

## Case Report

# Pleomorphic giant cell adeno-carcinoma gall bladder: a histological rarity and a surgical dilemma

M. S. Ray<sup>1</sup>, B. S. Deepak<sup>1\*</sup>, Aneeta Jassar<sup>2</sup>, Kunjan Pathania<sup>2</sup>

<sup>1</sup>Department of Surgery, Military Hospital, Jalandhar Cantt, Jalandhar, Punjab, India

<sup>2</sup>Department of Pathology, Military Hospital, Jalandhar Cantt, Jalandhar, Punjab, India

**Received:** 05 February 2017

**Accepted:** 03 March 2017

### \*Correspondence:

Dr. B. S. Deepak,

E-mail: [deepaksatyapal@gmail.com](mailto:deepaksatyapal@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

Undifferentiated pleomorphic giant cell adeno-carcinoma of the gall bladder (GB) is an extremely rare condition and is usually an incidental diagnosis. Here, we describe a rare case of gall bladder carcinoma in a 50 year old lady who presented with upper abdominal pain and palpable lump in the right hypochondrium. Computed tomography and Ultrasonography of the abdomen showed an ill-defined giant heterogeneous soft tissue mass involving gall bladder and adjacent liver parenchyma with obvious regional adenopathy. Metastatic work-up was abnormal and the patient underwent radical cholecystectomy. Histopathology and immunohistochemistry (IHC) study revealed Undifferentiated carcinoma or pleomorphic giant cell adenocarcinoma of gall bladder involving the adjacent hepatic parenchyma. Patient received post-op adjuvant chemotherapy and is under monthly follow-up. The present case emphasizes the need for better detection, evaluation and analysis of such rare entities, to identify their natural course and effective treatment modalities.

**Keywords:** Carcinoma gall bladder, Cholecystectomy, Giant cell, Pleomorphic, Undifferentiated

### INTRODUCTION

Undifferentiated carcinoma or giant cell adeno-carcinoma of the gall bladder is a rare condition with poor prognosis. Exact aetiology is not known. It is impossible to differentiate from other GB carcinoma based on clinical presentation and radiological investigation diagnosis is only possible by HPE and IHC. Computed tomography and Ultrasonography of the abdomen showed an ill-defined giant heterogeneous soft tissue mass involving gall bladder and adjacent liver parenchyma with obvious regional adenopathy.<sup>1</sup> Metastatic work-up was abnormal and the patient underwent radical cholecystectomy. Histopathology and immunohistochemistry (IHC) study revealed Undifferentiated carcinoma or pleomorphic giant cell

adenocarcinoma of gall bladder involving the adjacent hepatic parenchyma. Patient received post-op adjuvant chemotherapy and is under monthly follow-up.

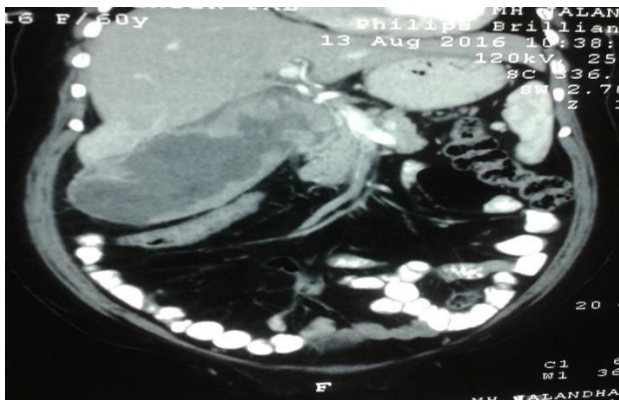
### CASE REPORT

A 50-year-old woman was admitted with a 12 month history of dull pain and mass in the right upper abdomen. No history of anorexia, anemia, asthenia, weight loss and jaundice. On general examination, she was well built and nourished with no jaundice or lymphadenopathy. Abdominal examination revealed palpable firm and non-tender globular mass in right hypochondrium, mild hepatomegaly and no ascitis. Laboratory investigation revealed normal haematological findings and Liver function tests were within normal limits. Tumor markers-

CA 19-9 was 173.67U/ml (Normal: <37), AFP was 48.98 ng/ml (N<10) and CEA was 3.32 ng/ml (N <3.00) were abnormally raised. Abdominal ultrasound and computed tomography (CECT) demonstrated a markedly distended gallbladder, measuring 16 x 9 cm, with cholelithiasis (Figure 1 and 2).



**Figure 1: Distended gall bladder with gross irregular wall thickening.**



**Figure 2: Axial section: large gall bladder (16x10x07) cm diffuse non-uniform thickening of the wall. maximum thickness 3.4 cm.**

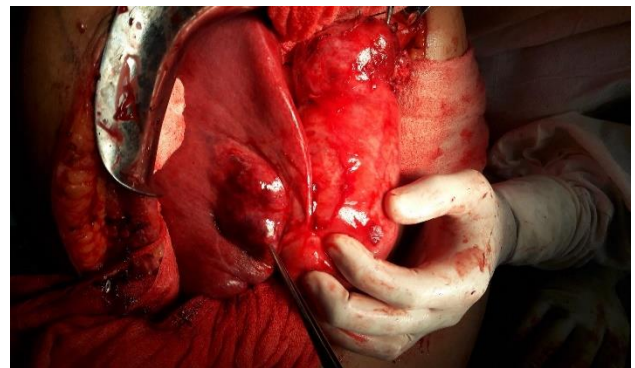


**Figure 3: Intra-op view: smooth surfaced “giant gall bladder”, size (16x10x07 cm).**

No biliary dilatation and regional adenopathy were noted, Chest X-ray was normal. Based on the patient's clinical picture and the results of the tumor markers and imaging studies, a working diagnosis of carcinoma of gallbladder was made and planned for radical cholecystectomy. At laparotomy, a large, bosselated, highly vascular mass was found arising mainly from fundus of the gallbladder with involvement of adjacent liver parenchyma with significant lymphadenopathy presumed to be lymph nodal metastases (Figure 3-5).



**Figure 4: Per-op view: giant gall bladder.**



**Figure 5: Per-op view: giant gall bladder showing infiltration to segment V & IVa liver; abutting transverse colon and displacing 2nd and 3rd part of duodenum.**



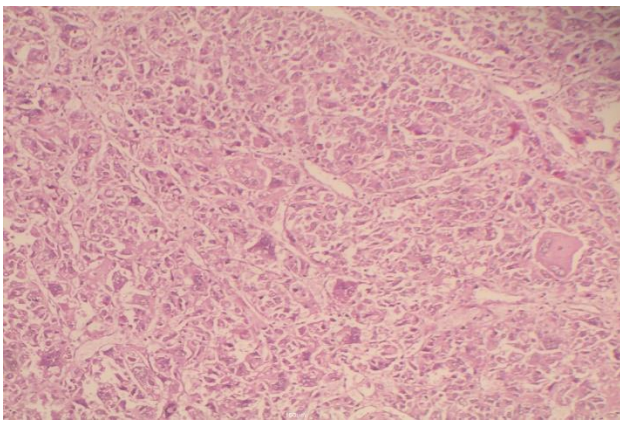
**Figure 6: A friable, fungating, exophytic mass filling the entire lumen of the gallbladder.**



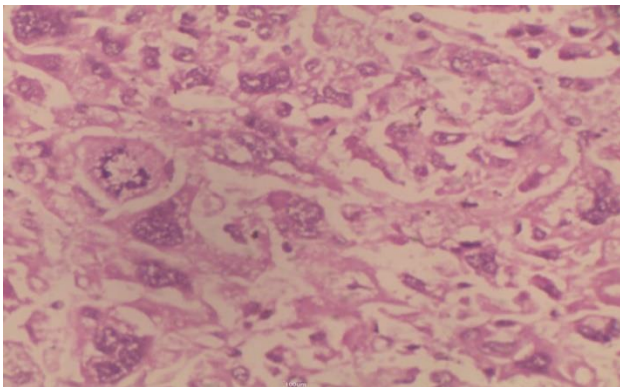
A radical cholecystectomy was under taken, resecting segments IV (a), IV (b) & V, en-mass with gall bladder and regional lymphadenectomy was done (Lymph node of Lund, peri-choledochal & retropancreatic chain and sentinel lymph node). Abdomen was closed en-mass with sub hepatic drains. Post-op recovery was uneventful, allowed oral feeds by 04<sup>th</sup> day post-op. Drains removed on 05<sup>th</sup> post-op day and sutures on the 15<sup>th</sup> day post-surgery and discharged home.

### Pathological findings

On gross examination, the gall bladder measured 12x12x6cm, while the attached portion of liver measured 9x3x1.2 cm. On cutting open, a fungating, exophytic and friable growth was seen involving the entire gall bladder (Figure 6) and extending into the adjoining liver.



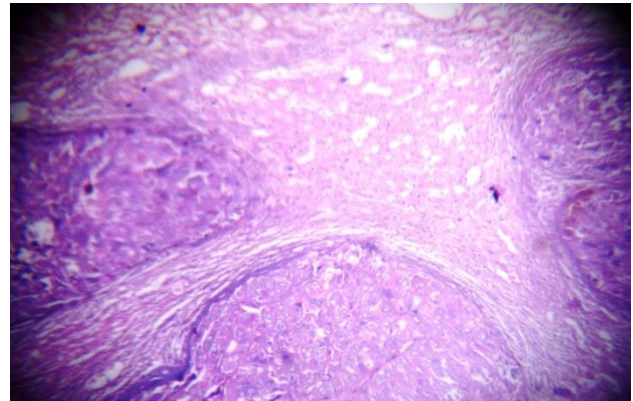
**Figure 7: Sheets and cords of pleomorphic polygonal neoplastic cells (H&E, 100X).**



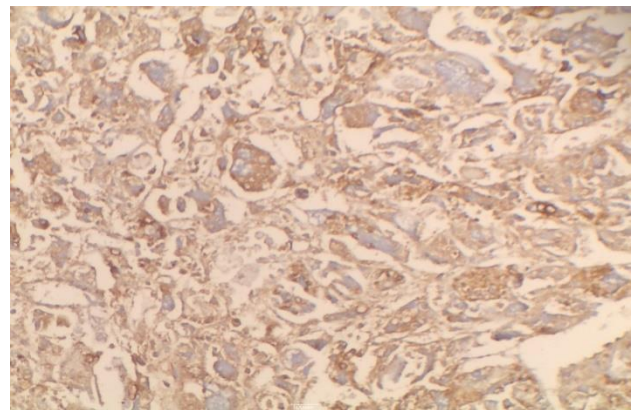
**Figure 8: Giant cells with marked pleomorphism (H&E, 400X)**

On microscopy, sections showed sheets, cords and nests of large neoplastic cells (Figure 7). These polygonal cells had abundant eosinophilic cytoplasm, pleomorphic vesicular nuclei and prominent nucleoli. Interspersed between the tumor cells were numerous giant cells with marked pleomorphism and bizarre nuclei (Figure 8 and 9). Occasional giant cells exhibited 'cellular cannibalism'. Numerous typical and atypical mitoses

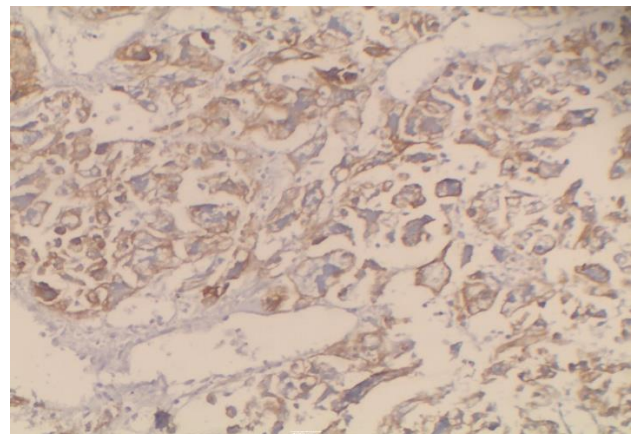
(>5/10HPF) were noted. There were no spindle cells, squamous cells, gland formation, mucin production or heterologous elements. There was widespread necrosis and lymphovascular invasion was present. The tumor had replaced the entire mucosa and muscular layer and was also seen infiltrating into the liver bed (Figure 10). However the surgical resection margins of the liver were free of tumor. Staging: pT3NxMx.



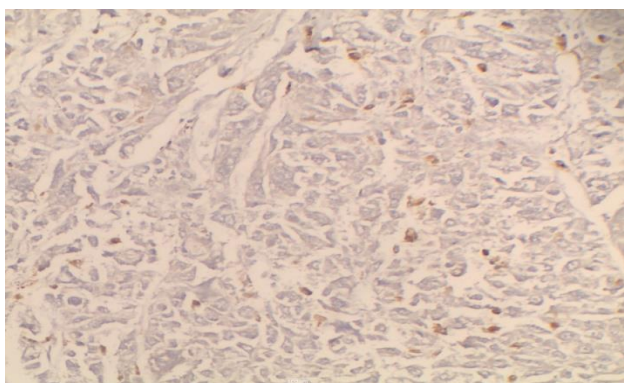
**Figure 9: Nests of tumor cells infiltrating the tumor bed (H&E, x100).**



**Figure 10: Positivity of tumor cells for pancytokeratin (CK, 200X).**



**Figure 11: Positivity of tumor cells for epithelial membrane antigen (EMA, 200X).**



**Figure 12: No staining of giant cells with CD 68 (CD 68, 200X).**

Immunohistochemistry revealed cytokeratin positivity in both the tumor cells and the giant cells (Figure 11). The latter were CD68 negative (Figure 12).

## DISCUSSION

The incidence of gall bladder carcinoma is 1.2 cases per 10,000 cases per year. Histologically rarer types, such as Clear cell, Mucinous, Squamous cell, Adenosquamous, signet ring cell, small cell, spindle cell, giant cell and undifferentiated carcinoma of gall bladder accounts for 10.4% to 10.9%, of all gall bladder carcinomas.<sup>1</sup> Undifferentiated carcinoma pleomorphic giant cell adenocarcinoma of the gall bladder has four histologic variants, namely Spindle and Giant cell type; Osteoclast cell (OC)-like giant cell type, Small cell type and Nodular or Lobular type.<sup>2</sup> The most common and most anaplastic variant is the Giant cell (GC) type, which was the diagnosis in this case.

Undifferentiated carcinoma or pleomorphic giant cell adenocarcinoma of gall bladder represent a group of neoplasms characterized by a wide spectrum of morphology and varying proportions of polygonal, round, spindle or multinucleated giant cells. Areas of well-differentiated adenocarcinoma are found in two-thirds of the tumors, representing a transition from the pleomorphic component to well-differentiated elements.<sup>3</sup> The final third of undifferentiated carcinoma cases, as in our case, consist exclusively of undifferentiated neoplastic cells. Our case too showed no areas of gland formation or mucin production after exhaustive sampling. Undifferentiated carcinoma or pleomorphic giant cell adeno-carcinoma with giant cells must be distinguished from undifferentiated carcinoma with Osteoclast-like giant cells.<sup>4</sup> While the former show pleomorphic giant cells with bizarre nuclei and immunohistochemical evidence of epithelial derivation (i.e. cytokeratin positivity), as was the case in our patient,

in undifferentiated carcinoma with Osteoclast-like giant cells, the giant cells are more monomorphic and of histiocytic origin (and therefore cytokeratin negative but CD 68 positive).<sup>5,6</sup> This case represents an unusual variant of undifferentiated carcinoma of the gall bladder. The presence of widespread necrosis, high mitotic index, serosal invasion and liver bed infiltration portends a poor post-surgical outcome in this case.

## CONCLUSION

Undifferentiated carcinoma or giant cell adeno carcinoma of the gall bladder is rare condition with poor prognosis. Exact aetiology is not known. It is impossible to differentiate from GB carcinoma based on clinical presentation and radiological investigation. Diagnosis is only possible by HPE and IHC. It is unusually diagnosed postoperatively based on histological findings and Immuno Histochemistry (IHC). Surgery is the mainstay of treatment with ill-defined role of chemo-radiotherapy with poor outcome. We present this case to highlight the rarity of this entity and utility of immunohistochemistry analysis.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

1. Guo KJ, Yamaguchi K, Enjoji M. Undifferentiated carcinoma of the gallbladder. A clinicopathologic, histochemical, and immunohistochemical study of 21 patients with a poor prognosis. *Cancer*. 1988; 61(9):1872-9.
2. Nishihara K, Tsuneyoshi M. Undifferentiated spindle cell carcinoma of the gallbladder: a clinicopathologic, immunohistochemical and flow cytometric study of 11 cases. *Hum Pathol*. 1993; 24(12):1298-305.
3. Medhi P, Dowerah S, Dutta U, Dutta A. Undifferentiated carcinoma of the gall bladder: a rare entity. *Ind J of Pathol Onco*. 2016;3(1):124-8.
4. Kang YK. Undifferentiated gallbladder carcinoma with osteoclast-like giant cells – a case report. *The Korean J of Pathol*. 2007;41:127-31.
5. Diebold-Berger S, Vaiton JC, Pache JC, d'Amore ES. Undifferentiated carcinoma of the gallbladder. Report of a case with immunohistochemical findings. *Arch Pathol Lab Med*. 1995;119(3):279-82.
6. Akatsu T, Kameyama K, Kawachi S, Tanabe M, Aiura K, Wakabayashi G, et al. Gallbladder carcinoma with osteoclast-like giant cells. *J Gastroenterol*. 2006;41(1):83-7.

**Cite this article as:** Ray MS, Deepak BS, Jassar A, Pathania K. Pleomorphic giant cell adeno-carcinoma gall bladder: a histological rarity and a surgical dilemma. *Int Surg J* 2017;4:1497-1500.