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Case Report Open Access

EUS-FNA Diagnosis Cytology of Endocrine Tumor Recurrence

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Abstract

We examined a recurrent endocrine tumor patient who had undergone preoperative diagnosis by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). The cytomorphology and immunostaining patterns at onset were different from those seen at recurrence, and according to WHO classification we diagnosed the former condition as well-differentiated endocrine tumor and the latter condition as well-differentiated endocrine carcinoma. Endocrine tumors show great diversity of cytomorphology according to their malignancy, and we consider that understanding this is important to conducting cytoscreening diagnosis by cytomorphology.

Keywords: Endocrine cancer; Recurrence; Salt-and-pepper chromatin; Intranuclear inclusion bodies; Spindle cells

Introduction

Pancreatic endocrine tumors are comparatively rare, accounting for approximately 1.5% to 2.0% of all pancreatic tumors [1,2]. Of those, 15% to 30% are non-functional tumors, of which over 60% are malignant with a 5-year survival rate of just 30% [3]. In our investigation we examined a patient with recurrence of non-functional endocrine tumor, performing a preoperative diagnosis based on cytomorphology and immunostaining of samples derived by EUS-FNA.

Case Report

A 60-year-old male patient underwent abdominal ultrasonography, which revealed border irregularity on the head of the pancreas, part of which comprised a solid tumor mass measuring approximately 20 mm in diameter. After EUS-FNA, pancreaticoduodenectomy was conducted, and the patient was diagnosed as having neuroendocrine tumor (UICC: pT4). About 2 years and 6 months later, 20mm mass and 30mm mass were detected in S4 and S5, respectively, in the liver, and recurrence was suspected. Liver metastasis and the remaining pancreatic body were excised.

Result

Cytological findings

FNA at the time of onset was performed using a 22G needle. We observed salt-and-pepper chromatin, rosette formation, nuclear eccentricity, and intranuclear inclusion bodies by Diff-Quik and Pap staining (Figure 1A). Immunostaining on cell blocks produced positive test results for CD56, synaptophysin, and chromogranin A, all giving definite diagnoses of endocrine tumor. Aspiration at the time of recurrence was performed with a 22G needle. We observed intranuclear inclusion bodies, nuclear positivity, sheet-like cluster (Figure 1B), anisokaryosis, cell division (Figure 1C), and spindle cells (Figure 1D) by Diff-Quik and Pap staining (Table 1).

Immunostaining on cell blocks produced a positive test result for CD56, synaptophysin, and a negative result for chromogranin A, giving a definite diagnosis of endocrine carcinoma. At the time of the onset, MIB-1 index was 20% and CK19 was positive (Figure 2A, B). At the time of recurrence, MIB-1 index was 25% and CK19 was positive (Figure 2C, D).

Discussion

Non-functional endocrine tumors, as seen in this patient, comprise 20% to 40% of pancreatic endocrine tumors. They show no increase in blood concentrations of hormones and are clinically asymptomatic [4].

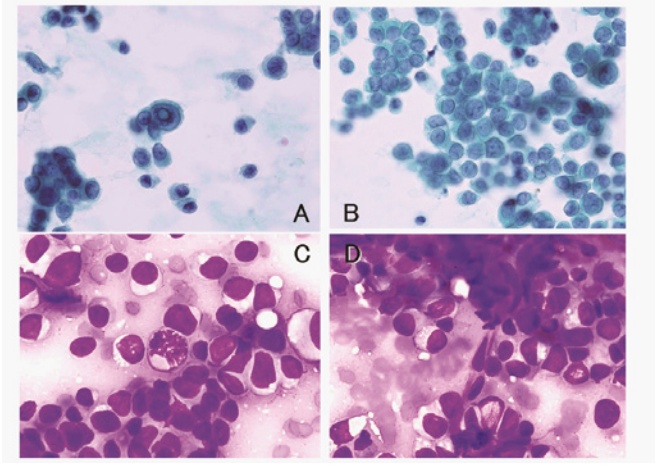

Figure 1: A: Intra-nuclear inclusion bodies by Pap (x1000). B: Sheet-like cluster of round uniform tumor cells predominate by Pap (x1000). C: Anisokaryosis, cell division by Diff-Quik (x1000). D: Spindle cells by Diff-Quik (x1000).

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Thus, early discovery by PET, CT, EUS-FNA or other types of imaging or cytoscreening is considered to be important.

Important indicators in cytoscreening for endocrine tumors are scattered cells, inclusion body cells, rosette formation, nuclear eccentricity, and salt-and-pepper chromatin morphologies. It has been reported that these cytomorphologies show clearly different cytological findings from those of adenocarcinoma and STPN [5,6]. We also observed these cytomorphologies in this patient at the time of onset, which we were able to diagnose through cytoscreening by Diff-Quik and Pap staining. At recurrence, in addition to the above-mentioned cytological findings, we also observed a variety of other cytological findings, such as nuclear positivity, spindle cells, cell division, inclusion body cells, and papillary growth. The difference in tumor cytomorphology between onset and recurrence is considered to be related to the malignancy of endocrine tumors. Mai et al. [7] carefully examined cytological findings in 30 pancreatic endocrine tumor patients, but because the cytological findings for well-differentiated endocrine carcinoma are also seen in other diseases besides endocrine tumor, a differential diagnostic method is necessary. We consider that the key points of cytoscreening in this case are that cells with salt-and-pepper chromatin (which are an important guide for cytodiagnosis of endocrine tumor) manifest sheet-like and papillary growth and show variation and lack of binding in the periphery of cell clusters. The observation of inclusion body cells at both onset and recurrence appears to be a cytological characteristic of this case and may be useful in cytoscreening of endocrine tumors.

cytomorphology	at the time of onset	recurrence
nuclear eccentricity	+	+
scattered	+	+
rosette formation	+	+
salt-and-pepper chromatin	+	+
inclusion bodies	+	+
papillary growth	-	+
sheet-like cluster	-	+
cell mitosis	-	+
spindle cells	-	+
Nucleolus	-	+
Immunostaining		
CD56	+	+
Synaptophysin	+	+
ChromograninA	+	-
MIB-1 index	20%	25%
CK19	+	+

Table 1: At the time of onset, recurrence of Cytomorphology and Immunostaining.

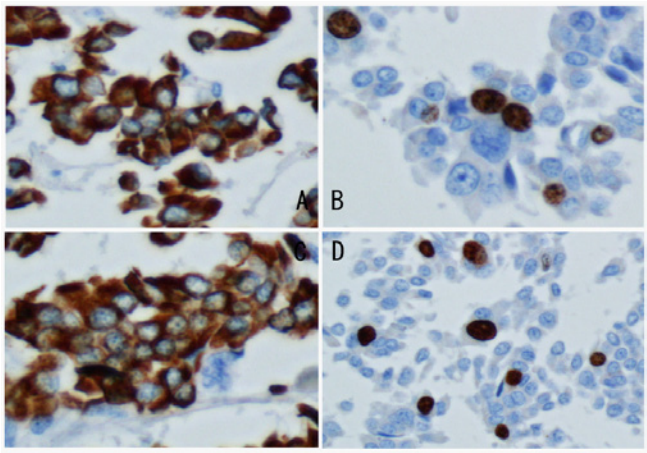

Figure 2: A: The tumor cells positive for CK19 of at the time of onset (x400). B: The tumor cells positive for MIB-1 of at the time of onset (x400). C: The tumor cells positive for CK19 of recurrence (x400). D: The tumor cells positive for MIB-1 of recurrence (x400).

Chromogranin A, synaptophysin, and cell adhesion molecule CD56 are typical markers of endocrine tumor. These markers can be diagnostic of tumor formation depending on tumor differentiation. In cases of endocrine tumor, synaptophysin and CD56 test positive with great frequency, regardless of malignancy or differentiation, but chromogranin A may sometimes test negative [8]. At the time of recurrence, the case we examined showed a positive test result both for synaptophysin and CD56, but a negative result for chromogranin A. These results appear to match with the cytomorphology that indicates endocrine carcinoma at recurrence. These evidences of tumor hormone production are often obtained by using operation materials to determine the malignancy of tumors, but we consider that by placing cell samples collected by EUS-FNA on cell blocks, it is possible to make a preoperative classification of the disease condition. Vikram et al. [9] reported that MIB-1 and CK19 are effective for the malignancy grade and prognostic factor of pancreatic neuroendocrine tumor [10,11]. In this case, the results of immunostaining at the time of the onset indicated that MIB-1 index was 20% and CK19 was positive, and so it was considered that when strong cellular atypia is detected through the cytoscreening at the time of the onset, it is possible to predict prognosis by conducting the immunostaining of MIB-1 and CK19.

The cellular morphology of this case showed great diversity and could be useful for the classification of endocrine tumors. We believe that continued research with more such cytologically diverse cases is necessary.

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