Papillary tumor of the pineal region presenting with Foster Kennedy sign

To the Editor: Foster Kennedy syndrome is defined as unilateral optic nerve atrophy, contralateral disc edema and anosmia. It was originally thought to be pathognomonic of space occupying lesions in the anterior fossa causing direct compression of the optic and olfactory nerves and later intracranial hypertension and contralateral disc edema. Subsequent reports of non-tumor and non-anterior fossa causes, most commonly bilateral sequential anterior ischemic optic neuropathy, have been described. We report a 29 year old man who presented with unsteady gait and diminution of vision over 2 months. He displayed findings typical of Parinaud’s syndrome, right disc edema and left optic atrophy. MRI revealed a large pineal tumor associated with hydrocephalus and evidence of increased intracranial pressure.

Papillary tumor of the pineal region (PTPR) was diagnosed on histopathology. To our knowledge, this is the first report of this very rare tumor, occurring in association with the Foster Kennedy sign.

Foster Kennedy syndrome consists of a triad of optic atrophy, contralateral optic nerve edema, and anosmia. Originally, it was thought to be pathognomonic of anterior fossa masses, causing direct compression and ipsilateral optic atrophy followed by intracranial hypertension with resultant contralateral papilledema. Devoid of viable neurons, the atrophic nerve fails to swell, leading to the fundoscopic disparity. Anosmia results from concomitant compression of the proximal olfactory nerve. The fundoscopic findings, although rare, have been reported in various tumors and nontumor conditions,1–7 and pseudo-Foster Kennedy syndrome or Foster Kennedy sign has been suggested as a more accurate designation of the isolated ocular manifestation.

Primary intracranial papillary tumors are exceptionally rare.8 Papillary tumor of the pineal region (PTPR), first described in 2003,8 has been recently classified by the World Health Organization9 as a new histopathologic entity, distinct from pineal tumors. With less than 100 cases reported, the typical clinicopathological spectrum and treatment protocols have yet to be established. Documenting PTPR cases will broaden our understanding of the spectrum of presentations and natural course with management implications that will ultimately influence survival.

A 29-year-old previously healthy man presented with a 4-month history of unsteady gait and 6 weeks of rapidly progressive asymmetric vision loss. He was alert and oriented, with a Glasgow Coma Score of 15/15 and completely intact central and peripheral nervous systems without reported anosmia. Visual acuities were 20/30 (R) and no perception of light (L), with bilateral dyschromatopsia [3/15 (R) and 0/15 (L)]. His extraocular movements were full with modest limitations of upgaze and convergence. Optokinetic testing indicated convergence–retraction nystagmus. Pupils were sluggishly reactive to light with a left afferent papillary defect; however, they were briskly reactive to attempted convergence, exhibiting light-near dissociation.

Dilated ophthalmoscopy revealed a grossly edematous right optic nerve and a modestly edematous (Figure 1A) and atrophic left optic nerve with gliosis and decreased arcuate nerve fibers and fine capillaries (Figure 1B). Subsequent right visual fields revealed general constriction. The anomalous eye movements and pupillary reflexes constitute Parinaud’s syndrome, whereas the ophthalmoscopic findings represent the Foster Kennedy sign. Systemic survey classified this malignancy as localized without metastases.

Contrast-enhanced neuroradiologic assessments of the brain and spinal columns revealed a large heterogeneous mass in the pineal region, compressing the tectal plates of the brain stem and occluding the aqueduct of Sylvius with significant hydrocephalus and intracranial hypertension (Figure 2A–C). The lateral and third ventricles were grossly distended, with the latter hanging low and appearing to compress the adjacent optic nerves and chiasm (Figure 2C).

The tumor was surgically debulked and a ventriculoperitoneal shunt was placed to manage the hydrocephalus. Histopathologic analysis revealed a low-grade tumor with epithelial and neuroendocrine differentiation and focal pseudopapillary pattern. Immunohistochemical staining was positive for cytokeratin (AE1/AE3 and CK18) and neural/neuroendocrine markers (synaptophysin, neurofilament protein, CD56 (neural cell adhesion molecule), and focal chromogranin), and negative for pan-germ cell markers (Figure 3). These findings are compatible with PTPR. The MIB-1 proliferation index, a measure of proliferation
and indicator of clinical behavior, was 2%. The patient underwent successful adjuvant radiation therapy and recovery was uneventful with complete resolution of hydrocephalus and no interval progression on subsequent brain magnetic resonance imaging.

Foster Kennedy sign, a rare finding with numerous etiologies, most commonly results from bilateral sequential anterior ischemic optic neuropathy.\(^1\)\(^-\)\(^3\)\(^,\)\(^6\)\(^,\)\(^7\) In our case, the anterior visual pathway was affected from a remote site, which suggests the involvement of an indirect pathogenic mechanism. Liang et al.\(^1\)\(^0\) proposed the following classification concerning possible pathogenic mechanisms for the Foster Kennedy sign associated with tumors: Type 1, direct optic nerve compression and intracranial hypertension as originally described; Type 2, bilateral asymmetric optic nerve compression; and Type 3, no nerve compression but asymmetric chronic papilledema. Variable contributions from asymmetric chronic papilledema and third ventriculomegaly compression (Figure 2A–C) were likely causes of this Foster Kennedy sign.

PTPR, a newly recognized distinct entity with both epithelial and neuroendocrine components, possibly represents aberrant proliferation of specialized ependymal cells in the subcommissural organ.\(^8\)\(^,\)\(^9\) Most reports, case presentations, and small series, present with hydrocephalus and Parinaud’s syndrome with local recurrences, but tumor dissemination is rare.\(^8\)\(^,\)\(^9\) Anecdotal success with various regimes, including surgical excision, radiotherapy, and chemotherapy, has been described previously. However, an evidence-based management protocol has yet to be established. This case of PTPR presenting exclusively with ophthalmic

**Figure 1.** (A) Dilated fundoscopy showing right optic disc edema and (B) left optic atrophy and evidence of old edema and perivascular gliosis and loss of superficial capillaries. Compared with the right side, there are less arcuate bundles bilaterally to the left.

**Figure 2.** (A) Brain and orbit magnetic resonance imaging, revealing a pineal region mass and hydrocephalus: (A) pre-contrast T2 axial view showing a large heterogeneous pineal region mass and lateral and third ventriculomegaly (arrows) with bilateral orbital optic nerve swelling; (B) post-contrast T1 axial view showing enhancement of the pineal mass; and (C) post-contrast T1 sagittal view showing lateral and third ventriculomegaly with low-hanging optic recess of the third ventricle (arrow).
manifestations of Parinaud’s syndrome and the Foster Kennedy sign, by direct and indirect mass effects, respectively, is a significant contribution to the catalog of presentations of this newly classified and very rare tumor.

CONFLICTS OF INTEREST
All contributing authors declare no conflicts of interest.

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Figure 3. (A) Histology of the pineal region tumor depicting focal papillary architecture in low magnification. (B) Intermediate magnification shows a solid epithelial tumor with minimal nuclear atypia and mitotic activity. The cells express (C) cytokeratin, (D) synaptophysin, (E) chromogranin, and (F) neurofilament protein.