



ORIGINAL RESEARCH PAPER

Pathology

MALIGNANT ASCITES OF UNKNOWN PRIMARY – A DIAGNOSTIC DILEMMA

KEY WORDS:

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ABSTRACT

Malignant ascites indicates the presence of malignant cells in the peritoneal cavity and is a grave prognostic sign with poor survival of the patient. Peritoneal carcinomatosis accounts for approximately 10% of all cases of ascites. Tumors causing carcinomatosis are more commonly secondary peritoneal surface malignancies which include: ovarian, colorectal, pancreatic and uterine; extra-abdominal tumors originating from lymphoma, lung and breast; and a small number of unknown primary tumors. The diagnostic accuracy of Exfoliative Effusion cytology is still a challenging task for cytopathologists. The diagnosis of metastases from carcinomas of unknown primary site (CUP) in serous effusions is distinctly difficult. We report an unusual case of a sixty year female who presented with ascites with no history of any known primary malignancy. The characteristic Indian file arrangement of the cells seen in the stained smears prepared from ascitic fluid raised the possibility of Lobular carcinoma breast which on subsequent detection of the lump breast, FNAC and histopathological examination was proved. Immunohistochemistry was applied as an adjunct to the cytological diagnosis which is otherwise a gold standard to the confirmation of diagnosis in malignant effusions. The aim of this case report is to highlight the diagnostic accuracy of conventional effusion cytology and to bring awareness of carcinoma breast among females, physicians and surgeons.

Introduction

Ascites is the accumulation of fluid in the peritoneal cavity that exceeds 25ml. It can be transudative or exudative in nature. Causes of ascites can be categorized as neoplastic and non-neoplastic. The most frequent non-neoplastic causes of ascites are: cirrhosis, portal vein thrombosis, chronic heart failure, nephrotic syndrome, pancreatitis and tuberculosis. Metastatic Ascites occurs in approximately 15-50% of patients with cancerous diseases, frequently in the ovarian, endometrial and gastrointestinal cancers. More rare causes of ascites include: breast cancer, non-Hodgkin's lymphoma, mesothelioma, multiple myeloma and melanoma [1]. The presence of malignant ascites is a grave prognostic sign. While survival in this patient population is poor, averaging about 20 weeks from the time of diagnosis, quality of life can be improved through palliative procedures [2]. The diagnosis of malignant ascites is a challenging problem both for the clinician and cytopathologist and the latter should be extra vigilant in reporting the malignant effusions.

Case report

Here we present a case of a 60 years old female with chief complaints of breathlessness and ascites since 2months. A sample of ascitic fluid received for malignant cells was centrifuged and smears stained with H&E, Giemsa and Papanicolou stains. Microscopic examination revealed singly scattered small round to elliptical cells, many of which were arranged in characteristic indian-file patterns consisting of 3 to 5 cells (fig 1). The tumor cells had scanty cytoplasm, rare cytoplasmic vacuoles and marked chromatin clumping with small, but prominent nucleoli. A presumptive diagnosis of metastasis of lobular carcinoma was suspected. Patient was re-examined and on complete physical examination, we noticed a right breast lump which was present since 15yrs. As the lump was asymptomatic, patient was not aware of that and therefore she did not seek any treatment for the same. FNAC of breast lump was done and smears so prepared were stained with H&E and Giemsa stains. Microscopic examination revealed small cells arranged in characteristic indian file pattern (fig 2). A presumptive diagnosis of lobular carcinoma breast with metastasis to peritoneal cavity was made. The specimen after modified radical mastectomy was obtained and subjected to histopathological examination, so as to classify special subtype of invasive breast carcinoma. Based on morphology and pattern, the diagnosis of classic Invasive lobular carcinoma breast (fig 3) was made and confirmed by immunohistochemical staining with loss

of E-cadherin expression in tumor cells (fig.4). Lymph nodes showed reactive hyperplasia.

Discussion

Carcinoma of the breast is a histologically heterogeneous disease. Invasive lobular carcinoma (ILC) accounts for 8–14% of all breast cancers [3, 4]. A negative E-cadherin stain is a sensitive and specific biomarker to confirm the diagnosis of invasive lobular carcinoma. Positive E-cadherin expression was also associated with tubulolobular variant of ILC. Data from a recent epidemiologic study [5] indicates that for unknown causes the incidence of this type of breast cancer is increasing, especially among postmenopausal women.

ILC is difficult to detect on clinical and radiological examination because of its diffuse infiltration and absence of well-defined margins [6]. Compared often to IDC, it has significantly different pathologic behavior that has marked clinical and treatment consequences. ILC is characterized by a unique growth pattern that displays an increased frequency for contralateral breast involvement and is often multifocal and multicentric [7, 8]. In the documented case it was a diffuse mass involving almost the whole of the right breast with no involvement of contralateral breast. Non cohesive cells and tendency to infiltrate could be linked to a higher probability of ILC recurrence and metastatic disease [9]. Most of the carcinoma breast spreads through lymphatic and haematogenous routes. Common sites of metastasis are - lungs, liver, bone and central nervous system for both ILC and IDC. ILC has been found to metastasize to the peritoneum-retroperitoneum, gastrointestinal tract and genitourinary organs [10, 11]. In the documented case we present a case of unusual metastatic spread of ILC to the peritoneal cavity, through the transcoelomic route bypassing the other common sites like liver, lung and bone. Other uncommon presentations of ILC include bilateral krukensberg tumor, vaginal bleeding etc.

Summary and Conclusion

The rationale of this case report is that ILC usually presents with lump and lymph node metastasis while in the present case it manifested as ascites. The registered case emphasizes the significance of careful examination of characteristic cell pattern and individual cell morphology in clinching the diagnosis of an unknown primary. In the absence of any clinical history, the alert cytopathologist, while examining the smears of malignant ascites

especially in females, should consider the possibility of primary from the abdominal organs as well as extra abdominal sites such as breast.

Furthermore, the statistics show that Carcinoma breast is inarguably the emerging malignancy seen in females in the Indian set up and hence there is a stringent need to sensitize the women about the disease and seeking early medical help to reduce the morbidity and mortality rates.

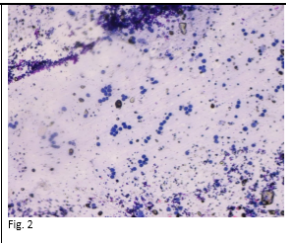
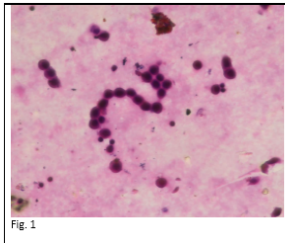


Fig. 1: [H&E, 40x]: Indian file arrangement of cells in ascitic fluid

Fig. 2: [Giemsa, 10x]: Single file arrangement of cells in breast lump

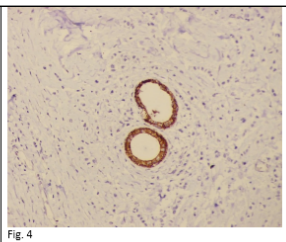
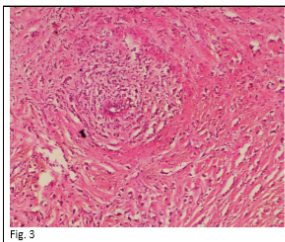


Fig. 3: [H&E, 10x]: Histopathology of lump breast showing onion skin lesion and single file arrangement of cells

Fig. 4: [20x]: Negative E-cadherin expression with positive control

REFERENCES

1. Terlikiewicz J, Marciniak L, Wodobrzusze. (Ascites). *Pol Med Paliat.* 2003; 2(2): 105-109 (in Polish).
2. Malignant ascites: A review of prognostic factors, pathophysiology and therapeutic measures. *World J Gastrointest Surg.* 2012 Apr 27; 4(4): 87-95
3. Martinez V, Azzopardi JG: Invasive lobular carcinoma of the breast: incidence and variants. *Histopathology.* 1979, 3: 467-488.
4. Borst MJ, Ingold JA: Metastatic patterns of invasive lobular versus invasive ductal carcinoma of the breast. *Surgery.* 1993, 114: 637-641. discussion 641-632
5. Li CI, Anderson BO, Porter P, Holt SK, Daling JR, Moe RE: Changing incidence rate of invasive lobular breast carcinoma among older women. *Cancer.* 2000, 88: 2561-2569. 10.1002/1097-0142(20000601)88:11<2561::AID-CNCR19>3.3.CO;2-O.
6. Harake MD, Maxwell AJ, Sukumar SA. Primary and metastatic lobular carcinoma of the breast. *Clin Radiol.* 2001; 56(8):621-630.
7. Doyle DJ, Relihan N, Redmond HP, Barry JE. Metastatic manifestations of invasive lobular breast carcinoma. *Clin Radiol.* 2005;60(2):271-274.
8. P.Carcoforo, et al., Infiltrating lobular carcinoma of the breast presenting as gastrointestinal obstruction: a mini review, *J.Cancer*3(2012)328-332.
9. T.Korhonen, et al., The impact of lobular and ductal breast cancer histology on the metastatic behavior and longterm survival of breast cancer patients, *Breast*22(6) (2013) 1119-1124.
10. Sastre-Garau X, Jouve M, Asselain B, et al. Infiltrating lobular carcinoma of the breast. Clinicopathologic analysis of 975 cases with reference to data on conservative therapy and metastatic patterns. *Cancer.* 1996; 77(1):113-120.
11. Harris M, Howell A, Chrissohou M, Swindell RI, Hudson M, Sellwood RA. A comparison of the metastatic pattern of infiltrating lobular carcinoma and infiltrating duct carcinoma of the breast. *Br J Cancer.* 1984; 50(1):23-30.