CASE REPORT

A Rare Case of Thyroid Metastasis from Pancreatic Adenocarcinoma

Michael E Kelly[1], John Kinsella[2], Charles d'Adhemar[3], Niall Swan[3], Paul F Ridgway[1]

[1]Professorial Surgical Unit, Department of Surgery; [2]Department of Otolaryngology; [3]Department of Histopathology; The Adelaide and Meath Hospital, Dublin Incorporating the National Children's Hospital. Dublin, Ireland

ABSTRACT

Context Thyroid metastasis from pancreatic adenocarcinoma is extremely rare, with only two previous cases in the literature. We report a case of pancreatic adenocarcinoma metastasising to the thyroid. We review the incidence, diagnosis, and management of this rare occurrence. **Case report** A 38-year-old man with a synchronous 6-month history of thyroid swelling, presented with epigastric pain and signs of obstructive jaundice. He was investigated by abdominal computerised tomography and endoscopic retrograde cholangiopancreatography. The diagnosis of pancreatic neoplasm was made. His thyroid neoplasm was investigated at another tertiary centre and thought to be a papillary neoplasm. He underwent a pancreaticoduodenectomy and recovered well post-operatively. Eight weeks later he had a total thyroidectomy. Histology confirmed that the thyroid mass was both morphologically and immunophenotypically similar to the pancreatic neoplasm. **Conclusion** This case demonstrates the importance of a full investigation when a patient with suspected neoplastic history presents with a thyroid nodule. We outline the crucial role that immunohistochemistry plays in detecting and classifying primary and secondary thyroid neoplasms. The detection of a solitary thyroid metastasis from pancreatic adenocarcinoma may indicate a poor prognosis, and it is debatable whether resection of the primary should be undertaken when it presents with a solitary metastasis.

INTRODUCTION

Treatment of patients with pancreatic adenocarcinoma with solitary metastasis to the thyroid is unknown. Improvement in diagnostic methods now facilitates to differentiate primary from metastatic disease. Recent autopsy studies have shown that the incidence of thyroid metastasis ranges between 1% and 24% in patients with a known history of neoplasm [1]. However, these are usually in the setting of patient with widespread disease. This case report highlights the rare incidence of thyroid metastasis and the paucity of evidence upon which management strategies are based. Furthermore histology and immunohisto-chemistry have a significant role in differentiating whether a thyroid nodule is a primary neoplasm or metastasis from other neoplastic sites, notably the pancreas.

Pancreatic neoplasm has an incidence of 10.3/100,000 males and 7.9/100,000 females in the United Kingdom [2]. Only 20-30% of cases are localized and potentially curable at diagnosis. Despite resection, five-year survival rates for pancreatic adenocarcinoma remain low, averaging 5% [2]. This poor survival is thought to be due to microscopic occult metastasis at the time of resection. Data are lacking to clarify survival rates in patients with pancreas carcinoma metastasising to the thyroid. The majority of thyroid metastasis occurs in the presence of widespread metastatic burden, unlike our case.

Received September 17th, 2010 - Accepted October 19th, 2010

Key words Carcinoma, Pancreatic Ductal; Neoplasm Metastasis; Thyroid Neoplasms

Correspondence Michael E Kelly
Department of Surgery; Adelaide and Meath Hospital Incorporating National Children's Hospital; Tallaght; Dublin 24; Ireland
Phone: +353-1.414.2000; Fax: +353-1.414.2212
E-mail: kellym11@tcd.ie

URL http://www.serena.unina.it/index.php/jop/article/view/3381/3661

CASE REPORT

We present the case of a 38-year-old man of Eastern European origin. He was transferred from a tertiary level institution with a 6-week history of vague epigastric pain, eight kilogram weight loss, and a seven-day history of obstructive jaundice. Of note, he also had a six-month history of a right neck swelling. There was no significant family history of thyroid or gastrointestinal neoplasms. However, he was an ex-smoker of twenty-five pack/year.

On examination, he was observably jaundiced with scleral icterus. A mass on the right side of his neck was noted to be mobile, soft, fluctuant, and moved with swallowing. Cervical lymphadenopathy and retro-sternal extension were not present. Abdominal examination was positive for Courvoisier's sign. He had an elevated CA 19-9 (2,322 U/mL; reference range: 0-39 U/mL).

At the referring centre, flexiscope laryngoscopy showed a normal larynx and vocal cords. A computerised tomography (CT) of the head and neck showed a 7 cm multiloculated mixed cystic and solid mass of the right thyroid lobe. Fine needle aspirates of the neck mass revealed small amount of follicular cells with papillary like architecture, but which did not demonstrate classical features of thyroid papillary carcinoma. Cytology reported a suspected atypical thyroid papillary carcinoma at multidisciplinary meeting.

Subsequently, on transfer to our centre, he had a contrast CT of the abdomen which reported an enlargement of the pancreatic head and uncinate process with dilation of both the pancreatic and common bile ducts. Retroperitoneal, para-aortic, and coeliac lymphadenopathy were noted. Furthermore, endoscopic ultrasound revealed a large irregular mass occupying the head of the pancreas. Endoscopic retrograde cholangiopancreatography with stenting, and biopsy were completed. Biopsy of the ampulla of Vater was positive for invasive, moderately differentiated adenocarcinoma. A staging laparoscopy was negative for peritoneal deposits. A pancreatico-duodenectomy was performed with resection of the tumour from the head of the pancreas (R0), and found that the tumour had invaded the ampulla of Vater, the duodenal wall, and the distal common bile duct. Seven of twelve regional lymph nodes, including aortocaval lymph nodes, were positive. Histology confirmed a moderately to poorly differentiated ampullary ductal type adenocarcinoma. The staging of the tumour was T4N1M1. He recovered well and discharged on day ten post-operatively.

Eight weeks later, he was electively re-admitted for a total thyroidectomy. The histology of the full specimen was similar to that of the pancreatic resection, indicating that the thyroid nodule was a pancreatic adenocarcinoma metastasis. He was commenced on palliative gemcitabine based chemotherapy. He is alive and well without any evidence of disease at nine-month follow-up.

DISCUSSION

To our knowledge, there are only two reported cases of thyroid metastasis from pancreatic malignant neoplasm [3, 4]. The efficacy of surgical treatment for solitary metastasis as seen in our case is unknown. More frequently, pancreatic adenocarcinoma spreads to local lymph nodes and organs such as the liver, lungs, adrenals and kidneys. However, rarer sites such as brain, larynx, and skin have also been reported [5].

Being a highly vascularised organ, the thyroid should be a prime centre for metastatic disease [6]. In the 1950's, Coman *et al*. researched on the embolic transition of tumour cells within rabbits, and concluded that tumour cells were more likely to lodge in capillaries of the kidneys, adrenals and the pituitary, rather than arterioles of the thyroid. This phenomenon was speculated to be related to haemodynamic factors such as blood flow and pressure. The tumour cells were more likely to lodge in capillaries because of differential blood flow and pressure. Furthermore, arteries and arterioles have lower amounts of calcium in their walls, resulting in tumour-cell emboli being less adhesive [7]. However, we recognise this metastatic phenomenon to be more complex than previously speculated. Tumour embolisation and deposition is a multi-factorial process that requires much further in depth analysis and investigation.

Secondaries to the thyroid are more common from primary neoplasms of the kidney, breast, lung, and colon [8]. However, recent research autopsy studies have shown an increased incidence of metastasis to the thyroid in patients with known history of neoplasm [1]. Interestingly, others have argued that the surge of fine needle aspiration of thyroid nodules have led to this rise in incidence of detecting thyroid metastasis [3]. This case report emphasises that patients with suspected history of neoplasm presenting with a thyroid nodule should be fully investigated to distinguish between primary thyroid carcinoma and metastasis from neoplasm elsewhere. However, there have not been studies reporting the incidence on treatment of thyroid metastasis from pancreatic adenocarcinoma.

Synchronous primary malignancies are a recognised, yet unusual occurrence. It is more common in individuals with familial/hereditary traits. Synchronous renal cell carcinoma and pancreatic neoplasm is associated with autosomal conditions such as Von-Hippel Lindau disease or Birt-Hogg-Dube syndrome [9]. According to the John Hopkins Polyposis Registry, patients with familial adenomatous polyposis can have synchronous extra-intestinal neoplasms. These patients have a relative risk increase of 7.6% for thyroid neoplasm and 4.46% increased risk of pancreatic adenocarcinoma [10].

Similar to our patient, nearly all patients with malignant thyroid neoplasms (primary or metastases) are euthyroid [11]. Fine needle aspiration (FNA) is the most common investigation for thyroid nodules. However, researches have shown that FNA specificity ranges from 72% to 98% depending on the publication and power of the study. Furthermore, it is limited by user experience and cytopathologist expertise [12]. FNA may be unable to distinguish primary thyroid carcinoma from secondary metastasis if the cells are highly anaplastic [11]. Therefore, histology and immunohistochemistry play a vital role in identifying primary thyroid neoplasm by staining for thyroid transcription factor-1 (TTF-1) and thyroglobulin. In our case report, macroscopic examination of the resected thyroid specimen revealed a cystic lesion subtotally replacing the right thyroid lobe, the inner lining of which showed focal papillary excrescences of fleshy, tan tissue. Microscopically, these foci consisted of moderately differentiated adenocarcinoma with a mixed tubular and irregular pseudo-papillary architecture (no true fibrovascular cores) associated

with significant acute inflammation. These tumour cells were predominantly columnar with prominent nucleoli. Although papillary thyroid carcinoma may present as a cystic lesion with similar macroscopic features, the cytonuclear features of the tumour present were not consistent with papillary thyroid carcinoma. Immunohistochemical staining demonstrated that the thyroid tumour cells were positive for cytokeratin 7 and 19 and had negative staining for cytokeratin 20, thyroid transcription factor-1, and thyroglobulin. While our cytokeratin profile could be seen with either a primary thyroid or pancreatic carcinoma, the negative staining for both thyroid transcription factor-1 and thyroglobulin favours a metastatic tumour over a primary thyroid neoplasm. Staining for galactin-3 was not performed because galactin-3 is expressed in both metastatic pancreatic cancer cells and thyroid neoplastic cells [13, 14]. Therefore, galactin-3 staining would not add further benefits to our immunohistochemical profile. After reviewing the histology slides from our patient's pancreatico-duodenectomy, we found that the morphology of the pancreatic tumour (ductal adenocarcinoma) was identical to that of the thyroid tumour deposits. This histological finding indicated that the thyroid neoplasm was a metastatic pancreatic ductal adenocarcinoma.

Metastasis to the thyroid from pancreatic malignancy is probably a poor prognostic indicator. Survival is reported to be ranging between 3 and 6 months, marking it as a terminal event in the course of the disease [15]. However, there is no series evidence to follow generalisable median survival data. As surgical resection is the most common modality of management of the thyroid, metastasectomy has been recommended in some centres [16]. However, there is no clear evidence that thyroidectomy or resection of the primary may prolong (or reduce) survival. In general, however, detection of typical metastases from pancreatic neoplasms mark limited short term survival [17]. We recommend that management of such cases be evaluated on a bespoke basis in a multidisciplinary forum.

CONCLUSION

This case emphasises the importance of a clinical suspicion as well as histology/immunohistochemistry profiling for a patient with suspected neoplastic history presenting with a thyroid nodule. Often, as in our case, the association is made retrospectively. In cases where the diagnosis is known preoperatively, management strategy in such cases cannot be guided by published data and therefore should be addressed at multidisciplinary conference.

There will never be randomised data to clearly define management in these rare cases, but pooling of cases may lend insight into the most efficacious therapy. Future studies should centre on quality of life as well as survival as it is reasonable to assume these cases to be palliative.

Imaging The images of this case report are available in the appendix at the end of the paper or in format of slide show at http://www.joplink.net/prev/201101/04.ppt.

Conflict of interest None

References

1. Nakhjavani MK, Gharib H, Goellner JR, Van Heerden JA. Metastasis to the thyroid gland. A report of 43 cases. Cancer 1997; 79:574-8. [PMID 9028370]

2. Ypsilantis E, Courtney ED, Warren H. Increase in annual number of pancreatic head resections does not affect mortality of pancreatic cancer in the United Kingdom. JOP. J Pancreas (Online) 2009; 10:462-3. [PMID 19581759]

3. Hsiao PJ, Tsai KB, Lai FJ, Yeh KT, Shin SJ, Tsai JH. Thyroid metastasis from intraductal papillary-mucinous carcinoma of pancreas. Acta Cytol 2000; 44:1066-72. [PMID 11127736]

4. Eriksson M, Ajmani SK, Mallette LE. Hyperthyroidism from thyroid metastasis of pancreatic adenocarcinoma. JAMA 1977; 238:1276-8. [PMID 578180]

5. Aksoy M, Sumer A, Sari S, Mete O, Salmaslioglu A, Erbil Y. Pancreatic ampullary carcinoma with neck metastases: a case report. Cases J 2009; 2:146. [PMID 19946517]

6. Wychulis AR, Beahrs OH, Woolner LB. Metastasis of carcinoma to the thyroid gland. Ann Surg 1964; 160:169-77. [PMID 14209716]

7. Coman DR, Delong RP, McCutcheon M. Studies on the mechanisms of metastasis; the distribution of tumors in various organs in relation to the distribution of arterial emboli. Cancer Res 1951; 11:648-51. [PMID 14859232]

8. Bae WK, Shim HJ, Choi YD, Kim JW, Cho SH, Kang HC, Chung IK. Severe hypothyroidism induced by thyroid metastasis of cholangiocarcinoma. Cancer Res Treat 2009; 41:56-8. [PMID 19688074]

9. Bharthuar A, Pearce L, Litwin A, LeVea C, Kuvshinoff B, Iyer R. Metastatic pancreatic adenocarcinoma and renal cell carcinoma treated with gemcitabine and sunitinib malate. A case report. JOP. J Pancreas (Online) 2009; 10:523-7. [PMID 19734629]

10. Giardiello FM, Offerhaus GJ, Lee DH, Krush AJ, Tersmette AC, Booker SV, et al. Increased risk of thyroid and pancreatic carcinoma in familial adenomatous polyposis. Gut 1993; 34:1394-6. [PMID 8244108]

11. Kim TY, Kim WB, Gong G, Hong SJ, Shong YK. Metastasis to the thyroid diagnosed by fine-needle aspiration biopsy. Clin Endocrinol 2005; 62:236-41. [PMID 15670202]

12. Gharib H, Goellner JR. Fine-Needle Aspiration Biopsy of the Thyroid: An Appraisal. Ann Intern Med 1993; 118:282-9. [PMID 8420446]

13. Berberat PO, Friess H, Wang L, Zhu Z, Bley T, Frigeri L, et al. Comparative analysis of galectins in primary tumors and tumor metastasis in human pancreatic cancer. J Histochem Cytochem 2001; 49:539-49. [PMID 11259457]

14. Barut F, Onak Kandemir N, Bektas S, Bahadir B, Keser S, Ozdamar SO. Universal markers of thyroid malignancies: galectin-3, HBME-1, and cytokeratin-19. Endocr Pathol 2010; 21:80-9. [PMID 20198455]

15. Hegedus L. Clinical practice. The thyroid nodule. N Engl J Med 2004; 351:1764-71. [PMID 15496625]

16. Liang HH, Wu CH, Tam KW, Chai CY, Lin SE, Chen SC. Thyroid metastasis in a patient with hepatocellular carcinoma: case report and review of literature. World J Surg Oncol 2007; 5:144. [PMID 18157914]

17. Hidalgo M. Pancreatic Cancer. N Engl J Med 2010; 362:1605-17. [PMID 20427809]

APPENDIX

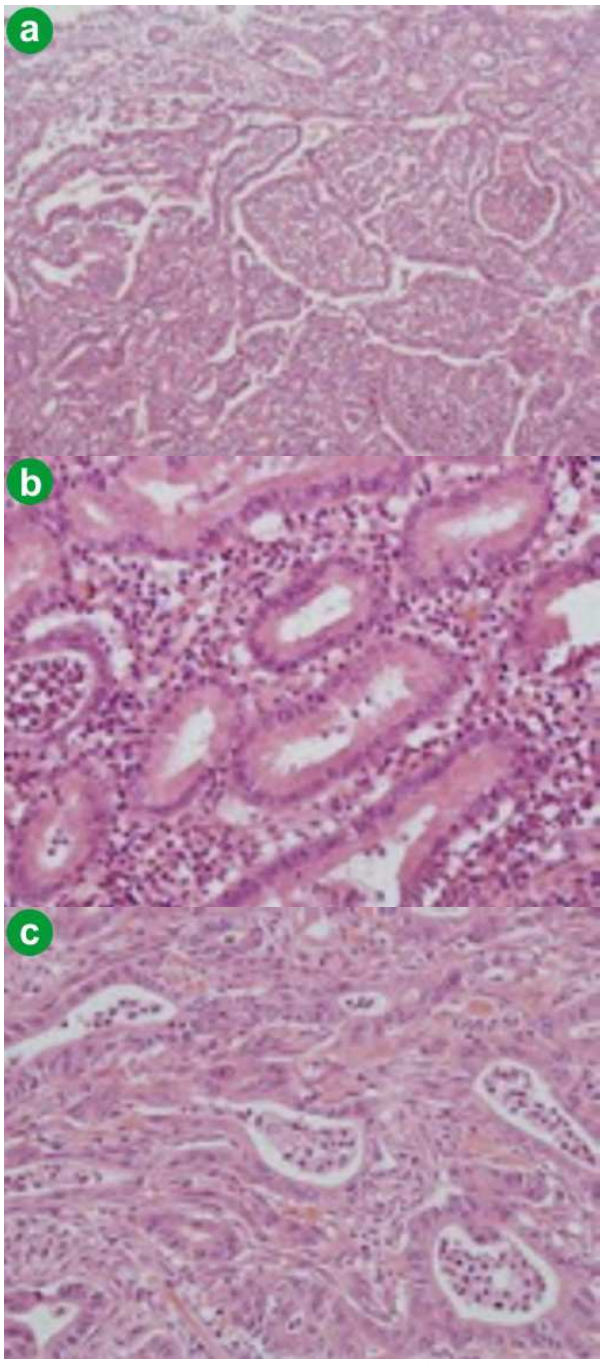

Figure 1. a. Low power photomicrograph of a thyroid tumour deposit showing tubular and pseudopapillary architecture (H&E 5x). **b.** Higher magnification of the deposit showing malignant glands lined by columnar cells with prominent nucleoli (H&E 20x). **c.** Primary pancreatic ductal adenocarcinoma showing similar cytomorphological features but with more typical ductal structures (H&E 20x).

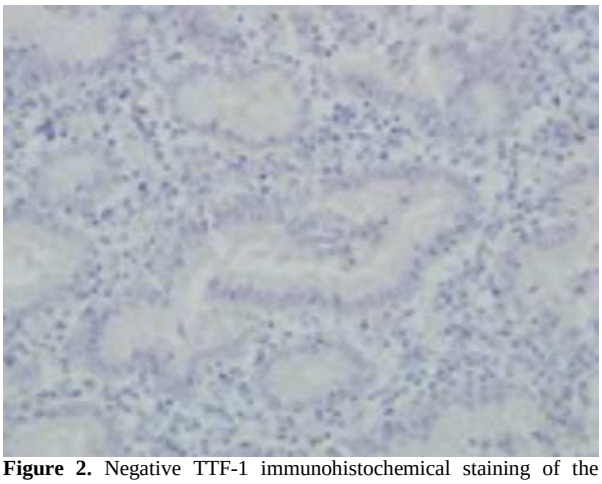

Figure 2. Negative TTF-1 immunohistochemical staining of the thyroid tumour (20x).

Figure 3. Computerised tomography of abdomen showing pancreatic neoplasm with pancreatic duct dilatation.

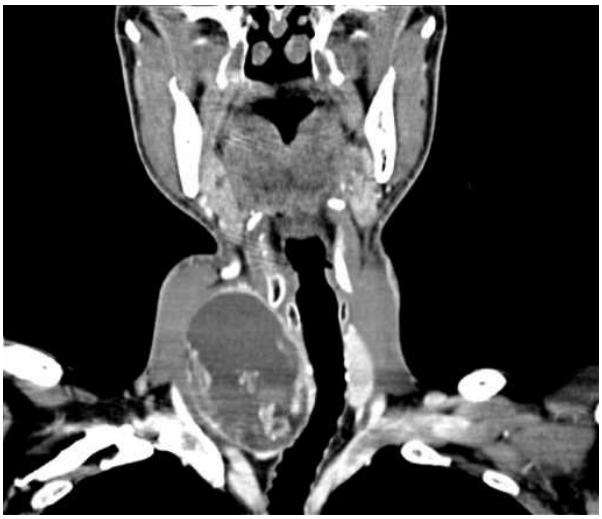

Figure 4. Computerised tomography of neck showing solid mass of the right thyroid lobe.