



## Letter to the Editor



# Intraneural metastasis of cholangiocarcinoma in a cow

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Dear Editor of American Journal of Cancer Science,

I have published the article entitled “*Osseous metaplasia in the mesenteric lymph node with metastatic cholangiocarcinoma in a cow*” [1] in Volume 1, Issue 1 of **American Journal of Cancer Science**. Although the article described briefly that the vagus nerve was involved with metastatic carcinoma, neither images illustrating such a finding nor relevant discussion on the subject were provided unfortunately. This letter gives more detailed explanation of this extremely rare intraneural metastasis of the carcinoma.

On postmortem gross examination, the cow had in the mediastinal space a firm mass consisting of large amounts of fibrous tissues, swollen mediastinal lymph nodes with metastatic lesions from cholangiocarcinoma, and thickened vagal nerve trunk. On histopathology, vagal nerve trunk in the mediastinal region was surrounded by abundant fibrous connective tissue. As shown in Fig. 1, perineural connective tissue of the vagal nerve exhibited frequent intravascular growths of cholangiocarcinoma cancer cells, most of which showed degenerative or necrotic features. Endoneural invasion of carcinoma tissue was also frequently found in nerve bundles, occupying nerve tissue to a varying degree. There was endoneural hemorrhage in association with carcinoma invasion. Mild sub-endoneural edema was occasionally observed and, to a varying degree, axonal degeneration (swellings) of nerve fibers was seen adjacent to metastatic lesions of cholangiocarcinoma.

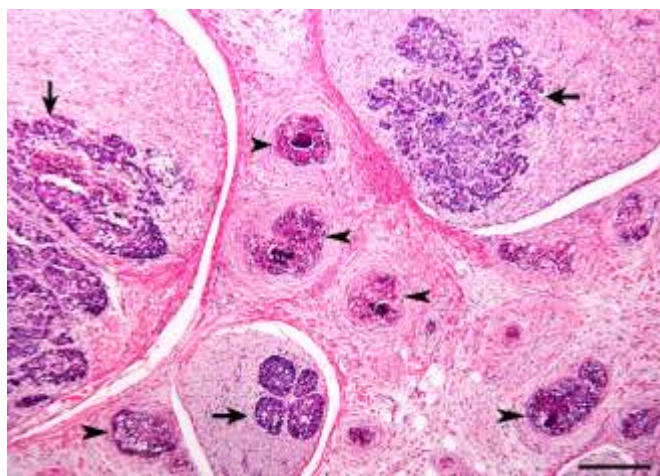
Intraneural metastasis has been reported in a variety of malignancies, including basal cell carcinoma [2], cystosarcoma phyllodes [3], mammary carcinoma [4], lymphoma [4], melanoma [5], synovial sarcoma [6], fibroxanthoma [7], renal carcinoma [8], and pancreatic ductal adenocarcinoma [9]. To the best of the author's knowledge, cases with intraneural metastasis from cholangiocarcinoma, as seen in the current cow, have never been described in the English medical and veterinary literature. Although pronounced rarity of carcinoma (or sarcoma) metastasis to tissue sites such as peripheral nerves and muscles is well known, its reason has not been fully explained. In peripheral nerves, a role of the blood-nerve barrier is suggested to be effective against carcinoma metastasis [10]. It is thought that intraneural metastasis of cholangiocarcinoma reported here might have occurred via hematogenous spread, taking into account the fact that tumor cells invaded blood vessels in the perineural connective tissue and metastatic carcinoma was associated with endoneural hemorrhage. The observation of intraneural metastasis of cholangiocarcinoma in this cow may be useful to those conducting research in the pathology of malignant tumors in man and domestic animals.

## References

1. Ohfuji S. Osseous metaplasia in the mesenteric lymph node with metastatic cholangiocarcinoma in a cow. *Am J*

*Cancer Sci.* 2012, 1:1-7

2. Mark GJ. Basal cell carcinoma with intraneural invasion. *Cancer*. 1977, 40:2181-2187
3. Grimes M M, Lattes R, Jaretzki A. Cystosarcoma phyllodes. Report of an unusual case, with death due to intraneural extension to the central nervous system. *Cancer*. 1985, 56:1691-1695
4. Meller I, Alkalay D, Mozes M, Geffen DB, Ferit T. Isolated metastases to peripheral nerves. Report of five cases involving the brachial plexus. *Cancer*. 1995, 76:1829-1832
5. Cantone G, Rath SA, Richter HP. Intraneural metastasis in a peripheral nerve. *Acta Neurochir (Wien)*. 2000, 142:719-720
6. Matsumine A, Kusuzaki H, Hirata H, Fukutome K, Maeda M, Uchida A. Intraneural metastasis of a synovial sarcoma to a peripheral nerve. *J Bone Joint Surg*. 2005, 87-B: 1553-1555
7. Dettrick A, Strutton G. Atypical fibroxanthoma with perineural or intraneural invasion: report of two cases. *J Cut Pathol*. 2006, 33: 318-322
8. Varin S, Faure A, Bouc P, Maugars Y, Berthelot J M. Endoneural metastasis of the sciatic nerve disclosing the relapse of a renal carcinoma, four years after its surgical treatment. *Joint Bone Spine*. 2006, 73: 760-762
9. Chatterjee D., Katz M H, Rashid A, Wang H, Luga A C, Varadhachary G R, Wolff R A, Lee J E, Pisters P W, Crane CH, Gomez H F, Abbruzzese J L, Fleming J B, Wang H. Perineural and intra-neural invasion in posttherapy pancreaticoduodenectomy specimens predicts poor prognosis in patients with pancreatic ductal adenocarcinoma. *Am J Surg Pathol*. 2012, 36: 409-417
10. Smith G J, Baqnell C R, Bakewell W E, Black K A, Bouldin T W, Earnhardt T S, Hook G E, Pryzwansky K B. Application of confocal scanning laser microscopy in experimental pathology. *J Electron Microscop Tech*. 1991, 18: 38-49



**Fig. 1** Lesions of cholangiocarcinoma invade endoneural areas (arrows) of the nerve bundles, and lumens of perineural blood vessels are filled with necrotic tumor cells (arrowheads). Hematoxylin and eosin stain. Bar = 360  $\mu$ m

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**Competing Interests:** The authors have declared that no competing interests exist.

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