflammations (formerly called orbital pseudotumor), and IgG4 lesions.

GPA can be a life-threatening disease, affecting many organs including the upper and lower respiratory tract and the kidneys (glomerulonephritis). GPA is characterized by vasculitis, gran-
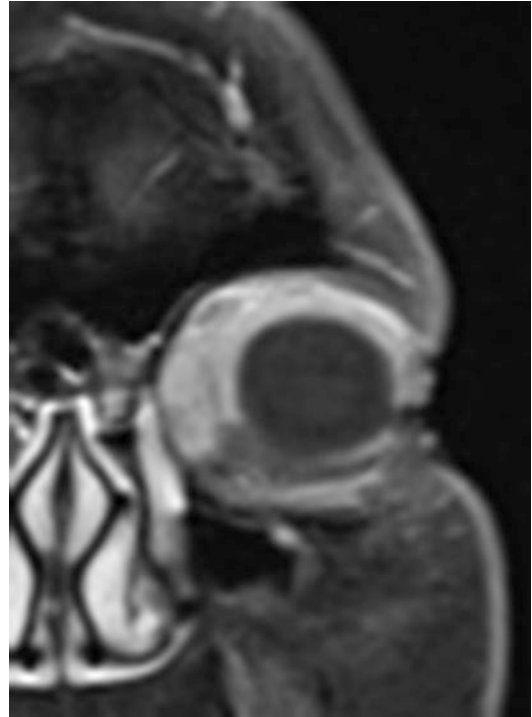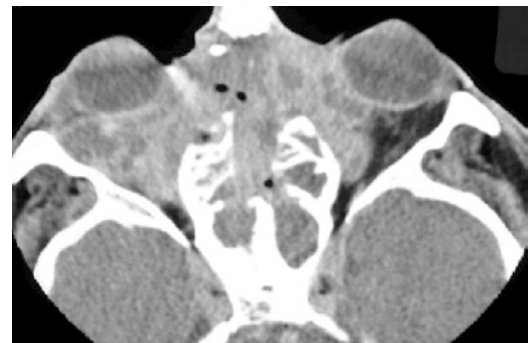

Fig. 7.20 Destructive granulomatosis with poly-angiitis of orbits and nose in a 52-year-old female

ulomatous inflammation, and tissue necrosis. The course is chronic with exacerbations and remissions. Involved orbits show proptosis and visual and motility impairment. CT scans show a destructive mass (Fig. 7.20). High c-ANCA (anti-neutrophil cytoplasmic antibodies) titers are highly specific for GPA. Interestingly, gingival

hyperplasia can be one of the early signs of GPA [26]. Classical treatment options are (combinations of) bactrimel, prednisone, azathioprine (Imuran), and cyclophosphamide (Endoxan). More recent treatment options are: mycophenolate mofetil (CellCept), daclizumab, and other monoclonal antibodies.

Idiopathic Orbital Inflammation

Idiopathic orbital inflammations (IOI) occur everywhere in the orbit and are relatively common. By definition, these polymorphous lymphoid infiltrates are restricted to the obit only. Apart from exophthalmos and motility impairment leading to diplopia, they are associated with (severe) pain (Fig. 7.21).

A special form is orbital myositis (Figs. 7.21 and 7.22), in which not only the involved extraocular muscle(s) is/are enlarged, but in more than 50% also the muscular insertion tendons. As such the condition can be distinguished from GO. Orbital myositis can 'jump' from one muscle to another and also to the contralateral orbit. Except for those with excessive fibrosis, IOIs usually respond in a few days to oral prednisone. Response to prednisone, however, does not prove the existence of an IOI. Other entities including orbital NHLs may also improve after steroid treatment. Preferably, a biopsy is taken prior to treatment. Recalcitrant
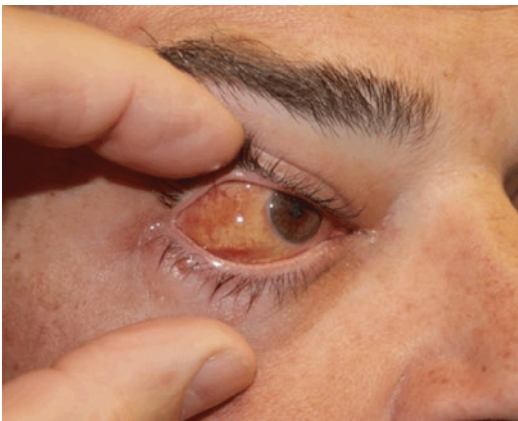

Fig. 7.21 Young adult with orbital myositis, conjunctival swelling and severe pain. All symptoms disappeared in 2 days after treatment with 40 mg prednisone

Fig. 7.22 MRI scan of the same patient as shown in Fig. 7.21 with enlarged medial rectus muscle

forms can be treated with monoclonal antibodies such as rituximab.

Fibrous Dysplasia

Fibrous dysplasia is a nonmalignant, nonhereditary developmental disease which leads to the formation of abnormally weak, 'fibrous' bone. It is seen in young adults. The disease manifests itself either as a monostotic form or as a polyostotic form and can be related to endocrine and skin disorders (McCune–Albright syndrome). Involvement of the frontal bone causes facial asymmetry and exophthalmos, and may lead to narrowing of the orbital foramina with compression of vascular and neural structures that run through them. CT scans typically show a 'ground-glass' appearance of the lesion. Surgical treatment requires a multidisciplinary approach.

Neurofibromatosis

Neurofibromatosis type I (NF-1) (formerly called von Recklinghausen disease) is an autosomal hereditary disease that affects 1 in every 3000 births. In 50% it concerns a new mutation. So-called café-au-lait spots on the skin are present from early childhood. A plexiform neurofibroma in the lateral part of an upper eyelid causes a S-shaped swelling. Other manifestations of NF-1 are pulsating exophthalmos due to a defect

in de sphenoid bone and neurofibromas of the skin and other parts of the body.

Diseases with Enophthalmos

Orbital Fracture

This is the most common cause of enophthalmos. Orbital fractures are in discussed in Part 5 of this book.

Orbital Varix

Most orbital varices are congenital distensible venous anomalies. In rest they show enophthalmos. Exophthalmos and an unpleasant sensation occur when the vessels of the lesion are filled with blood. This happens, for instance, when the patient bends forward to tie his/her shoelaces or during a Valsalva maneuver. These intermittent swellings of the varix cause atrophy of orbital fat tissue and enophthalmos in rest (Fig. 7.23).

Superficially located varices are seen as dark, dilated vessels of the eyelid or conjunctiva. Combinations of superficial and deeper varices also occur.

Varices are prone to spontaneous bleeding and thrombosis. Increase in size is a typical phenomenon seen in CT scans and MRI scans during the Valsalva maneuver. Management of orbital varices is challenging. Fortunately, most of them do not need treatment.

Fig. 7.23 Enophthalmos in a 62-year-old lady with a history of an orbital varix since her early years

Silent Sinus Syndrome

The silent sinus syndrome or imploding antrum syndrome (Figs. 7.24 and 7.25) is a condition in which a chronic negative pressure in the maxillary sinus (due to osteomeatal obstruction) and subsequent reduction in aeration of the antrum causes a downward translation of the orbital floor, together with inward bowing of the medial

Fig. 7.24 Silent sinus syndrome of the right maxillary sinus. (Courtesy of Dr. P. Gooris)

Fig. 7.25 CT scan of the same patient as shown in Fig. 7.24. (Courtesy of Dr. P. Gooris)

and posterolateral walls of the maxillary sinus [27]. These, in turn, cause enophthalmos and hypoglobus. Treatment includes restoration of the normal sinus drainage and reconstruction of the orbital floor.

Metastasis of Mammary Carcinoma

One would think that a metastasis in the orbit would always create proptosis due to the space-occupying nature of the tumor, and in general this is true. However, a scirrhous metastasis of a tubular malignancy of the breast is the exception, as it causes retraction to the globe and impaired motility and, hence, results in enophthalmos (Figs. 7.26). We have seen such presentations as the first sign of mammary carcinoma in women who had a negative mammography [28]. One should realize that the sensitivity of mammography is not higher than 85%. Ophthalmic symptoms are seen in up to 5% of women with otherwise asymptomatic breast cancer.

Fig. 7.26 Female with right-sided enophthalmos due to diffuse intraconal metastasis of breast carcinoma

References

1. Wagenmann A. Ernst *Hertel. Graefes*. Arch Ophthalmol. 1943;145:511–3.
2. Mourits MP, Lombardo SH, Van Der Sluijs FA, Fenton S. Reliability of exophthalmos measurement and the exophthalmometry value distribution in a healthy Dutch population and in Graves' patients. An exploratory study. Orbit. 2004;23:161–8.
3. Wu D, Liu X, Wu D, Di X, Guan H, Shan Z, Teng W. Normal values of Hertel exophthalmometry in a Chinese Han population from Shenyang, Northeast China. Sci Rep. 2015;5:8526.
4. Kashkouli MB, Beigi B, Noorani MM, Nojoomi M. Hertel exophthalmometry: reliability and interobserver variation. Orbit. 2003;22:239–45.
5. Gil B, de Montes F, Pérez Resinas FM, Rodríguez García M, González OM. Exophthalmometry in Mexican adults. Rev Investig Clin. 1999;51:341–3.
6. Beden U, Ozarslan Y, Oztürk HE, Sönmez B, Erkan D, Oge I. Exophthalmometry values of Turkish adult population and the effect of age, sex, refractive status, and Hertel base values on Hertel readings. Eur J Ophthalmol. 2008;18:165–71.
7. Pereira TS, Kuniyoshi CH, Leite CA, Gebrim EMMS, Monteiro MLR, Pieroni Gonçalves AC. A comparative study of clinical vs. digital exophthalmometry measurement methods. J Ophthalmol. 2020;2020:article 1397410.
8. Genders SW, Mourits DL, Jasem M, Kloos RJ, Saeed P, Mourits MP. Parallax-free exophthalmometry: a comprehensive review of the literature on clinical exophthalmometry and the introduction of the first parallax-free exophthalmometer. Orbit. 2015;34:23–9.
9. Davanger M. Principles and sources of error in exophthalmometry. A new exophthalmometer. Acta Ophthalmol. 1970;48:625–33.
10. Naugle TC Jr, Couvillion JT. A superior and inferior orbital rim-based exophthalmometer (orbitometer). Ophthalmic Surg. 1992;23(12):836–7.
11. Rootman J. Pathophysiologic patterns of orbital disease. In: Rootman J, editor. Diseases of the orbit: a

multidisciplinary approach. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. p. 43–52.

12. Claus AB, Bondy ML, Schildkraut JM, Wiemels JL, Wrensch M, Black PM. Epidemiology of intracranial meningioma. Neurosurgery. 2005;57(6):1088–95.

13. Saeed P, Tanck MWR, Freling N, Baldeschi L, Mourits MP, Bennink RJ. Somatostatin receptor scintigraphy for optic nerve sheath meningiomas. Ophthalmology. 2009;116:1581–6.

14. Huang M, Patel J, Patel BC. Optic nerve glioma. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2020.

15. Kloos R, Mourits D, Saeed P, Mourits MP. Orbital apex cavernous hemangioma: beware of the pear. Acta Ophthalmol. 2013;91:328–9.

16. McNab AA, Wright JE. Cavernous haemangiomas of the orbit. Aust New Zeal J Ophthalmol. 1989;17:337–45.

17. Khan AA, Niranjan A, Kano H, Rondziolka D, Flickinger JC, Lunsford LD. Stereotactic radiosurgery for cavernous sinus or orbital hemangiomas. Neurosurgery. 2009;65:914–8.

18. Dutton JJ. Radiology of the orbit and visual pathways. Philadelphia, PA: Saunders Elsevier; 2010.

19. Mourits MP, Koornneef L, Voûte PA. Treatment or orbital rhabdomyosarcoma. Ned Tijdschr Geneeskd. 1985;129:948–51.

20. Jurdy L, Merks JH, Pieters BR, Mourits MP, Kloos RJ, Strackee SD, Saeed P. Orbital rhabdomyosarcomas: A review. Saudi J Ophthalmol. 2013;27:167–75.

21. Van Der Poel NA, De Witt KD, Van Den Berg R, De Win MM, Mourits MP. Impact of superior ophthalmic vein thrombosis: a case series and literature review. Orbit. 2019;38:226–32.

22. Plaisier MB, Sie-Go DMDS, Berendschot TTJM, Petersen EJ, Mourits MP. Ocular adnexal lymphoma classified using the WHO classification: not only histology and stage, but also gender is a predictor of outcome. Orbit. 2007;26:83–8.

23. Fenton S, Slootweg PJ, Dunnebier EA, Mourits MP. Odontogenic myxoma in a 17-month-old child: case report. J Oral Maxillofac Surg. 2003;61:734–6.

24. Hartman LJ, Mourits MP, Canninga-Van Dijk MR. An unusual tumor of the lacrimal gland. Br J Ophthalmol. 2003;87:363.

25. Fenton S, Sie-Go DMDS, Mourits MP. Pleiomorphic adenoma of the lacrimal gland in a teenager, a case report. Eye. 2004;18:77–9.

26. Hanisch M, Fröhlich LF, Kleinheinz J. Gingival hyperplasia as first sign of recurrence of granulomatosis with polyangiitis (Wegener's granulomatosis): case report and review of the literature. BMC Oral Health. 2016;17:33.

27. Hobbs CGL, Saunders MW, Potts MJ. "Imploding antrum" or silent sinus syndrome following nasotracheal intubation. Br J Ophthalmol. 2004;88:974–5.

28. Mourits MP, Saeed P, Kloos JHM. Enophthalmos as first sign of breast cancer. Ned Tijdschr Geneesk. 2015;159:A9114.