HOW TO DISTINGUISH PSEUDOPAPILLEDEMA FROM PAPILLEDEMA

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LEARNING OBJECTIVES
1. Review the cardinal clinical signs of papilledema versus pseudo-papilledema in patients presenting with an elevated optic nerve appearance
2. Describe the best use ancillary tests and tailor the investigative approach in patients with possible papilledema versus pseudo-papilledema

CME QUESTIONS
1. Does the patient in the case presented have papilledema or pseudo-papilledema?
2. Is this a case of optic disc drusen?
3. How can we differentiate benign causes of an elevated optic nerve appearance from causes of raised intracranial pressure?

KEYWORDS
1. Papilledema
2. Pseudopapilledema
3. Optic Disc Drusen
4. Ultrasonography
5. Fluorescein Angiography

INTRODUCTION
The differentiation of optic disc drusen (ODD) from true optic disc edema (ODE) is of critical importance, because ODE may represent a life-threatening condition requiring urgent and costly ancillary testing, whereas ODD is most often a benign process requiring only observation. In cases of ODD located on the disc surface, diagnosis may be straightforward, but with intrapapillary ODD (“buried drusen”), the optic disc appearance may mimic that of ODE. Ancillary testing has been utilized to aid in identification of ODD, including B-mode ultrasonography1, CT imaging, and fluorescein angiographic “autofluorescence.” 2-5 Recently, specific fluorescein angiography (FA) criteria for differentiating ODD from ODE have been published6. Optical coherence tomography (OCT) is also evolving as a modality for differentiation of ODD from ODE.7-11

ILLUSTRATIVE CASE
A 36-year-old obese woman reports a 3-week history of headache, increased in frequency over her baseline migraine pattern. She has occasional blurring of vision but no transient visual obscurations. She denies pulse synchronous tinnitus or diplopia. Her only medications include occasional over the counter analgesia for her headaches.

Examination shows the visual acuity is 20/15 each eye, with equivocally sluggish pupils but no relative afferent pupillary defect. Eye movements are normal as is the remainder of the neuro-ophthalmic examination except for the fundus. The optic discs are elevated, with blurred margins and no visible cup, as shown in the fundus photos (Figure 1). No spontaneous venous pulsations are observed. Visual fields demonstrate bilateral inferior constriction (Figure 2).

Figure 1

Figure 2
AUDIENCE RESPONSE QUESTION
What test would you use to determine whether this is a case of papilledema versus pseudo-papilledema?

The diagnostic test options are:

1. B-scan ultrasonography
2. Fluorescein angiography with assessment for autofluorescence
3. OCT, both time domain and spectral domain.
4. Cranial and orbital MRI with venography
5. Lumbar puncture

PANEL DISCUSSION
What would you choose as your “money test” and why?”

CASE CONCLUSION
B-scan ultrasonography was negative for calcified ODD (Figure 3). Fluorescein angiography did not demonstrate autofluorescence (Figure 4). Time-Domain OCT showed nerve fiber layer thickening but no characteristic feature to differentiate ODD from ODE (Figure 5).

The entire angiographic sequence showed no early leakage, with progressive circumferential peripapillary staining with nodularity; no disc hyperfluorescence was present (Figure 6).

The findings were typical for buried ODD.

DISCUSSION
When ODD are visible on the optic disc surface, identification is straightforward. The clinical features of intrapapillary (buried) ODD include optic disc elevation, blurred optic disc margins without obscuration of peripapillary retinal vessels, and nodular border of the optic disc, in the absence of features of optic disc edema, such as retinal nerve fiber opacification with obscuration of retinal vessels, microvascular abnormalities such as optic disc surface capillary net dilation, telangiectasia, retinal hemorrhages, and exudates. In this scenario, it is not infrequently difficult to distinguish ODD from ODE with certainty.

The detection of autofluorescence of the optic disc on pre-injection photography is confirmatory for ODD (Figure 7), but the technique is most effective when the ODD are on or near the disc surface, in which case ancillary testing is unnecessary. For intrapapillary ODD, sensitivity is low; Kurz-Levin and Landau documented autofluorescence in only 15 of 82 (18%) cases of “buried” ODD. Computed tomography (CT) (Figure 8) is limited not only by 1.5 mm thickness of orbital sections, which often may miss ODD, but by the requirement for calcification of ODD for their detection. B-mode ultrasonography (Figure 9) similarly detects only calcified ODD. While no study has clearly identified the percentage of ODD which are calcified, Kurz-Levin and Landau found positive ultrasonography in only 39 of 82 (48%) of eyes with “buried” ODD. In the study of Pineles and Arnold, 30 eyes with proven ODD had also undergone B-scan ultrasonography, 8 of which were negative.
Fluorescein angiography has been studied as a tool to identify ODD and differentiate from ODE. Sanders and Ffytche⁴ and Mustonen and Nieminen⁵ reported on FA findings in ODD, describing “early fluorescence” and “nodular, well demarcated late hyperfluorescence” seen without leakage. Cartlidge, et al.⁷ compared the FA findings of eyes diagnosed with “pseudo-papilledema” to those of eyes with true papilledema, emphasizing the “increased vascularity seen more often in papilledema.” Others²,⁸ have commented on findings in ODD, and a simplified criterion of “disc leakage vs disc staining” has been the standard discriminating feature. A clear distinction between “hyperfluorescence,” staining, and leakage, a critical appraisal of intrapapillary vs peripapillary hyperfluorescence, and a comparison of the findings of the entire FA sequence between ODD and ODE was recently published⁶. Intrapapillary ODD are characterized by either no early staining, or a characteristic early nodular staining (Figure 10a), unlike ODE, which is characterized by early diffuse leakage (Figure 10b). Intrapapillary ODD also often demonstrate a characteristic late peripapillary staining, either nodular, circumferential, or both (Figure 11a), not seen in ODE, in which capillary dilation and tortuosity, early and late fluorescein leakage (Figure 10b) are seen. Coexistent ODE and ODE may be distinguished by these features. Our case demonstrated the late nodular and circumferential peripapillary stain without leakage characteristic of buried ODD, despite a fundus appearance which suggested ODE.
Johnson et al. suggested time-domain (TD) OCT criteria for differentiating ODD from ODE, based on the internal optic nerve contour and the subretinal hyporeflective space (Figure 12a).

More recently, Yi et al., Lee et al., and Sarac et al. have documented that the increased resolution of spectral-domain (SD) OCT may provide a clearer image of buried ODD (Figure 12b) and may also distinguish superimposed ODE.

**SUMMARY**

FA in our case confirmed the presence of ODD without ODE. Ultrasonography, autofluorescence, and TD-OCT were not useful in differentiating ODD from ODE. The use of SD-OCT may be the preferred diagnostic modality in the future.

**CME ANSWERS**

1. Pseudopapilledema
2. Yes
3. Fluorescein angiography is an accurate and reliable method of differentiating pseudopapilledema from papilledema

**REFERENCES**