Foster-Kennedy Syndrome: literature review and development of a diagnostic algorithm

Síndrome de Foster-Kennedy: revisão da literatura e algoritmo diagnóstico

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ABSTRACT

Foster-Kennedy Syndrome (FKS) is a rare neurological disorder characterized by symptoms such as unilateral optic disc atrophy, contralateral papilledema, and anosmia, often associated with tumors like meningiomas in the anterior cranial fossa. Pseudo-Foster Kennedy Syndrome (PFKS) mimics FKS but is caused by various other conditions, leading to optic disc edema and unilateral optic nerve atrophy. To improve diagnosis, a diagnostic algorithm was developed from a review of 79 PubMed articles on FKS, with 20 ultimately included in the study. This review highlighted the importance of recognizing the clinical differences between FKS and PFKS and their diverse causes. It also emphasized the need for cross-specialty awareness among ophthalmologists, otorhinolaryngologists, and general physicians for early detection. The proposed diagnostic algorithm guides investigations for patients with specific symptoms, underscoring the critical role of timely referral and management. The study calls for increased awareness and interdisciplinary collaboration to ensure optimal care for patients with FKS or similar conditions, highlighting the significance of education and communication across medical fields.

Keywords: *Foster-Kennedy Syndrome; Pseudo-Foster Kennedy; Unilateral papilledema; Optic atrophy*

RESUMO

A Síndrome de Foster-Kennedy (SFK) é uma desordem neurológica caracterizada por atrofia do disco óptico, papiledema contralateral e anosmia, frequentemente associada a lesões expansivas da fossa craniana anterior, como meningiomas. A Pseudo-Síndrome de Foster Kennedy (PSFK) simula a SFK, mas é causada por condições outras que geram edema do disco óptico e atrofia óptica unilateral. Visando auxiliar o diagnóstico da SFK e o diagnóstico diferencial com causas de PSFK, foi desenvolvido um algoritmo diagnóstico a partir da revisão de 79 artigos do PubMed sobre SFK, com 20 selecionados para este estudo. Esta revisão busca facilitar o reconhecimento das diferenças clínicas entre SFK e PSFK e suas diversas causas. Também enfatiza a necessidade da interdisciplinaridade entre oftalmologistas, otorrinolaringologistas e médicos generalistas para a detecção precoce da síndrome. Ademais, o algoritmo diagnóstico proposto objetiva guiar a investigação de pacientes com sintomas sugestivos, ressaltando a importância do diagnóstico e manejo precoces, a fim de evitar sequelas.

Palavras-chave: *Síndrome de Foster Kennedy; Pseudo Foster Kennedy; Papiledema unilateral; Atrofia óptica*

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INTRODUCTION

Foster-Kennedy Syndrome (FKS) is a rare neurological disorder first described in 1911, that historically consists of the triad: unilateral optic disc atrophy, contralateral papilledema, and anosmia. Nowadays, the term FKS is used to describe only the ipsilateral optic atrophy and the contralateral papilledema, excluding, most times, the presence of anosmia. Back in 1911, it was believed to be pathognomonic of anterior fossa tumors, but it is currently known that FKS can be caused by any expansive lesion with direct or indirect asymmetric compression of both optic nerves[1-3].

Pseudo FKS (PFKS) presents with unilateral optic atrophy and contralateral papilledema in the absence of intracranial mass. Any condition that develops optic disc edema and generates unilateral optic nerve atrophy can simulate FKS, and anterior ischemic optic neuropathy (AION) is the main cause. PFKS is a diagnosis of exclusion and should be considered when complementary exams are negative for intracranial masses[3-5].

METHODOLOGY

A literature review was conducted through PubMed, using the descriptor "Foster Kennedy Syndrome", filtering for English language, resulting in 79 articles. No publishing date restriction was applied. After reading the abstracts, 32 articles were selected; and 20 articles were ultimately used after a complete reading of each article. With the information gathered from the literature review, a diagnostic algorithm was designed.

RESULTS

Multiple conditions can mimic FKS, which comprises PFKS, and being an exclusion diagnosis requires a thorough investigation to avoid delay in diagnosis and treatment of any operable intracranial lesion. This algorithm (Figure 1) proposes the investigation of any patient that presents with painless bilateral visual loss, which is evidenced by unilateral optic atrophy and contralateral

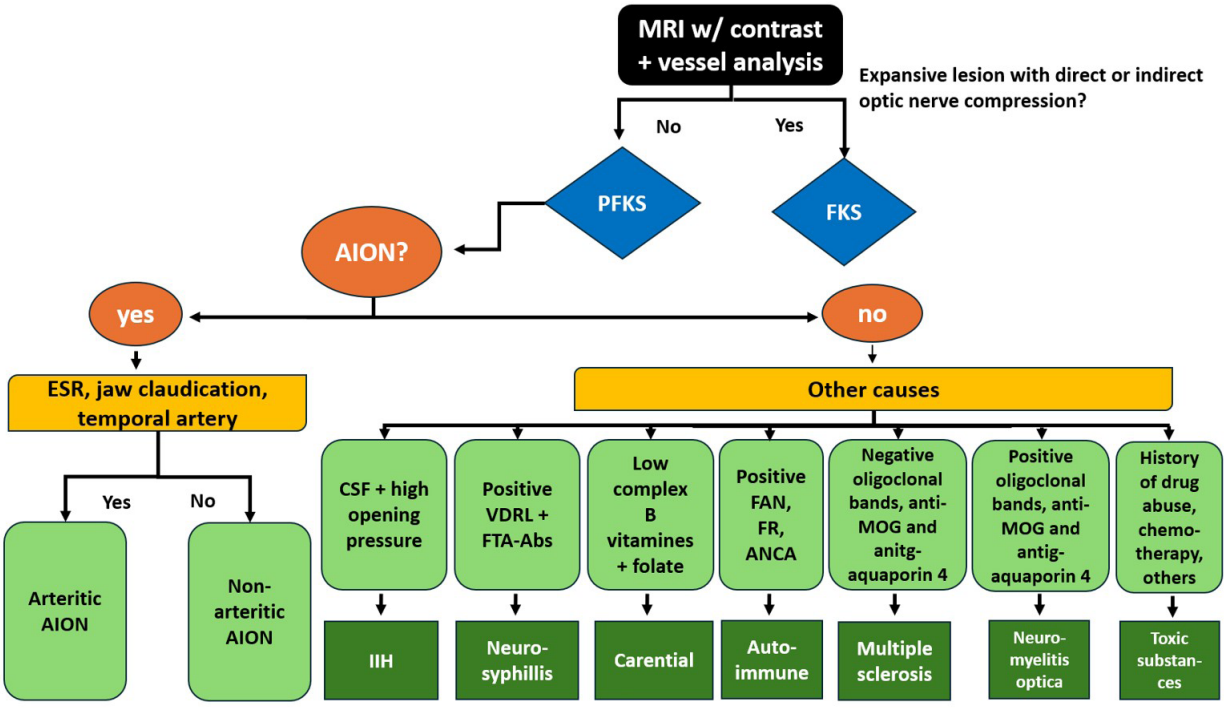

Figure 1. Investigation algorithm for patients with FKS.

papilledema, associated or not with headache, olfactory disturbances, psychiatric alterations or other neurological deficits.

Therefore, we propose an investigation algorithm for patients with suspected FKS (Table 1)

DISCUSSION

Foster Kennedy published, in 1911, a case series describing six patients with unilateral optic atrophy, contralateral papilledema and unilateral anosmia - these findings, in association, were coined Foster-Kennedy Syndrome. It was suggested that this was a localizing syndrome, with a voluminous frontal tumor, ipsilateral to the atrophy and contralateral to the papilledema. Most cases were caused by solid intracranial tumors, usually frontal basal, olfactory groove and sphenoid wing (medial third) meningiomas.

Papilledema as a localizing sign was also discussed at the end of the XIX century, by Hughlings Jackson and Marcus Gunn. In Germany, 1905, the signature triad was observed by Schulz-Zehden, a patient with an epidermoid cyst at the chiasmatic cistern. Between 1880-1890, it was already evidenced that relief of intracranial pressure, secondary to an intracranial tumor, led to the disappearance of optic atrophy and papilledema. Gowers and Paton, in 1909, observed the phenomenon of unilateral optic atrophy, with central scotoma, and papilledema.

One of the key cases for the establishment of the syndromic triad was of a patient called Mary Cowie Cameron, who presented with unilateral papilledema and contralateral optic atrophy. During surgery, conducted by Victor Horsley in 1908, an intracranial frontal tumor was observed, contralateral to papilledema and contralateral to the optic atrophy[6].

Currently, the term FKS is used to describe only the ipsilateral optic atrophy and the contralateral papilledema, not considering, most times, the presence of anosmia[2,5]. Nowadays, it is known that those findings can be caused by non-tumoral lesions and lesions that do not occupy the anterior fossa, more usually by ischemic anterior optic neuropathy. Despite these exceptions, it is usually caused by olfactory groove, sphenoid wing and subfrontal meningiomas; but can also be secondary to frontal lobe, olfactory and optic gliomas, and craniopharyngiomas[4,5].

A case series, composed of 169 patients, demonstrated that 32% of these were not caused by tumoral lesions, and 17% of the lesions were not localized in the frontal lobe[7].

Table 1. Proposed investigation algorithm for patients with suspected FKS.

I	Anamnesis and physical examination. Search for any signs of expansive lesions: headache, behavioral changes, focal neurological deficits, epilepsy. Physical examination: campimetry, visual acuity, olfaction, frontal symptoms.
II	Complementary imaging studies with contrast enhancement and vessel analysis - preference: Magnetic Resonance Angiography. In case of unavailability, a Computerized Angio tomography can be performed initially.
III	Ophthalmological evaluation + Optical Coherence Tomography
IV	In the presence of anterior ischemic optic neuropathy -> differentiate between arteritic and non-arteritic: erythrocyte sedimentation rate, history of jaw claudication, headache and scalp pain. In case of suspected temporal arteritis, perform a temporal artery biopsy.
V	In the absence of anterior ischemic optic neuropathy, active search for differential diagnosis for PFKS is mandatory: a) Female, obese, childbearing age -> consider Idiopathic Intracranial Hypertension (IIH): lumbar puncture with CSF opening pressure measurement; b) Infectious disease stigmas with systemic manifestations -> syphilis, meningitis: CSF with infectious/inflammatory signs, CSF-VDRL test, antibiogram, serum VDRL and FTA-Abs; c) Chronic alcoholism, previous bariatric surgery, veganism/vegetarianism: complex B vitamin and folate dosages, complete blood count; d) Personal or familiar history of autoimmune diseases, systemic manifestations secondary to autoimmune/inflammatory diseases -> rheumatoid factor, FAN and ANCA analysis; e) Neurological symptoms that occurred at different points in time, and evidence of damage in separated areas of CNS -> Multiple Sclerosis, Neuromyelitis Optica: oligoclonal bands in CSF, anti-MOG, anti-aquaporin 4 test. f) Prior use of toxic substances harmful to the optic nerve.

During the pre-MRI era, it was already a rare condition, present in approximately 0,9% of intracranial tumors, and 0,5-3,5% of frontal tumors - 24% of olfactory groove meningiomas and 4,7% of sphenoid wing meningiomas presented with FSK[2]. With the advent and greater availability of MRI, there is an increase in intracranial tumor diagnosis, further reducing the likelihood of diagnosing the classic triad in bulky lesions.

Visual loss presents in 70% of cases, visual field defects (mainly central scotoma) in 9%, and ocular motor paresis in 6%[8]. Anosmia was present in 73% of cases[4].

Despite the well-recognized and characteristic ophthalmological pattern and anosmia, not all FKS originate from the same pathophysiological mechanisms. Thus, there are distinct types of FKS, as shown in Table 2 and illustrated in Figure 2: type 1, with direct and unilateral compression of the optic nerve, with intracranial hypertension (ICH); type 2, with bilateral direct optic nerve compression without ICH; type 3, with ICH and optic nerve atrophy, with direct compression of the optic nerve. Type 1 FSK is the classical presentation, described by Foster Kennedy at the beginning of the 20th century. Type 2 FSK presents with asymmetrical bilateral optic nerve compression, with optic atrophy in the most compromised nerve (chronic) and papilledema in the other (acute). In type 3 FKS, there is no direct compression, and the optic atrophy is assigned to a final stage of chronic, asymmetric papilledema secondary to chronic ICH. The visual prognosis depends on the duration of papilledema, since the atrophic optic nerve is, already, permanently damaged[9].

The main mechanism responsible for papilledema and visual loss is axoplasmic flow stasis in the intraorbital portion of the optic nerve. The elevated intracranial pressure increases CSF pressure around the optic nerves, which, in turn, modifies the normal gradient between the intraocular and retrolaminar pressures, as they are covered by a meningeal sheath, being transmitted to the nerve as an increase in pressure. As a consequence, there is an impairment of the metabolic processes mediated by axoplasmic flow. Furthermore, CSF stasis decreases venous blood flow, further increasing pressure inside the subarachnoid space above the intraorbital optic nerve.

Table 2. FKS subtypes according to the optic nerve presentation.

Subtype	Optic Nerve		ICH
	Atrophy	Papilledema	
FKS 1	Direct Ipsilateral Compression	Contralateral secondary to ICH	Yes
FKS 2	Chronic direct compression (most compromised side)	Contralateral secondary to acute compression (less compromised side)	No
FKS 3	Chronic indirect compression (ICH)	Contralateral secondary to indirect compression; initial stage (ICH)	Yes

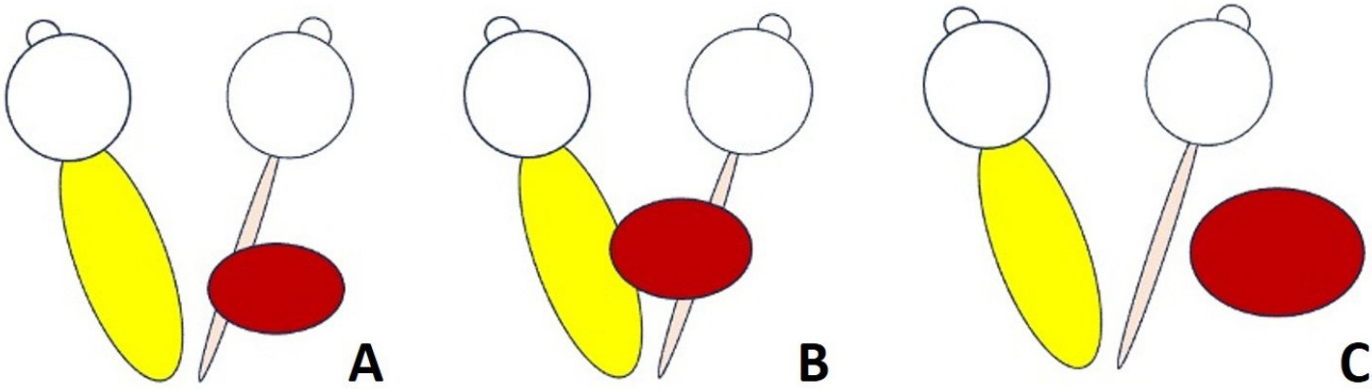

Figure 2. FKS subtypes according to the optic nerve presentation. (A) FKS 1, direct ipsilateral compression. (B) FKS 2, bilateral asymmetric compression. (C) FKS 2, indirect compression.

During the acute stage of papilledema, there is an increase in the blind spot. If the process is not resolved, nervous fibers lesion ensues, leading to visual field defects, usually corresponding to the optic disk topography. Central visual loss (central scotoma) occurs after optic nerve atrophy[10].

Another hypothesis suggests that the contralateral papilledema can also be caused by transmission of increased pressure through the intraorbital subarachnoid space from the mechanical compressed side, affecting the contralateral nerve, illustrated in Figure 3[11].

During slit lamp exams, findings on the optic disc can be observed. Papilledema can be characterized by optic disc swelling, with blurred disc margins, venous dilation and tortuosity. Optic disc atrophy, on the other hand, presents with a retracted and pale optic disc[5].

Analogous to the optic nerve, the increase of intracranial pressure can compromise the olfactory nervous system, since it is also covered by a meningeal sheath encompassing the subarachnoid space. In addition, an extensive lymphatic system surrounding the olfactory nerves contributes to CSF reabsorption - with the compression of this lymphatic network, CSF stasis develops, which further increases the pressure upon the olfactory nerves, impairing axoplasmic flow. In advanced stages, functional loss and anosmia prevail[12].

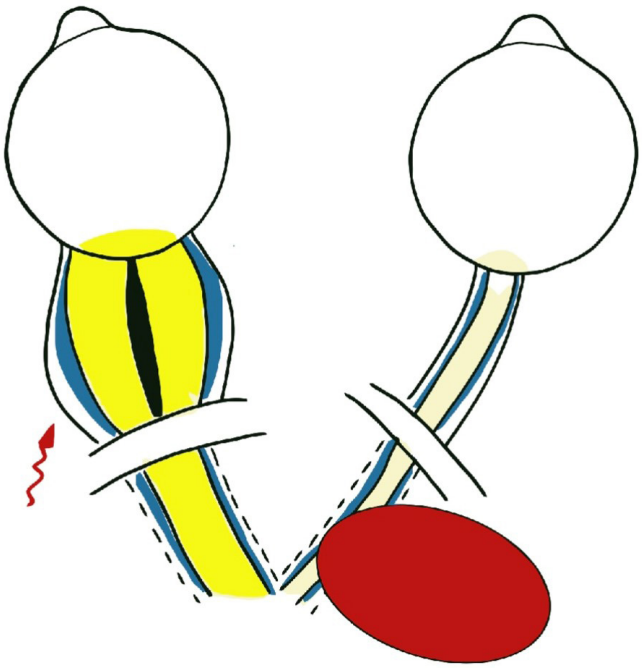

Figure 3. Schematic representation of SFK pathophysiology. Expansive lesion causing direct compression to the ipsilateral optic nerve, with atrophy; and contralateral edema, secondary to increased CSF pressure and decreased venous blood flow.

Pseudo FKS (PFKS) presents with unilateral optic atrophy and contralateral papilledema in the absence of intracranial mass, typically secondary to bilateral sequential optic neuritis or anterior ischemic optic neuropathy[13]. Any condition that initially develops optic disc edema and generates unilateral optic nerve atrophy can simulate FKS: demyelination (optic neuritis, multiple sclerosis), ischemia (anterior ischemic optic neuropathy), infections (syphilis), autoimmune diseases (sarcoidosis, systemic lupus erythematosus, Sjögren syndrome, Wegener granulomatosis), hereditary conditions (dominant optic neuropathy - type Kjer), nutritional deficits (vitamin B1, B2, B6 and B12 deficits) and chemical substances (ethambutol, amiodarone, methanol, methotrexate, cyclosporine, vincristine, cisplatin, ethanol and tobacco)[13]. Therefore, PFKS is a diagnosis of exclusion and should be considered when complementary exams are negative for intracranial masses[14,15].

Anterior ischemic optic neuropathy is the most common form of non-granulomatous optic atrophy in the elderly, and the main cause of PFKS. It can be divided into arteritic (secondary to temporal/giant cells arteritis) and non-arteritic (atheromatous etiology). Patients present with sudden painless visual loss, associated with optic disc swelling and visual field defects, justified by involvement of optic disc. Involvement of the contralateral eye occurs in 25% of cases in 3 years, defining the PFKS, in which the initially committed eye presents with optic atrophy signs, and the contralateral one, under acute process, develops papilledema[15].

Miller et al. published a case of temporal arteritis with PFKS, comprising the classical ophthalmological findings, associated with jaw claudication, rheumatic polymyalgia, headache and increase in erythrocyte sedimentation rate[7].

Papilledema, by definition, does not affect central visual acuity; it compromises the visual field by progressive compression, especially the nasal field. Vertical visual field deficits are a hallmark of optic nerve circulatory insufficiency in regions close to the cribriform plate, which generates optic disc swelling. In these cases, it is seldom to consider anterior ischemic optic neuropathy and giant cell arteritis as probable diagnoses. Beyond that, a swollen and pale optic disc does not correspond to the diagnosis of papilledema, and being usually associated with ischemic etiologies[7].

Bansal et al.[14] described a case of a preschooler with concomitant hydrocephalus and optic nerve congenital hypoplasia - therefore, the patient had an optic disc atrophy and a contralateral papilledema.

Macieli et al.[16] described a case of IIH causing PFKS. IIH occurs when there is an isolated increase in intracranial pressure, not related to intracranial mass lesions, venous thrombosis or meningeal inflammation. Papilledema is present in most cases; asymmetric cases are not uncommon; and ¼ of patients develop secondary optic atrophy and permanent visual loss. Intracranial hypertension findings are independent of etiology: empty sella, perioptic subarachnoid space distension and vertical tortuosity of the orbital segment of the optic nerve[17].

Semeraro et al.[17] described a case of PFKS in a patient with a meningioma associated with superior sagittal sinus infiltration, causing intracranial hypertension, and a venous anastomosis between the anterior third of the latter and left superior ophthalmic vein (sinus pericranii). Despite being a mass lesion, with a classic FKS as the initial diagnosis, there was no direct compression caused by the tumor, mainly because of its location (outside of the anterior fossa); and the visual repercussions were secondary to intracranial hypertension and venous anatomic variation.

Some cases of PFKS are secondary to trauma, especially by anterior fossa arachnoiditis, described by Yaskin, during the pre-tomography era[8]. Similarly, but with a different etiological origin, autoimmune (rheumatoid arthritis, sarcoidosis, Wegener granulomatosis, Churg-Strauss syndrome) and infectious diseases (syphilis, neurotuberculosis) can cause pachymeningitis, with involvement of cranial nerves, including the optic nerve[18].

Optic Coherence Tomography (OCT) is a non-invasive imaging test that maps the retina utilizing light waves, analog to ultrasound, to create seriated sectioned images of the retina. It is also used as a tool to analyze the optic nerve, studying the nervous fibers layer and the width of the ganglionic cells layer. Distances and microstructures are measured based on the way light waves are reflected or scattered in the medium they hit[19]. In the scenario of FKS, changes in the width of the nervous fibers layer are the most common feature, especially at the nasal macula: decrease in width in cases of optic atrophy, and width increases when in the presence of papilledema. OCT can also show different patterns of optic nerve atrophy, being able to help localize the lesion[20].

CONCLUSIONS

FKS is a rare presentation of expansive intracranial lesions, manifested as ophthalmologic patterns that can be common to various other diseases. In the presence of optic atrophy and contralateral papilledema, the first step is to exclude intracranial lesions. In the case of PFKS, the diagnostic algorithm developed by the authors helps guide the differential diagnosis and refer the patient to the right specialties, ensuring early diagnosis and treatment.

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