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Case Report

Amenorrhea along with renal and thyroid metastasis: Unusual presentation of pancreatic adenocarcinoma

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ARTICLE INFO

Article history:

Received 20 December 2016

Accepted 25 September 2017

Available online 28 November 2017

Keywords:

Ectopic β -hCG

Endoscopic ultrasound

Pancreatic adenocarcinoma

Renal metastasis

Thyroid metastasis

Case report

A 30-year old female patient presented with a thyroid swelling for 6 months, amenorrhoea for 4 months, and upper abdominal pain, anorexia and weight loss for one month. She denied any exposure to carcinogens like tobacco, exposure to chemicals or a family history of malignancies. On examination; there was pallor, diffuse thyromegaly with retrosternal extension and a well defined intra-abdominal retroperitoneal lump measuring 10×8 cm occupying the epigastrium, right and left hypochondrium and umbilical regions. Urine pregnancy test was positive. Various haematological and biochemical tests revealed anaemia, euthyroid status, normal serum calcium and a raised β -hCG level (10,000 IU/ml). An ultrasonography of abdomen suggested a pseudopancreatic cyst with no evidence of an intra uterine pregnancy. Transvaginal Ultrasonography (TVS) was suspicious for a right ectopic pregnancy. A diagnostic laparoscopy was done which ruled out an ectopic pregnancy with normal bilateral tubes and ovaries (Fig. 1). Ultrasonography of the neck revealed a hypoechoic nodule measuring $8.6 \times 5.6 \times 6.4$ cm in the right lobe and 1.5×1.9 cm nodule in the left lobe of thyroid gland. Contrast Enhanced Computed Tomography (CECT) abdomen revealed a $8.6 \times 11.6 \times 9.0$ cm enhancing multi-septated thick walled fluid collection in the body and tail of pancreas extending into the peripancreatic region, abutting the stomach and splenic vein, along with para-aortic and celiac lymphadenopathy. There was also a solid lesion with necrosis in the right kidney along with ascites (Fig. 2). An Endoscopic Ultrasonography (EUS) was done which revealed a

Introduction

Synchronous malignancies in pancreas, thyroid and kidney occur rarely and do not fit into any of the previously described syndromes. Also, pancreatic adenocarcinomas metastasise infrequently to the thyroid and kidney. We herein highlight the diagnostic challenges and dilemma while caring for a young female patient with synchronous malignancies in thyroid, kidney and pancreas with ectopic β -hCG production.

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0377-1237/© 2017 Published by Elsevier B.V. on behalf of Director General, Armed Forces Medical Services.

Fig. 1 – Diagnostic laparoscopy photographs. (A). No evidence of ectopic pregnancy. (B). The pancreatic mass bulging through the lesser sac.

Fig. 2 – CT scan axial images showing: (A). A large complex cystic lesion involving pancreas with para-aortic lymph nodes. (B). Exophytic solid enhancing lesion involving the parenchyma of right kidney. Areas of necrosis noted at the periphery.

9X8 cm solid cystic mass in the head and body of pancreas with extension into retroperitoneum, adjacent stomach and duodenum. A EUS-guided biopsy was done which was suggestive of adenocarcinoma pancreas. Fine Needle Aspiration Cytology (FNAC) from thyroid and right kidney showed malignant cells similar in morphology to each other (Fig. 3). Positron Emission Tomography (PET) CT showed FDG avidity only in the region of thyroid, pancreas and right kidney. A final working diagnosis of β -hCG producing adenocarcinoma pancreas metastatic to thyroid and kidney was made. In view of unresectable primary, the patient was started on cisplatin/taxane based chemotherapy. The patient developed severe neutropenia post the first cycle of chemotherapy and unfortunately, succumbed to her illness.

Discussion

Tumours occurring simultaneously in different organs can be either synchronous as in syndromic tumours or metastatic from a primary site. Synchronous renal cell carcinoma and pancreatic neoplasm has been seen in association with certain autosomal syndromes like Von-Hippel Lindau disease or Birt-Hogg-Dube syndrome. Also has been seen that patients with

familial adenomatous polyposis (FAP) may harbour synchronous non-intestinal neoplasms like thyroid and pancreatic cancers.^{1,2} However a known syndrome describing synchronous adenocarcinoma of pancreas, thyroid and kidney could not be found despite an extensive literature search.

Pancreatic tumours are known to metastasise frequently to the liver, lungs, and adrenals. Uncommon sites reported in the literature include brain, kidneys, larynx and skin. Also, Non-thyroid Malignancies (NTM) occur commonly from primary cancers of lung, breast, kidney, colon and rectum. The high and fast arterial flow and iodine content in the thyroid gland is said to be responsible for its low incidence of metastasis.³ These NTM occur more frequently in glands with pre-existing disorders like goitre, thyroiditis probably due to decreased iodine content and vascularity associated with these.⁴ As mentioned by Delitala et al., metastasis to the thyroid gland from pancreatic adenocarcinoma has been reported in three cases only with theirs being the fourth one.³ However, none of these cases had associated renal metastasis.

The optimum management of such cases remains a diagnostic challenge, mainly due to the rarity of such cases. Since a surgical resection has been the most widely practiced treatment modality for thyroid tumours, metastatectomy has been followed by some centres.⁵ However, there is no

Fig. 3 – Photomicrographs. (A) EUS guided trucut biopsy from pancreatic mass showing pleomorphic tumour cells having large hyperchromatic nuclei with abundant eosinophilic cytoplasm (adenocarcinoma pancreas) (H&E, 40×). (B) FNAC from the renal mass showing pleomorphic cells having anisocytosis, multinucleation with cytoplasmic vacuolation (consistent with ductal adenocarcinoma) (H&E, 40×). (C) FNAC from the thyroid swelling showing pleomorphic malignant cells having anisocytosis, intranuclear inclusions, margination of cytoplasmic granularity and cytoplasmic vacuolation (H&E, 40×).

definitive data to prove that a surgical resection of the thyroid or the primary may enhance survival. Also such options of thyroidectomy in cases with NTM seem more logical (even though it might still be investigational due to small numbers of such cases) in patients having isolated thyroid metastasis, a resectable primary tumour and situation with this additional metastatectomy does not add to an increased patient morbidity or mortality.

Thyroid metastasis from pancreatic malignancy may represent a poor prognostic indicator with a reported survival of three to six months. Thus, thyroid metastasis may be a terminal event in the natural history of the disease. Since these are rare manifestations of pancreatic malignancy, there is no robust evidence to derive a median survival in such patients. Even otherwise, once metastases from pancreatic cancer occur, it heralds a limited survival.⁶

β -hCG levels are elevated in 40–56% of pancreatic cancers.⁷ β -hCG production has been associated with a more aggressive clinical course and poor prognosis with no difference in the surgical options when compared with similar non β -hCG producing tumours.⁸

In literature, multifocal malignancies have been reported. Triple synchronous malignancies too, have reported.^{9–11} In our patient, who presented with a simultaneous tumour in pancreas, kidney and thyroid, a probability of malignant multifocal neuroendocrine carcinoma, primary synchronous

malignancy involving these three organs and pancreatic carcinoma metastatic to kidney and thyroid were considered. PET CT ruled out malignancy at other sites. Image guided biopsy/cytology helped to find out the histological type of the malignancy, which revealed pancreatic tumour to be an adenocarcinoma. The tumour cells in thyroid and kidney depicted similar cytological features to that of pancreatic cancer. Hence a diagnosis of adenocarcinoma head of pancreas with β -hCG production and isolated renal and thyroid metastasis was made. Though not done, an immunohistochemical staining for confirming a pancreatic origin (CK 19, CK 7 and CK 20) and ruling out primary thyroid malignancy (CK 7, TTF 1 and thyroglobulin) or renal cell carcinoma (CD 10, Vimentin and PAX 8) could have further confirmed our diagnosis while ruling out synchronous primaries. This was not done due to logistical constraints at our centre. Since, the pancreatic malignancy was unresectable at presentation, the patient was given chemotherapy. The presence of β -hCG production and thyroid metastasis were additional poor prognostic indicators in this patient.

Conclusions

Synchronous malignancies in the body can pose diagnostic challenges. Imaging and cytology can help delineating their extent and type respectively. Ectopic β -hCG production and

thyroid metastasis in a case of pancreatic adenocarcinoma worsen the prognosis of the disease. Due to scarcity of such cases, optimal management of these cases should be individualised with multimodal treatment being usually beneficial. Surgery should be reserved for those with satisfactory performance status and resectable primary disease.

Conflicts of interest

The authors have none to declare.

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