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DOI: 10.1056/NEJMc1601361

Malignant Transformation of *Hymenolepis nana* in a Human Host

TO THE EDITOR: Muehlenbachs et al. (Nov. 5 issue)¹ describe a case of malignant transformation in a cestode, *Hymenolepis nana*, and transformation resulting in individual proliferating cells invading host tissues. The authors cite some earlier cases as examples of proliferating parasites that maintained recognizable metazoan tissues. Although their report is mostly accurate, it understates the century-long history of numerous reports of transformations among cestodes that infect humans and other animals, with typically fatal outcomes. Earlier reports used different terminology that is more consistent with invertebrate zoology, such as “aberrant” or “anomalous,” but the developmental and morphologic criteria for neoplasms and malignant transformations would apply as well. Most recent are our descriptions of aberrant interepithelial and epitheliomesenchymal interactions resulting in transformation into abnormal new (neoplastic) structures in metacestodes, including mesocestoides² and spirometra species,³ thus producing the malignant proliferative disseminated lethal infections previously reported in many host species.⁴ In retrospective analysis, the transformations we reported appear to be identical to all known cases, including the earliest human cases in Japan in 1905 and Florida in 1908.⁵

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Conn notes the long history of atypical infections with tapeworm larvae. We agree that many of these aberrant forms probably share an underlying disease process. We urge caution in considering them as one entity, however, since malformed larvae are typically not considered to be neoplasms despite rapid cellular proliferation. Moreover, atypical infections often occur in atypical hosts or immunocompromised patients, as in the most similar previous case reports.¹ This fact suggests that the absence of normal host-defense signals stimulates abnormal tapeworm growth,² tissue dissemination, and ultimately neoplasia. We propose that these infections represent a spectrum of disease (as in cancer in humans), from the stimulated proliferation of normal tapeworm stem cells to the acquisition of somatic mutations, clonal overgrowth, and frank neoplasia (i.e., from low-grade to high-grade malignant transformation). Fundamental questions remain: Do atypical proliferative infections contain somatic mutations? Have true neoplasms been observed previously? Do somatic mutations contribute to aggressive behavior in more common tapeworm infections, including racemose cysticercosis and late-stage echinococcosis? Our finding that aberrant tapeworm development can include neoplasia lends credence to these inquiries.

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The findings and conclusions in this letter are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Since publication of their article, the authors report no further potential conflict of interest.

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DOI: 10.1056/NEJMc1600490

Thyroid Nodules

TO THE EDITOR: Burman and Wartofsky (Dec. 10 issue)¹ describe a clinical approach to thyroid nodules and indicate that a “radioisotopic (iodine-123 or technetium-99m) scan with measurement of radioisotope uptake to confirm autonomous function is indicated only if the thyrotropin level is suppressed.” We think that a thyroid radioisotope scan may be considered in patients with findings on thyroid fine-needle aspiration that are suggestive of a follicular neoplasm, particularly if the thyrotropin level is in the lower end of the normal range. Although there is a low likelihood of finding a functioning nodule when thyrotropin levels are not suppressed, this approach might spare some patients from undergoing unnecessary surgery.

Our suggestion is consistent with the revised 2009 guidelines of the American Thyroid Association (ATA) on thyroid nodules.² The 2015 ATA guidelines, however, remained silent about this issue.³

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1600493

TO THE EDITOR: In their review of palpable thyroid nodules, Burman and Wartofsky do not discuss incidentally detected nodules and only

briefly address overdiagnosis and overtreatment of incidentally detected papillary thyroid cancers. These lesions outnumber palpable cancers by orders of magnitude in clinical practice.¹

The current guideline of the American College of Radiology was not mentioned in the article. It calls for no follow-up at all for incidentally detected nodules that are smaller than 1.0 cm in diameter in patients who are younger than 35 years of age or smaller than 1.5 cm in diameter in patients who are 35 years of age or older.²

Readers and patients would benefit from awareness of the low probability of cancer in small, incidentally detected nodules. They also would benefit from knowing that with appropriate evaluation and therapy, a favorable prognosis is associated with nodules that are found to be histologically malignant.

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1600493

THE AUTHORS REPLY: The combined guidelines of the American Association of Clinical Endocrinologists–Associazione Medici Endocrinologi–European Thyroid Association do not recommend the performance of a radioisotope scan when findings on thyroid fine-needle aspiration are suggestive of a follicular neoplasm.¹ The 2015 ATA guidelines have removed this recommendation,² which was present in the 2009 ATA guidelines and based on expert opinion.