RAEDER'S PARATRIGEMINAL SYNDROME

By *Tan Tian Cho, M.B.B.S.

and

†J. L. Da Costa, M.B.B.S., M.R.C.P.(Edin.), M.R.C.P.(Glas.)

Raeder's paratrigeminal form of Horner's syndrome is characterized by ocular sympathetic paralysis and trigeminal symptoms with or without variable involvement of the II, III, IV and VI parasellar nerves (Raeder, 1918 and 1924). The ocular sympathetic paralysis differs from the complete Horner's syndrome (Horner, 1869) in having no detectable facial anhidrosis or vasomotor disturbance. The trigeminal symptoms may occur singly or as a combination of neuralgia, motor paralysis and involvement of one or more divisions of the sensory root.

Raeder's first two patients (Raeder, 1918 and 1924) were shown at autopsy to have a tumour lying between the Gasserian ganglion and the internal carotid artery (described as an endothelioma and a meningioma respectively). Two other patients had fractures involving the base of the skull, but the aetiology in yet two other cases was undetermined. Raeder demonstrated that the oculopupillary sympathetic paralysis with trigeminal symptoms was produced by a lesion localized to a limited space just posterior to the cavernous sinus and lying between the foramen lacerum and foramen ovale. He used the designation "paratrigeminal" first suggested by Monrad-Krohn (Raeder, 1924) to describe this form of Horner's syndrome.

The rarity of this syndrome coupled with the importance of differentiating it from the complete Horner's syndrome because of its localizing value has prompted us to report in this paper, the clinical and laboratory findings of a patient with this syndrome due to a nasopharyngeal carcinoma.

CASE REPORT

The patient T.K.H. an intelligent Chinese housewife aged 35 was admitted to hospital on July 15th 1966. About 2½ months before admission, she experienced a "pulling" pain over the left zygomatic region which radiated two days later to an area behind and below the left ear. This pain was also "pulling" in nature, present throughout the morning and often recurring at night. On the third day after the onset of the pain, she began to hear a "wooshing" sound in the left ear which persisted until she came to hospital. While in hospital, this was replaced by a "buzzing" sound. Three weeks prior to admission she gradually became aware of increasing numbness over the left side of the face and the left side of the palate, tongue and buccal mucosa. She was also rather surprised to find she could not bite well on the left side though she had habitually used this side for mastication. Whereas previously she could sew for a prolonged period, her eyes now became blurred after sewing for a short while and she had to strain before she could see distant objects clearly. The left nostril appeared blocked. She denied the occurrence of any epistaxis. Dizziness not accompanied by nausea or vomiting was occasionally present.

Clinical examination revealed a well-nourished afebrile patient with no detectable cervical lymphadenopathy. No abnormality was observed in the cardiovascular and respiratory systems. Examination of the eyes revealed normal visual acuity on both sides. Intraocular pressure (Schiotz) was 11 mm.Hg. in both eyes. There was a left-sided ptosis and miosis, the diameter of the pupils being 2·5 mm. and 6·5 mm. on the left and right respectively (Fig. 1). Both pupils reacted briskly to light and accommodation. Instillation of 2% homatropine into both eyes resulted in dilatation of the left pupil to 3·5 mm. and the right to 8 mm. respectively. Instillation of 4% cocaine had no dilatory effect on the left pupil. Perimetry showed no field defects while fundoscopy was normal. A diplopia was present on extreme deviation of eyes to the left. The corneal and scleral sensitivity was equal in both eyes and there was no epiphora.

The area on the left side of the face supplied by the maxillary and mandibular divisions of the sensory root of the left trigeminal nerve showed diminished sensation to pin prick, light touch with cotton wool and temperature (hot and cold). Sweating could be elicited on both

* Research Assistant, Department of Medicine, University of Singapore.
† Lecturer, Department of Medicine, University of Singapore.

sides of the face by subjecting the patient to radiant heat and giving her a hot drink. Pain and temperature sensations were also diminished on the left side of palate, the buccal mucosa, the gums, the lips and also the tongue in its anterior two-thirds. Taste perception to sugar and vinegar was diminished over the same area of the tongue. There was also weakness of the masseter, temporalis and pterygoids on the left side (Fig. 1).

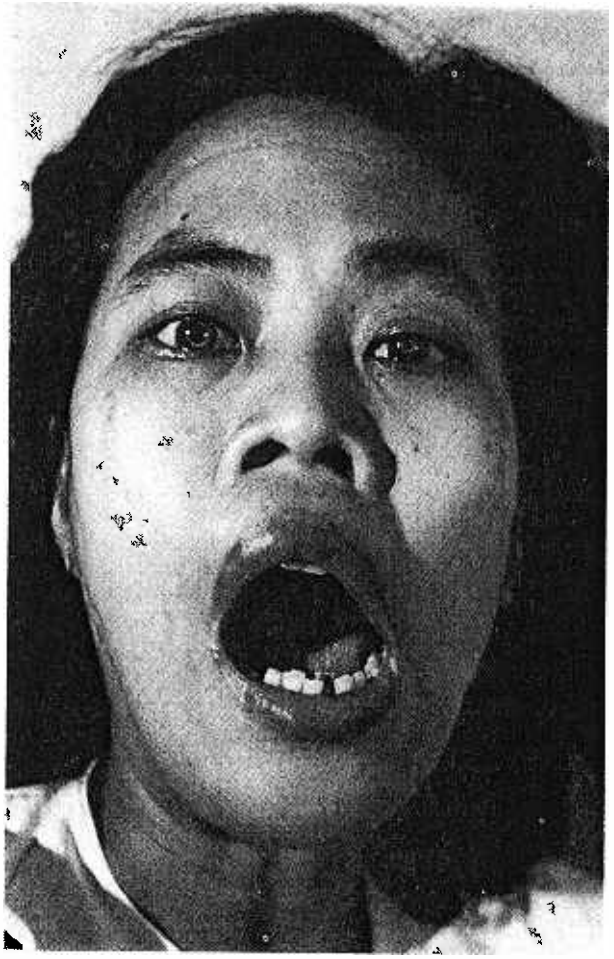

Fig. 1. T. K. H. Showing left sided ptosis, miosis and deviation of jaw to the left on opening of mouth.

Subjectively, she complained of a "block" in the left nostril and was unable to smell coffee powder and olive oil when the right nostril was occluded (this was thought to be due to a nasal stenosis). Both ear drums were intact. Rinne's and Weber's tests revealed a left ear conduction deafness which was confirmed by an audiogram. High note sounds, *e.g.* rubbing of hair close to the ears and the ticking of a watch were not audible.

SUMMARY OF NEUROLOGICAL INVOLVEMENT

1. Left oculopupillary sympathetic paralysis without enophthalmos, impairment of sweating or facial vasomotor disturbance.
2. Left trigeminal nerve lesion involving the motor root and also the maxillary and mandibular divisions of the sensory root.
3. Left VI nerve paresis.
4. Left ear conduction deafness.

Investigations

Haemoglobin 13 G%, total leucocyte count 5,600/c.mm. (normal differential count); E.S.R. 4 mm./hr. C.S.F. clear, pressure 300 mm. of water. Queckenstedt's test revealed no block; no abnormality detected microscopically or biochemically. Blood and C.S.F. Kahn tests were negative. Roentgenologic examination of the base of skull with contrast study of nasopharynx revealed a soft tissue opacity in the roof and left wall of the nasopharynx with suggestive erosion of foramina in the left middle cranial fossa. Examination of the nasopharynx revealed a growth on the left side of the roof of the post-nasal space and an enlarged left Eustachian cushion. Histological examination of the growth showed an undifferentiated nasopharyngeal carcinoma.

ANATOMICAL CONSIDERATION

Recapitulation of the anatomy of the sympathetic innervation of the face and eyes is desirable in order to understand the neurological manifestations of the paratrigeminal syndrome. From the hypothalamus the first-order neurones pass down to synapse in the ciliospinal centre situated in the spinal cord at the level of C-7, c-8 and T-1 segments (Fig. 2). Second-order preganglionic fibres ascend in the cervical portion of the sympathetic chain through the inferior and middle cervical ganglia to synapse in the superior cervical ganglion. From here some of the post-ganglionic fibres accompany the external carotid artery to innervate the sweat glands of the face, while the majority course up around the internal carotid plexus. From these plexuses four groups of fibres arise: one passing to the Gasserian ganglion to join the ophthalmic branch of the trigeminal nerve to innervate the dilator pupillae, another accompanying the oculomotor nerve to innervate the superior palpebral muscle, a third passing to the sphenopalatine ganglion via the deep petrosal nerve to innervate the orbital muscle of Muller and lastly the sympathetic root to the ciliary ganglion supplying the ocular blood vessels.

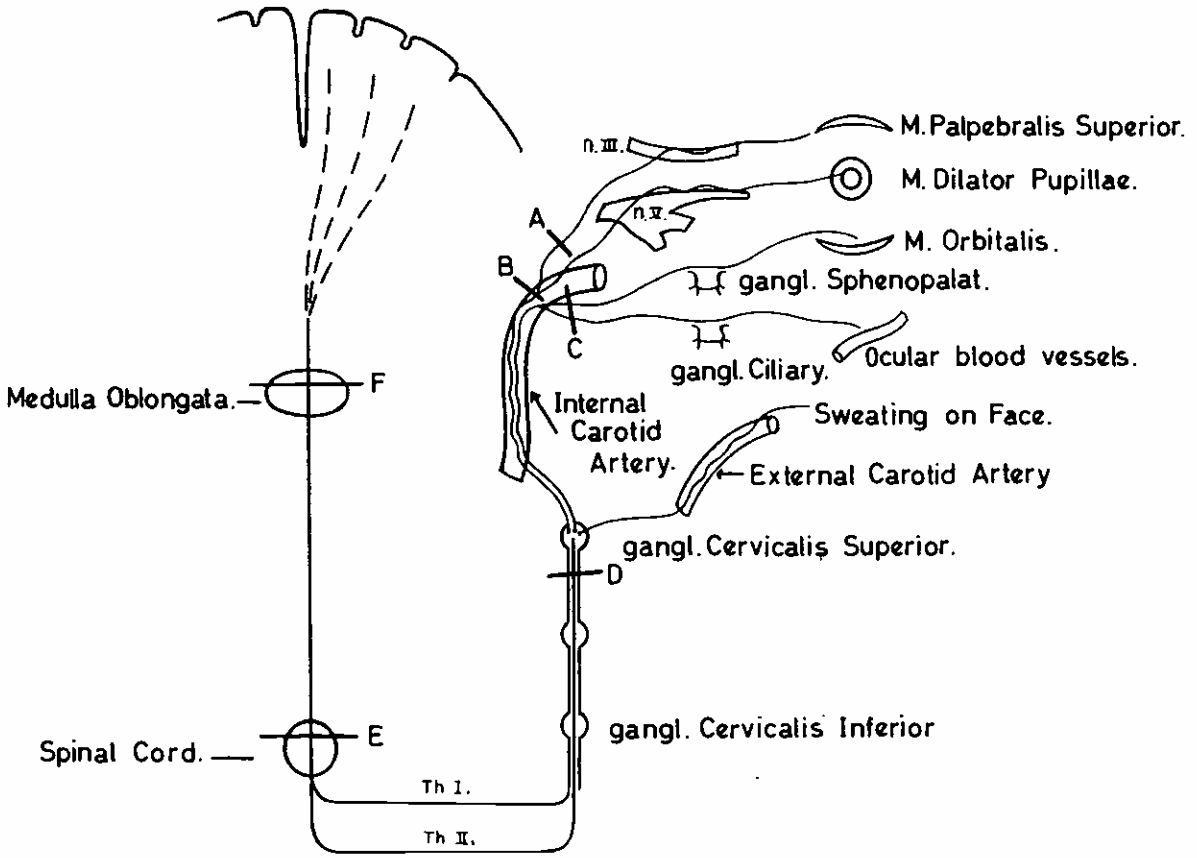

Fig. 2. Outline of cervical sympathetic pathway and its innervation. A lesion at D, E or F could produce Horner's syndrome with homolateral loss of facial sweating; a lesion at A, B or C would produce Horner's syndrome with preservation of facial sweating. Modified from Walsh, F. B. Clinical Neuro-ophthalmology, Baltimore. Williams & Wilkins Company, 1957 Fig. 76.

The clinical syndrome of Horner may result from a lesion at any place in the course of these fibres, but the completeness of the syndrome varies with the localisation of the lesion (Fig. 5). A lesion in the cervical trunk (D) will usually produce all the symptoms. When the lesion involves the spinal cord (E) or brain stem (F), the symptoms are less complete but are accompanied by other neurological signs, as in syringomyelita, or thrombosis of the posterior inferior cerebellar artery. An intracranial lesion of the postganglionic fibres could produce the paratrigeminal form of Horner's syndrome associated with variable cranial nerve involvement depending on the site of the lesion (A, B or C).

DISCUSSION

Boniuk and Schlezinger (1962) suggested dividing Raeder's paratrigeminal syndrome into two groups because of differences in pathogenesis, prognosis and treatment (Table 1). Group I would include cases of ocular sympathetic paralysis, trigeminal symptoms (sensory with or without motor involvement) and variable parasellar cranial nerve involvement. This association was originally described by Raeder in five out of the six original cases (Raeder, 1918 and 1924). To our knowledge no further cases have been reported in the English literature. However, cases were reported in the Continent by Cords and Klauber (1917, 1918), Raeder, (1924) Sales (1939) and Touissaint (1959). The lesion in this group has been shown to lie in the paratrigeminal area but the aetiology is variable *e.g.* tumour (Raeder 1918 and 1924; Toussaint, 1959), trauma to base of skull (Raeder, 1924) and syphilitic ostetitis (Toussaint, 1959). The prognosis and treatment in this group depends on the underlying aetiology but as malignancy is the commonest cause, the outlook is usually poor. It is therefore mandatory that patients presenting with Group I criteria be intensively investigated to exclude a neoplasm.

Group II would include cases of ocular sympathetic paralysis with trigeminal neuralgia alone without parasellar cranial nerve involvement. Since Raeder described one case in 1924. we have been able to trace twenty seven further cases in the English literature (Jaffe, 1950: Bedrossian, 1952; Klingon and Smith, 1956; Ford and Walsh, 1958; Boniuk and Schlezinger, 1962; Lucchesi and Topaziah, 1962; Minton and Bounds, Jr., 1964). The aetiology is still obscure and neoplasms have not been reported as a

TABLE I

RAEDER'S PARATRIGEMINAL SYNDROME

Group I	Group II
Pathology	**Pathology**
Lesion in paratrigeminal area *e.g.* Tumour (primary or metastatic) Fracture base of skull Syphilitic osteitis ? Aneurysm of internal carotid artery.	Obscure—often associated with: Migraine Chronic inflammatory disease of middle ear, sinuses or teeth. Hypertension Herpes Zoster of Gasserian ganglion.
Incidence	**Incidence**
Very rare	Rare
Sex	**Sex**
Predominantly in males	Predominantly in males
Clinical Features	**Clinical Features**
Ocular sympathetic paralysis Trigeminal symptoms (Sensory with or without motor involvement) Variable parasellar nerve involvement.	Ocular sympathetic paralysis Trigeminal neuralgia.
Prognosis	**Prognosis**
Depends on underlying cause; usually poor.	Good; spontaneous, partial or complete recovery.

causative lesion. A variety of associated diseases have been found in these patients *e.g.* migraine (Ford and Walsh, 1958; Smith, 1958; Minton and Bounds, Jrs., 1964), hypertension (Jaffe, 1950; Smith, 1958; Minton and Bounds Jr., 1964), chronic inflammation of sinuses, teeth and middle ear (Bedrossian, 1952; Boniuk and Schlezinger, 1962; Lucchesi and Topazian, 1962; Minton and Bounds Jrs. 1964). This group has been noted to pursue a benign course, has a good prognosis was either spontaneous, partial or complete recovery. Treatment has been directed mainly towards the associated diseases and the relief of the trigeminal neuralgia with analgesics.

In a detailed study of the ophthalmoneurological symptoms of 454 cases of malignant nasopharyngeal tumours, Godtfredsen (1944) could only find one possible case with a paratrigeminal syndrome out of seven cases with ophthalmoplegia, trigeminal symptoms and Horner's syndrome as the other six had associated cervical lymph node metastases. He also showed how a nasopharyngeal carcinoma from its primary site in the roof and lateral walls of the nasopharynx, could spread upwards through the preformed weak points—the foramina lacerum and ovale, into the middle cranial fossa. The immediate relationship on entry through the foramen lacerum is the cavernous sinus, and for the foramen ovale the mandibular division of the sensory root of the trigeminal nerve and the Gasserian ganglion. The region of the cavernous sinus and the paratrigeminal space are both limited areas and even a small lesion or growth could cause a varying combination of ophthalmoplegia, trigeminal symptoms and sympathetic paralysis.

In a recent combined Scandinavian-British series (Godtfredsen and Lederman, 1965) out of a total of 673 patients with malignant nasopharyngeal tumours, 35% of the patients had ophthalmoneurological symptoms. Of these, about 50% had the combination of trigeminal

and ocular nerve involvement. Horner's syndrome was present in 16% of the 75% of patients with eye signs. With such a high incidence of ophthalmoneurologic involvement in malignant nasopharyngeal tumours it is surprising that Raeder's paratrigeminal syndrome has been so rarely reported in association with malignant nasopharyngeal tumours. Failure to recognise the syndrome and differentiate it from the complete Horner's syndrome could be a major reason for its apparent rarity.

The above-mentioned patient had a nasopharyngeal carcinoma involving the roof and left wall of the nasopharynx encroaching on the Eustachian cushion and causing tubal obstruction. This together with involvement of the tensor tympani could account for the tinnitus and left-sided conduction deafness. It is postulated that the upward infiltration of the neoplasm eroded the foramina in the base of the skull on the left side and thus encroached upon the limited "paratrigeminal" area in the left middle cranial fossa. This led to involvement of the Gasserian ganglion, the motor root of V, the VIth nerve as well as the sympathetic filaments bridging the internal carotid plexus and the Gasserian ganglion thus giving rise to the left trigeminal symptoms, ocular sympathetic paralysis and the VI nerve paresis. Our patient could thus be classified under the very rare Group I Raeder's paratrigeminal syndrome (Boniuk and Schlezinger, 1962). The loss of taste sensation in the anterior two-thirds of the tongue on the left side supports Harris' observation (1952) that the presence of general sensibility in the palate and the anterior half of the tongue plays an important part in the recognition and appreciation of taste. However, direct infiltration of the greater superficial petrosal nerve which may form an alternative pathway for transmission of taste from the anterior two-thirds of the tongue to the geniculate ganglion and nervus intermedius into the pons (Schwartz and Weddell, 1938) or downward infiltration involving the chorda tympani cannot be excluded at present.

SUMMARY

A patient with Raeder's paratrigeminal syndrome (Group I type) due to a nasopharyngeal carcinoma is described. The importance of recognising this syndrome and differentiating it from the complete Horner's syndrome because of its localizing value is stressed. Raeder's syndrome should be separated into two distinct groups. This is essential because of difference in pathogenesis, prognosis and management. The rarity of this syndrome (Group I) in malignant nasopharyngeal tumours is surprising in spite of the high incidence of ophthalmoneurologic involvement in these tumours and it is suggested that this could largely be due to a failure in recognizing this syndrome.

ACKNOWLEDGEMENTS

We wish to thank Professor G. A. Ransome for his advice and encouragement, Professor R. Kanagasuntheram and Dr. N. B. Bhonsale for their advice and verification of anatomical considerations and also Dr. F. Y. Khoo for the contrast study of the nasopharynx.

REFERENCES

1. Bedrossian, E.H. (1952): "Raeder's Syndrome", A.M.A. Arch. Ophth., 48, 620-623.
2. Boniuk, M. & Schlezinger, N.S. (1962): "Raeder's Paratrigeminal Syndrome", Am. J. Ophth., 54, 1074-1084.
3. Ford, F.R. & Walsh, F.B. (1958): "Raeder's Paratrigeminal Syndrome", Bull. Johns Hopkins Hosp., 103, 296-298.
4. Godtfredsen, E. (1944): "Opthalmologic and Neurologic symptoms at Malignant Nasopharyngeal Tumours", Copenhagen, Einar Munksgraard.
5. Godtfredsen, E. & Ledernan, M. (1965): "Diagnostic and Prognostic Roles of Ophthalmoneurologic Signs and Symptoms in Malignant Nasopharyngeal Tumours", Amer. J. Ophth., 59, 1063-1069.
6. Harris, W. (1952): "The Fifth and Seventh Cranial Nerves in relation to the Nervous Mechanism of Taste Sensation. A new approach", Brit. Med. J., 1, 831-836.
7. Horner, F. (1869): "Uber eine Form von Ptosis", Klin. Monatsbl. f. Augenh. 7, 193-198.
8. Jaffe, W.S. (1950): "Localization of Lesions causing Horner's Syndrome", A.M.A. Arch. Ophth., 44, 710-728.
9. Klingon, G.H. & Smith, W.M. (1956): "Raeder's Paratrigeminal Syndrome", Neurology, 6, 750-753.
10. Lucchesi, F.J. & Topazian, D.S. (1962): "Raeder's Syndrome", Oral Surg., Oral Med. and Oral Pathology, 15, 923-926.
11. Minton, L.R. & Bounds, Jr., G.W. (1964): "Raeder's Paratrigeminal Syndrome", Amer. J. Ophth., 58, 271-275.
12. Raeder, J.G. (1918): "Et tilfalde av intrakraniel sympaticuslammelse", Norsk mag. laegevidensk. 79, 999-1015.
13. Raeder, J.G. (1924): " 'Paratrigeminal' Paralysis of Oculo-Pupillary Sympathetic", Brain, 47, 149-158.
14. Sales, M. (1939): "Raeder's Paratrigeminal Syndrome (Horner's Syndrome with Paralysis of the Sixth Cranial Nerve and Neuralgia of the Ophthalmic Branch) Report of a Case", Arq. lust. Penido Burnier, 5, 231-237.
15. Schwartz, H.G. & Weddell, G. (1938): "Observations on the Pathways transmitting the Sensation of

Taste", Brain 61, 99-115.
16. Smith, J.L. (1958): "Raeder's Paratrigeminal Syndrome", Am. J. Ophth., 46, 194-201.
17. Toussaint, D. (1959): "Contribution a l'etude du syndrome de Raeder ou syndrome paratrigeminal du sympathique oculaire", Acta Neur. & Psychiat. Belg., 59, 892-914.
18. Walsh, F.B. (1957): Fig. 7b., Clinical Neuro Ophthalmology 2nd Ed., 1957. Williams and Wilkins Co., Baltimore.