Neuroendocrine carcinoma of the gall bladder in a young lady presenting with upper abdominal heaviness: a common complaint and a rare diagnosis

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Accepted 21 March 2019

DESCRIPTION

A 34-year-old woman was referred from internal medicine with complaints of occasional upper abdominal heaviness and pain for 4 months. Her WHO performance score was 1. On examination, she was icteric and had multiple, brownish nodular skin lesions on limbs and back that were soft to firm in consistency. On per abdominal examination, the liver span was approximately 5 cm below the right subcostal margin at midclavicular line. She underwent CT scan of the abdomen, which revealed an ill-defined heterogeneously enhancing lesion in the gall bladder fossa infiltrating adjacent liver parenchyma, duodenum and the common bile duct at the porta hepatis (figure 1A–L). Her biopsy revealed liver parenchyma infiltrated by tumour cells with hyperchromatic nucleus, fine chromatin, inconspicuous nucleoli and scant cytoplasm (figure 2A,B). Tumour cells were positive for synaptophysin and showed high MIB1 labelling index (figure 2C,D). A diagnosis of neuroendocrine carcinoma of gall bladder was made. She was discussed in tumour board and was offered palliative chemotherapy.

Primary neuroendocrine tumours (NETs) of the gall bladder (GB) are rare entities, and they represent only about 0.5% of all NETs.[1] They have a variable age of presentation and a slight female preponderance of about 2:1.[2] It was initially believed that they arise by migration from the neural crest cells, but now it is accepted that they arise from pluripotent stem cells in the gastrointestinal system.[3] GB-NETs may arise from endocrine cells appearing in the neck, body and fundus of the gall bladder, induced by gastric or intestinal metaplasia.[4 5] They can be associated with neurofibromatosis type 1 (NF-1), which is one of the most common hereditary cancer syndromes and has an autosomal dominant inheritance pattern. When associated with NF-1, cutaneous lesions much precede the gastrointestinal manifestations, and there is a general paucity of symptoms.[6] Symptoms tend to be non-specific and compose of upper abdominal discomfort or pain, jaundice and weight loss. The development of a carcinoid syndrome is rare. Cholelithiasis may be an associated finding.[5] As per WHO, GB-NETs are classified as grade 1 NET, grade 2

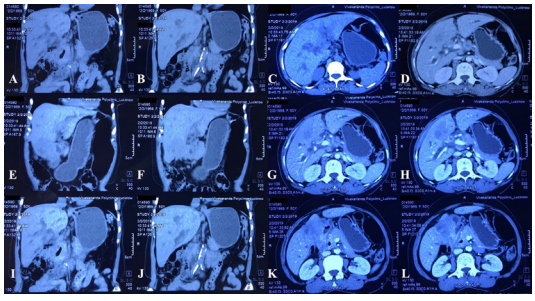

Figure 1 CT scan of the abdomen reveals approximately 52×48 mm ill-defined heterogeneously enhancing lesion involving the gall bladder fossa, which has invaded the adjacent liver parenchyma. The lesion has also invaded the duodenum and the common bile duct at the porta hepatis. The confluence of the hepatic duct is patent.

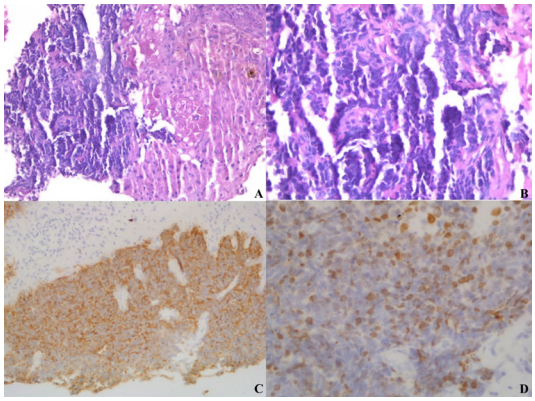

Figure 2 Section shows liver biopsy infiltrated by tumour cells (A) (H&E 200×). Higher power shows tumour cells with hyperchromatic nuclei, fine chromatin, inconspicuous nucleoli and scant cytoplasm (B) (H&E 630×). Tumour cells are positive for synaptophysin (C) (200×). Tumour cells show high MIB1 labelling index (D) (200×).

Learning points

- Neuroendocrine tumours of the gall bladder are rare, aggressive tumours that present with non-specific symptoms.
- Gall bladder neuroendocrine tumours may be associated with an underlying hereditary tumour syndrome, and there is a need to screen for gastrointestinal malignancies in such patients.
- Overall survival is poor even with multimodality treatment.

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To cite: Chakrabarti D, Qayoom S, Ghosh A, *et al*. *BMJ Case Rep* 2019;**12**:e229684. doi:10.1136/bcr-2019-229684

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NET, neuroendocrine carcinoma (large cell or small cell type) and mixed adenoneuroendocrine carcinoma.[7] They express neuroendocrine markers on immunohistochemistry.[7] GB-NETs have an aggressive clinical course and are often unresectable at the time of diagnosis. En bloc surgical resection forms the best chance for cure in early lesions, but patients develop recurrent or metastatic disease even after complete surgical resection.[8] Most cases are managed by palliative chemoradiotherapy. Data from the Surveillance, Epidemiology and End Results Program database report a median survival of only about 10 months, with a 5-year survival rate of 36.9% in carcinoids and 0% in small cell carcinoma.[5]

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Contributors DC: concept, design, manuscript writing and image acquisition. SQ: supervision, histopathological work-up, image acquisition and critical analyses. AG: concept, design and image acquisition. RG : supervision and critical analyses. All authors read and approved the final draft.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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