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Case report

Bilateral congenital absence of the abducens nerve

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Summary. A patient with lifelong, bilateral horizontal gaze palsies is presented. The anatomical findings of bilateral absence of the abducens nerve as it affected the brainstem, the course of the cranial nerves to the extraocular muscles, and muscle innervation are described. The possible relationship of these findings to Duane's syndrome and Möbius syndrome is discussed.

Key words: Abducens nerve – Cranial nerve – Ophthalmoplegia

Patients with congenital horizontal gaze disorders due to lateral rectus muscle palsy constitute a small but significant percentage of individuals with ophthalmoplegia (Rush and Younge 1981; Shrader and Schlezinger 1960). Congenital unilateral or bilateral paralysis of the lateral rectus has been described as an isolated neuro-ophthalmological abnormality, as well as in association with other ocular and/or neurological problems (Philips et al. 1932; Yee et al. 1982). Duane's syndrome (the Stilling-Turk-Duane syndrome) includes variable degrees of globe retraction, limitation of adduction and palpebral fissure narrowing on attempted abduction, in addition to lateral, rectus paralysis (Duane 1905; Huber 1974). Möbius syndrome involves paralysis of muscles innervated by the facial nerve as well as extraocular muscle paralysis (Möbius 1888; Henderson 1939).

The pathological basis for the eye movement disorder in all of these conditions which exhibit horizontal gaze palsy rests on only a few fully evaluated cases; nevertheless, congenital absence of the abducens (sixth cranial) nerve appears to be the anatomical abnormality common to these disorders (Dalloz and Norton 1964; Henderson 1939; Hotchkiss et al. 1980; Hoyt and Nachtigaller 1965; Heubner 1900; Miller et al. 1982; Philips et al. 1932; Spatz and Ullrich 1931). We present the case of a woman with bilateral

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congenital absence of the abducens nerves and propose that simple congenital paralysis of horizontal gaze, Duane's syndrome, and Möbius syndrome represent different points on a continuum of increasing severity in a single embryonic disorder.

Report of a case

A 78-year-old woman was admitted to Brigham and Women's Hospital in mid-January 1981 with severe back pain and haemoptysis. She had a lifelong history of an eye movement disorder. Optometric records of an eye examination in May of 1977 describe bilateral lateral rectus muscle palsies. In the position of primary gaze, there was a mild divergent strabismus by Hirshburg test. Pupillary reflexes were equal and normal. Refraction revealed correctable bilateral hyperopia.

At the time of her final hospitalization the neurological evaluation on admission again documented bilateral, complete lateral rectus muscle paralysis. The examiner did not record the presence of either globe retraction or palpebral fissure narrowing. The remainder of her neurological and opthalmological examination was normal, except for a mild, bilateral hearing loss. She was too ill at the time for an extensive neuro-ophthalmological evaluation.

Discovery of a lung mass, multiple vertebral compression fractures, severe anaemia, and thrombocytopaenia led to a bone marrow biopsy that disclosed marrow replacement by a small cell anaplastic malignancy, presumed to be of lung origin. The patient's precarious respiratory status deteriorated rapidly despite therapy. She became hypotensive and expired on January 29, 1981.

Pathological findings

Post-mortem examination revealed widely metastatic small cell carcinoma of the lung with metastases in the hilar lymph nodes, liver, and multiple bones. No metastases were present in the skull or brain. The cause of death was haemorrhage of 700 ml of blood into the right pleural space.

After opening the skull, and carefully reflecting the forebrain, it was noted that the abducens nerves were absent bilaterally (Fig. 1). Detailed inspection of the skull and the base of the brain ruled out accidental evulsion of the nerves. The dural openings near the rostral end of the clivus, through which these nerves exit the cranial vault, were likewise absent (Fig. 2). All the other cranial nerves were present in their normal positions.

The brain stem was embedded in paraffin and serial histological sections were made. These sections were stained with either haematoxylin and eosin (H&E), cresyl violet, Bodian silver impregnation, or luxol fast blue and period acid-Schiff (LFB-PAS) stains. Comparison was made with selected brainstem sections from two age-matched controls. Examination of the sections from the patient's brainstem revealed only scattered neurons in the area of the pontine tegmentum where the sixth cranial nerve nucleus should have been situated. No well-organized abducens nuclei could be found in their usual location beneath the genu of the seventh cranial nerve (Fig. 3). In this area of the pontine tegmentum no evidence of prior damage or old gliosis was found. In the basis pontis, near the ponto-medullary junction, the roots of the sixth cranial nerves could not be detected. The oculomotor and trochlear nuclei, as well as the other cranial nerve roots and nuclei, were present in their usual positions, and were morphologically normal.

Inspection of the base of the skull and the cavernous sinuses was performed to follow the course of the third and fourth cranial nerves. No evidence of the sixth cranial nerve was found. On the right side, in the posterior recess of the orbit, the inferior division of the oculomotor nerve divided into many fine branches; by gross inspection, two of these went to the right lateral rectus muscle (Fig. 4). On the left side, the roots entering the lateral rectus muscle from the third cranial nerve were more numerous and of finer calibre.

Bilateral, total orbital exenterations were performed. Gross and histological examinations of both globes revealed no major abnormalities. The extraocular muscles were all present

Fig. 1 A, B. Ventral surface of the brainstem from the present patient (**A**) and from a normal individual (**B**). The sixth cranial nerves are identified by the arrowheads in (**B**)

and exhibited normal origins and insertions. Histological evaluation of these muscles using H&E, Masson trichrome, and phosphotungsic acid haematoxylin (PTAH) stains disclosed no evidence of muscle denervation, fibrosis, or disproportionate atrophy; these findings include both lateral rectus muscles. It is concluded that the lateral recti were innervated by aberrant branches of the inferior division of the third cranial nerves. This innervation presumably accounts for the fact that they were not atrophic or fibrotic; the observed functional abnormalities of the lateral recti are probably also attributable to their aberrant innervation.

Discussion

Congenital absence of one or both abducens nerves is a rare anatomical occurrence. It occurs as part of the congenital facial diplegia syndrome of Möbius (Dalloz and Norton 1964; Henderson 1939; Heubner 1900; Spatz and Ullrich 1931) or it may occur as an isolated abnormality. Philips et al. (1932) reported absence of both sixth cranial nerves and associated hypoplasia of their nuclei in a girl who clinically exhibited horizontal gaze paralysis. Another individual case was reported by Matteuci (1946) concerning a patient with unilateral horizontal gaze palsy and globe retraction. In this latter case, the abducens nerve was missing on the affected side, the corresponding cranial nerve nucleus in the pontine tegmentum was hypoplastic, and the lateral rectus muscle was fibrotic. In addition, Hoyt and Nachtigaller (1965), Tillack and Winer (1962), and Bremer (1921) have all reported isolated examples of the absence of the sixth cranial nerve as anatomical oddities.

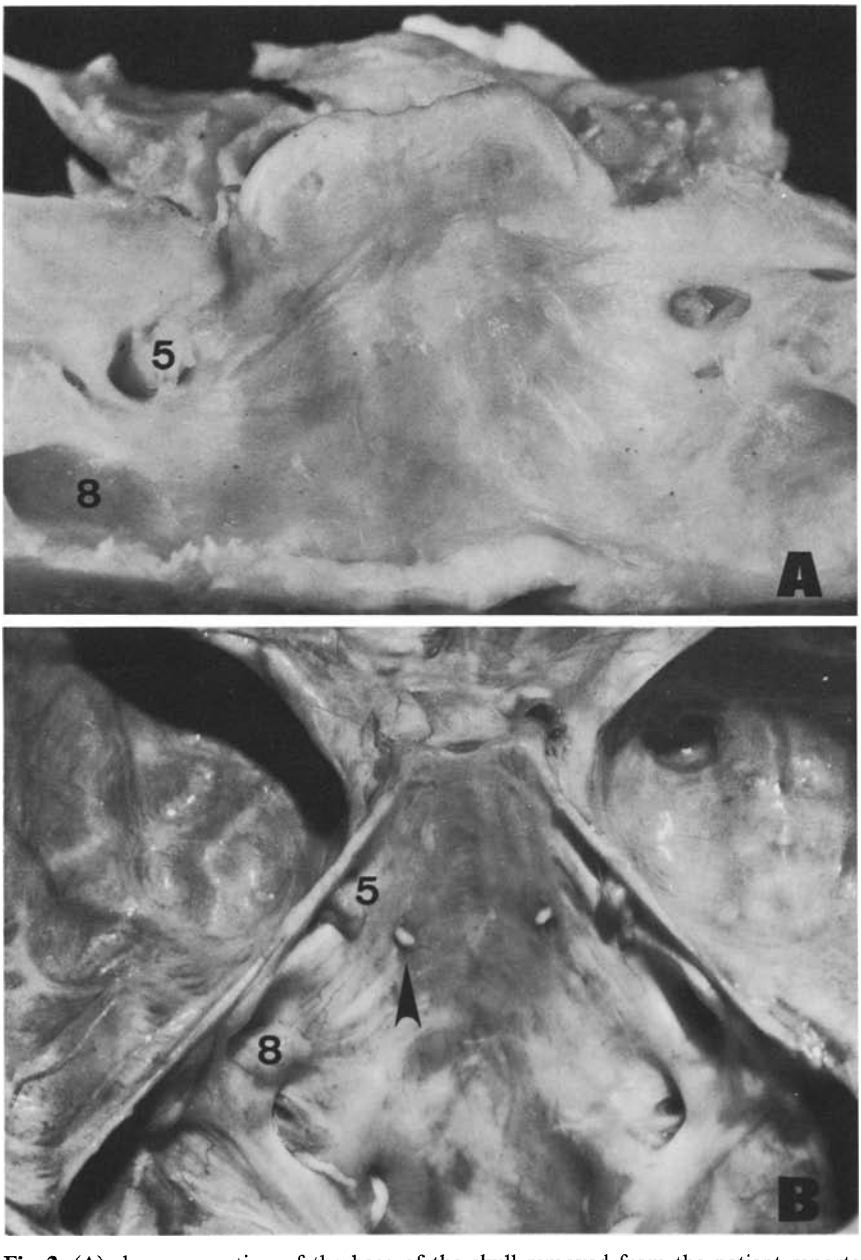

Fig. 2. (**A**) shows a portion of the base of the skull removed from the patient reported; (**B**) is the same area from a normal patient. *5* and *8* mark the exits of the fifth and eighth cranial nerves respectively. The *arrowhead* in (**B**) indicates the site of exit of the left abducens nerve; these foramina are absent in (**A**)

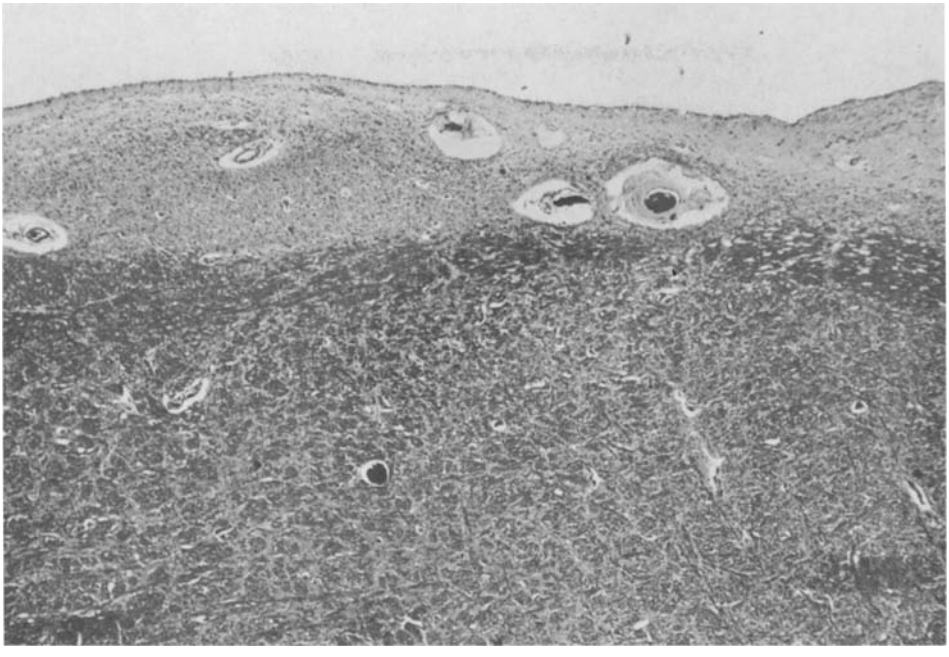

Fig. 3. A photomicrograph of the pontine tegmentum beneath the genu of the seventh cranial nerve. Note that the genu is slightly flattened, and in the tegmentum there are few, scattered neurons where the abducens nucleus should be. No evidence of gliosis or damage is noted. (H&E, 125 ×)

Fig. 4. Lateral view of the dissected right cavernous sinus. *3* indicates the main trunk of the oculomotor nerve; *3i* identifies a branch of the oculomotor nerve that entered the right lateral rectus; *0* is the ophthalmic nerve, and *4* is the trochlear nerve

In the recent past, two thoroughly evaluated cases of Duane's syndrome have demonstrated bilateral (Hotchkiss et al. 1980) and unilateral (Miller et al. 1982) absence of the abducens nerves with associated hypoplasia of the nerve nucleus and innervation of the lateral rectus muscle on the involved side by aberrant branches of the oculomotor nerve. There is a marked similarity between the two cases and the pathological findings in the case reported here.

Although the pathological study of the above-mentioned cases has not fully elucidated the aetiology of all congenital horizontal gaze palsies, there does appear to be a common factor among them: congenital absence of the sixth cranial nerve. From the evaluation of the present case and those previously described, it is possible to conclude that the cause of the absence of the abducens nerve is not a grossly destructive intraparenchymal event. All the histological descriptions describe hypoplasia and disorganization in the area of the sixth nerve nuclei, but anatomical evidence of a prior episode of tissue damage is lacking.

Based on these observations, a teratogenic event during the second month of gestation can be postulated to account for the abnormality (Hotchkiss et al. 1980). Likewise, based on the anatomical findings in all reported instances, it can be proposed that congenital horizontal gaze paralysis, Duane's syndrome, and Möbius syndrome represent points of increasing severity in a single spectrum of developmental aberration. In these conditions the same small area of the pontine tegmentum is found to be disorganized and hypoplastic.

The similarities among these three clinical complexes extend beyond the brainstem. All are often attended by a similar constellation of visceral and musculoskeltal malformations, and can occur as a genetically determined problem (Cross and Pfaffenbach 1972; Ehrenberg et al. 1980; Dalloz and Norton 1964; Henderson 1939; Okihiro et al. 1977; Pfaffenbach et al. 1980; Riley and Swift 1979; Skyberg and Vander Hagen 1965; Walsh and Hoyt 1969; Yee et al. 1982). Indeed, some patients with clinically apparent horizontal gaze problems can actually be classified as Type I Duane's syndrome since they do have inapparent globe retraction which is detectable only by electro-physiological study of the extraocular muscles (Huber 19747). The clinical overlap of these conditions is further demonstrated by some patients who have Duane's syndrome coupled with varying degrees of congenital facial muscle palsies (Pfaffenbach et al. 1972; Walsh and Hoyt 1969). In addition, tests on other brainstem functions in patients with Duane's syndrome suggest that the inherent abnormalities are not limited solely to the abducens nerve (Blodi and Van Allen 1964; Gourdeau et al. 1981; Jay and Hoyt 1980).

Since the brainstem neurons destined to become the various cranial nerve nuclei differentiate in an orderly sequence during a short period in embryo formation (Shaw and Alley 1981), it is possible that a brief disturbance of the brainstem microenvironment could induce a lesion manifest clinically as abducens nerve paralysis. If such a disturbance persisted or was more

widespread, a more severe syndrome would occur. In the light of current concepts of neural differentiation and the establishment of neuronal interconnections (Edelman 1981), such a hypothesis is not unreasonable.

At present the number of cases of congenital horizontal gaze paralysis, Duane's syndrome, and Möbius syndrome that have been fully evaluated anatomically are few. More data are needed before the underlying pathological similarity of these conditions can be fully established.

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