

Uncommon small blue cell tumours of the uterine cervix. A report of five cases



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INTRODUCTION

The most common carcinoma of cervix is HPV associated Squamous cell carcinoma (SCC), the most frequently diagnosed patterns being non-keratinizing and basaloid. The latter two impart a blue cell appearance to the tumour, however other small blue cell malignancies are known to occur in the cervix and include small cell neuroendocrine carcinoma (SCNEC), lymphoma and PNET. We report five such cases diagnosed at our centre.

CASE REPORT

Clinical features: All cases presented with bleeding and/or white discharge per vagina. Local examination in all but case 1, revealed an ulcero-proliferative growth. In case 1 there was no visible growth. The clinical features are summarized in table 1.

Pathologic findings: In cases 1, 4 and 5, we received small biopsy. In cases 2 and 3 radical hysterectomy was done. In all cases, microscopy revealed lesion with small blue cell appearance with indiscernible cytoplasm. The lesional cells showed architecture as follows: A round cell appearance with discrete monomorphic cells was seen in case 1; In cases 2, 3 and 5 organoid nests, trabeculae, insular patterns and islands were seen; In case 4 rosette like pattern was distinct in addition to islands; Nuclear moulding and crush artefact were seen in cases 4 and 5. Necrosis was seen in cases 1, 2 and 4. In case 5, additional malignant component was seen with obvious squamous differentiation. The immunoprofile of all cases is summarized in table 2.

Diagnosis: Diffuse large B cell lymphoma (DLBCL), non GCB type in case 1; SCNEC in cases 2,3 and 4; SCC admixed with SCNEC in case 5.

DISCUSSION

Neuroendocrine neoplasms (NEN):

- Rare tumours of the female genital tract (FGT); they are classified into NE tumours (NET) and NE carcinomas (NEC).¹ NET comprises Grade 1 (carcinoid) and Grade 2 (atypical carcinoid), more common in ovary whereas NEC is more common in cervix and can be small cell (SCNEC) or large cell type (LCNEC).¹
- The mean age at diagnosis for NEC is 48.1 years.¹
- Among the NE IHC markers synaptophysin is most sensitive and chromogranin is most specific. CD 56 is less specific, however it contributes to diagnosis when there is appropriate morphology, as in case 5 of present report.
- NEC cervix has a poor prognosis. The mean 5 year overall survival rate was found to be 34% despite aggressive treatment with radical surgery, neoadjuvant or adjuvant chemotherapy and radiotherapy.²
- NEC cervix has been strongly linked to HPV 18, 16 infection, thus HPV vaccination can confer protection against these aggressive tumours.³

FGT Lymphoma (FGTL):

- Rare as primary or secondary tumours, the former were more common in a study by Kosari F et al.⁴ Mean age is 50.4 years, but affects all ages. Cases were recorded in 7 months old as well as 89 years old.⁴
- FGTL, primary or secondary, most often involve adnexa followed by mixed, uterine corpus, cervix, vagina, portio and vulva in descending order. Most common subtype is DLBCL followed by Follicular lymphoma and Burkitt lymphoma.⁴
- In the cervix, 95% were primary in a study by Kosari F et al,⁴ who considered extragenital (nodal or extranodal) invasion as secondary FGTL.
- Krol et al⁵ defined extranodal lymphomas (ENL) as lymphomas that originate and dominate at extranodal sites even when associated with disseminated disease. Primary FGTL comprise 0.2-1.1% of all ENL. They often present at an early stage (Ann Arbor stage I/II), probably due to mass effects and B symptoms are infrequent.⁶

In case 1 though initial symptoms were related to involvement of cervix, patient defaulted and presented 7 months later with stage III DLBCL.

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Table 1: Clinical features

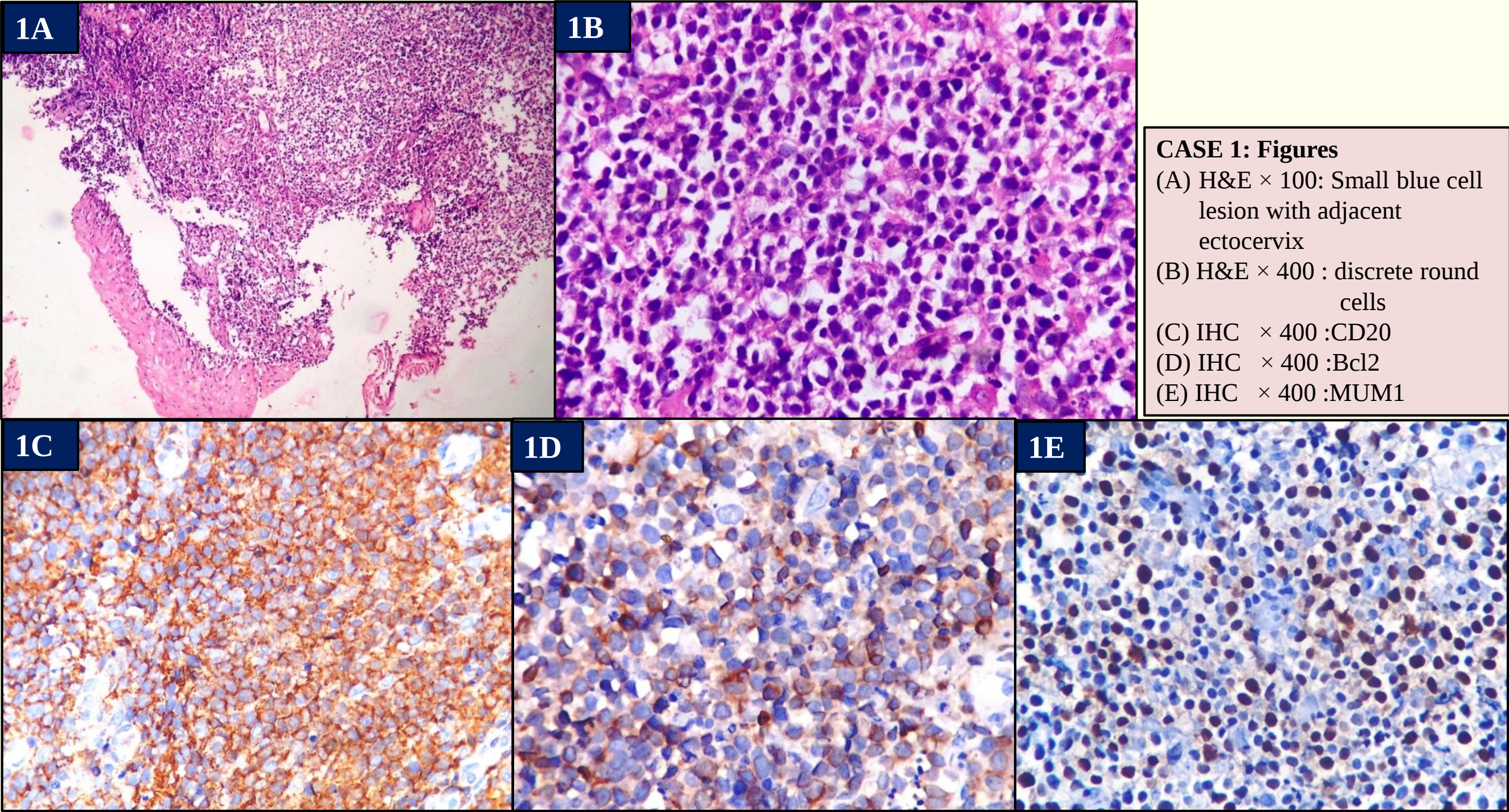
Case	Age (yrs)*	Duration	T stage	Clinical course
1	57	2m*	Pelvic wall involved	Defaulted for 7 months after initial diagnosis, then presented with clinical stage III DLBCL, received 6 cycles of R-CHOP, had a DFI* of 1 year 10 months, recurred with stage IV disease, planned for 2 cycles of BR
2	40	2m*	pT2a1	Underwent radical hysterectomy, received RT* and CT*; LTFu* later
3	58	2w*	pT1b1	Received Radical hysterectomy, RT*, CT*, developed RIT* refused further treatment, LTFu*
4	35	6m*	cII B	Recent diagnosis. Treatment not planned yet
5	71	n/k*	cIII B	Bone scan revealed multiple skeletal metastases. Planned for palliative therapy. Recent diagnosis

*yrs, years; m, months; w, weeks; n/k, not known; DFI, disease free interval; RT, radiotherapy; CT, chemotherapy; LTFu, lost to follow up; RIT, radiation induced toxicity.

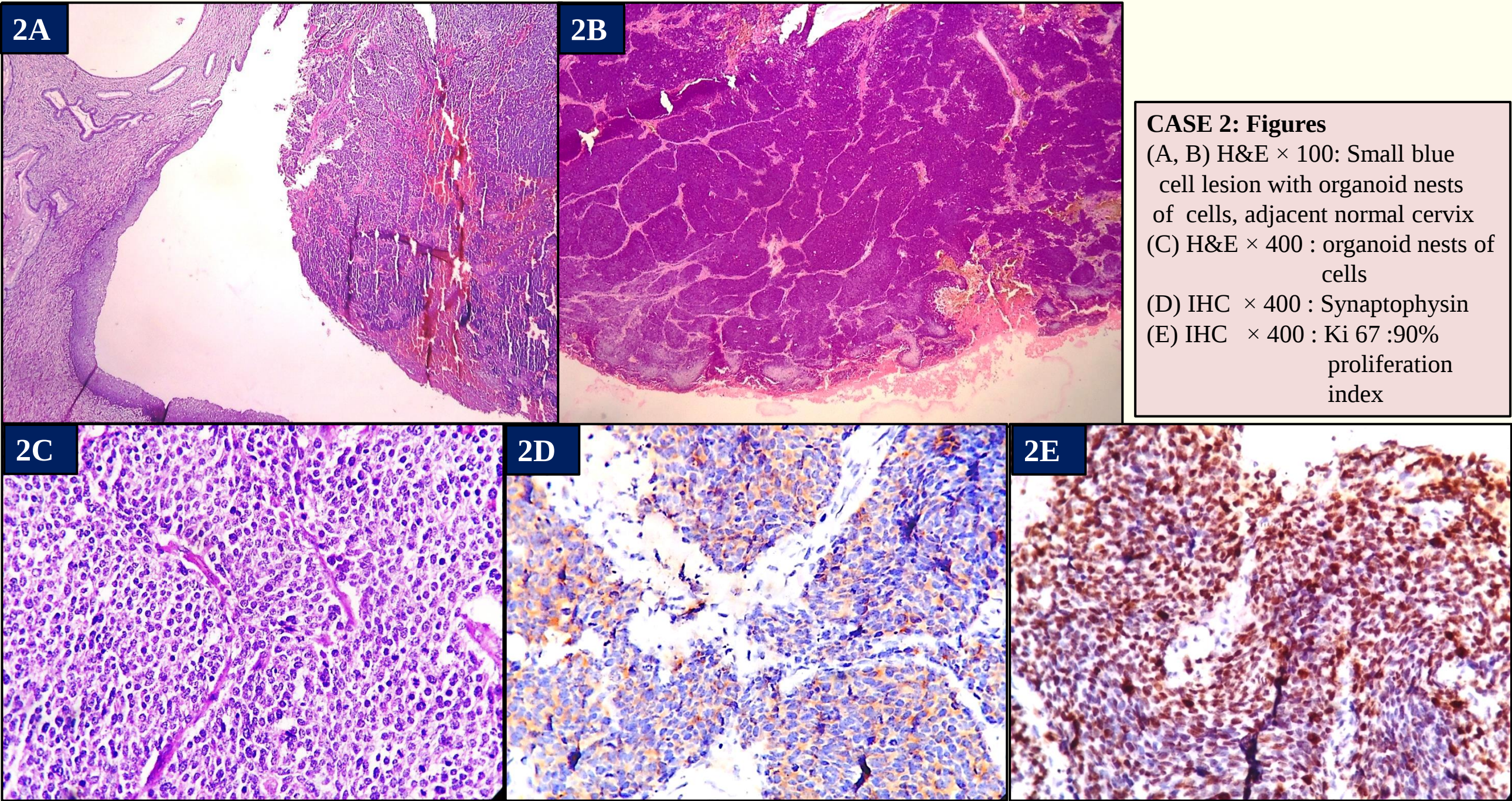
Table 2: IHC profile

Case	Neuroendocrine markers			Ki67 (%)	Other positive markers	Other negative markers
	CD56	Synapto-physin	Chromo-granin			
1	N/d#	Negative	Negative	60	CD20,Bcl2, Bcl6, Mum1	CD3,CD5, CD10, Cyclin D1,Tdt
2	N/d#	Positive	Negative	60	CK 7 (pnd)#	P63
3	N/d#	Positive	Positive	90	CK 7 (pnd)#	P40, p63
4	Positive	Positive	N/d#	60	Nil	P40
5	Positive	Negative	N/d#	60	Nil	Nil

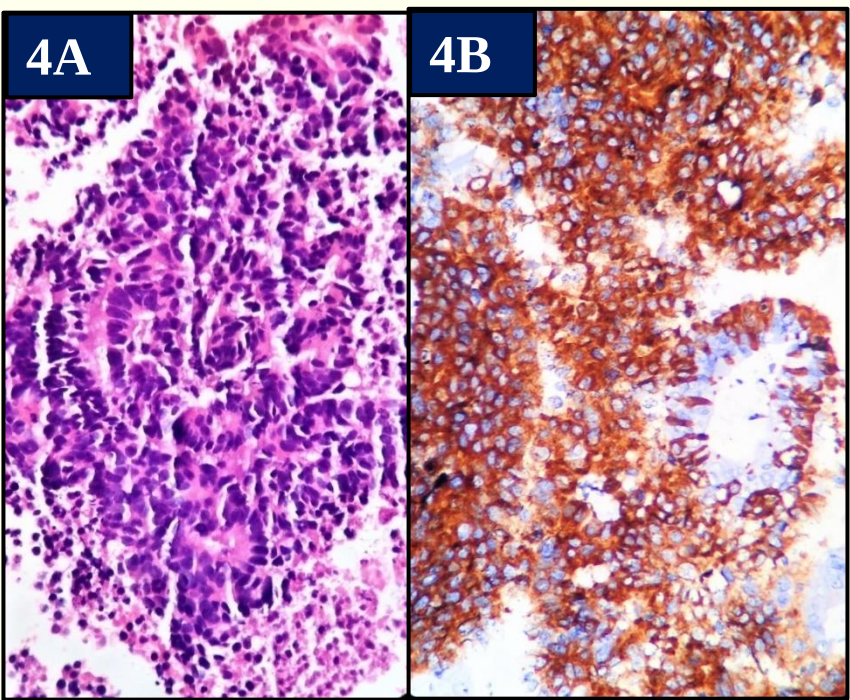
N/d, not done; pnd, perinuclear dot positive



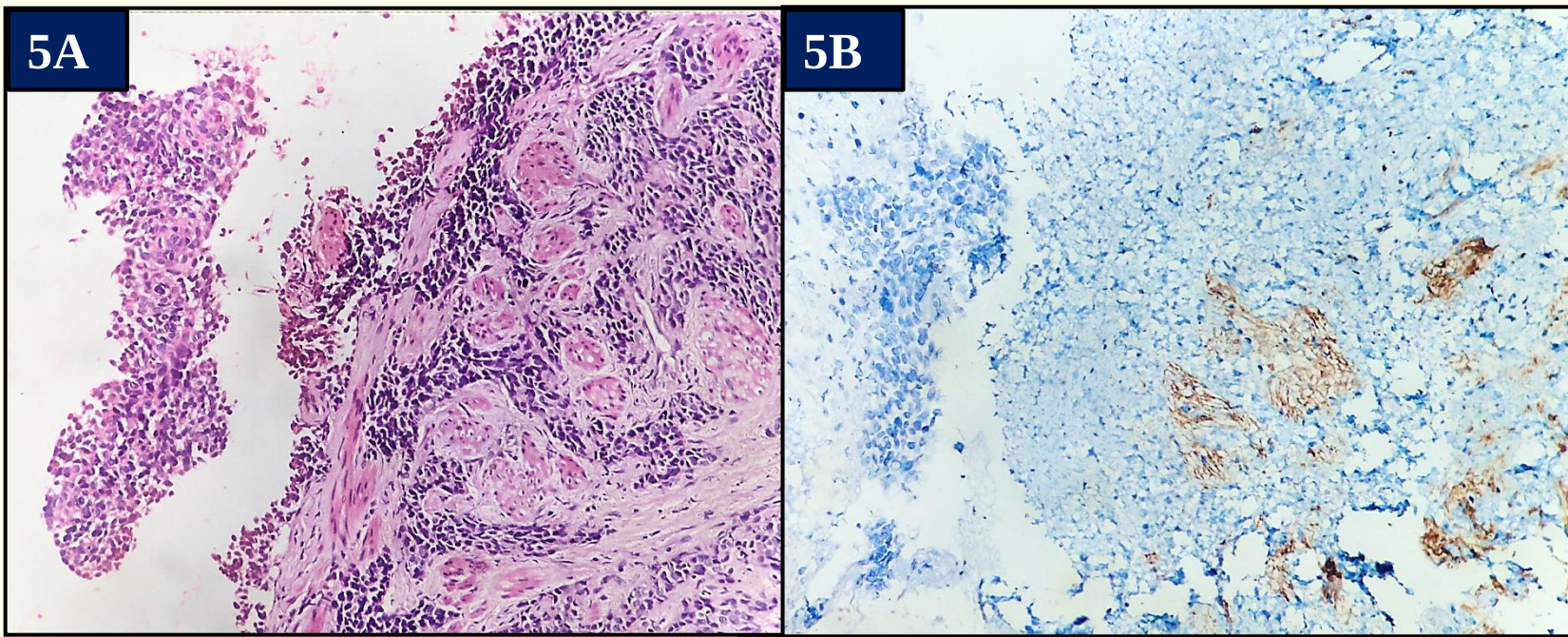
CASE 1: Figures
(A) H&E × 100: Small blue cell lesion with adjacent ectocervix
(B) H&E × 400 : discrete round cells
(C) IHC × 400 :CD20
(D) IHC × 400 :Bcl2
(E) IHC × 400 :MUM1



CASE 2: Figures
(A, B) H&E × 100: Small blue cell lesion with organoid nests of cells, adjacent normal cervix
(C) H&E × 400 : organoid nests of cells
(D) IHC × 400 : Synaptophysin
(E) IHC × 400 : Ki 67 :90% proliferation index



CASE 4: Figures
(A) H&E ×400: Rosette like pattern
(B) IHC × 400 : Synaptophysin



CASE 5: Figures
(A) H&E ×200 : SCC (right) with SCNEC (left)
(B) IHC × 200: CD56 highlights SCNEC