RESULTS

The present study was carried on several types of adrenal tumors. These tumors were obtained from patients surgically during the period from (1985 - 2002). The studied tumors fixed in 10% buffered formalin for 24 hours and processed as usual for the preparation of paraffin wax blocks. These blocks stored in the archive bank of the urology and nephrology center, Mansoura University. The patients were followed postoperatively in the outpatient clinic for available periods. They also examined clinically to determine the body weight, hypertension and blood pressure.

Histological and immunohistochemical investigations were also applied on the tumor sections. However, histopathological examination of the excised adrenal tumors revealed that these tumors could be divided into two main classes; adrenal cortical tumors (ACT) and adrenal medullary tumors (AMT). Forty patients with a percentage of 35.3% represented the cortical tumors. These tumors were subdivided into two subdivision, adenoma and carcinoma with a percentage of 24.7% and 10.6%, respectively. Moreover, 73 patients with a percentage of (54.7%) represented the medullary tumors. These tumors were subdivided into two main types, pheochromocytoma and neuroblastoma groups. The last group was subdivided, on some histopathological criteria, into neuroblastoma, ganglioneuroblastoma and ganglioneuroma (Table 5).

Meanwhile, the pheochromocytoma was represented by 39 patients (32 benign and 7 malignant). Of the 39 patients, 21 were males and 18 females. A total number of 34 patients represented the neuroblastoma

group. The number of patients was 13, 12, and 9 for NB, GNB and GN, respectively.

It could be observed that more than 60% of cases were medullary tumors. The pheochromocytoma represents the high frequency, while ganglioneuroma represent the lowest one. in view of the fact that these tumor represent different clinical entities, their results will be individually displayed.

I-Clinical findings:

A- Adrenal Cortical Tumors:

1- Adrenal cortical adenoma (ACA):

In this study, 28 patients had cortical adenoma with a percentage of (24.7%). The clinical data of these patients is outlined in Table (6).

Age distribution:

Age distributions in patients with ACA are shown in table (6a). Most of the cases (57.1%) were in the 6^{th} decades of life. While, in the first and second decades there is no patients were recorded. The age of patients ranged from 22-60 years (the average was 46.8 years).

Sex distribution:

Sex distribution in patients with ACA is shown in table (6b). 28 patients had cortical adenoma with a percentage 24.7%. There were 12 males and 16 females. The male to female ratio was 1:1.3.

Tumor Size:

The tumor size in patients with ACA is recorded in table (6c). The size ranged from 2 to 10 cm. with an average 6.65 cm. More than 60 % of

the tumors have sizes ranged from 6-10 cm. while less than 40 % of them possessed sizes ranged from 0-5 cm.

2-Adrenal cortical carcinoma:

12 patients had cortical carcinoma with a percentage 10.6%. They were 5 males and 7 females. The male to female ratio was 1:1.4. The clinical data of patients with cortical carcinoma is outlined in table (7).

Age distribution

The age of the patients ranged from 10 up to 53 years with an average age of 42 years. Nine cases were equal to or above 42 years and three cases were below the age of 42 year. Most cases are in 5^{th} decade of life.

Tumor size:

Tumor sizes recorded in all cases of ACC are shown in table (7). The average diameter was 12.8 cm. that ranged from 10-to18 cm. A male patient with an age of 24 year represented the largest ACC tumor size, while three patients represented the smallest one. Their age ranged from 42-53 years. One patient was female and the other two patients were males.

B- Adrenal Medullary Tumors (AMT):

1- Pheochromocytoma:

The clinical data of the patients with pheochromocytoma is outlined in table (8). Thirty-nine cases of pheochromocytoma were examined clinically to illustrate the sex and age of patients. In addition, the size of the tumors was recorded. The patients were followed for a definite period. Most of them were died after a follow up period reaching 58 months.

Age distribution:

The age distribution among the patients with pheochromocytoma is outlined in table (8a). The age of patients ranged from 19 up to 61 years with an average age of 36.4 years. Most of the cases are in the 4^{th} and 5^{th} decade of life.

Sex distribution:

Sex distribution in patients is represented in table (8b). 39 cases of pheochromocytoma were 15 males with a percentage 38.46% and 24 were females with a percentage 61.54%. The male to female ratio was 1:1.6.

Tumor size

The tumor size in patients with pheochromocytoma is outlined in table (8c). The sizes ranged from 4 -14 cm. with an average size 8.543 cm.

2- Neuroblastoma and ganglioneuroblastoma:

The clinical data in patients with neuroblastoma represented by 13 patients and ganglioneuroblastoma represented by 12 patients is outlined table (9).

Age distribution:

The age distribution among the patients with neuroblastoma and ganglioneuroblastoma is outlined in Table (9a). The age of patients ranged from 4 months up to 44 years (average age 6 years). Most cases are in the first year of life.

Sex distribution:

Sex distribution among the patients with neuroblastoma and ganglioneuroblastoma are recorded in table (9b). There were 13 male with percentage 52% and 12 females with a percentage 48%. The male to female ratio is 1.08:1.

Tumor Size:

The size of tumor in 25 patients with neuroblastoma and ganglioneuroblastoma is recorded in table (9c). The size of tumors ranged from 9.5 to 20 cm. with the average size of 14.56 cm.

3- Ganglioneuroma:

Nine patients had ganglioneuroma; there were five males and four females. The male to female ratio was 1.25:1. The clinical data are shown in table (10).

Age distribution:

Age distribution in patients with ganglioneuroma is recorded in table (10). The age of the patients ranged from 15 up to 35 years with average value (23.2) years. Most of the cases are in the 2nd decade of life.

Tumor size:

Tumor size was recorded in nine patients with ganglioneuroma with an average diameter of 11.7 cm. The size of tumors ranged from eight to 14cm (Table10).

The outcome of patients:

All patients were followed postoperatively in the out patient clinic for available periods ranged from 12 to 168 months for ACA and from 11 to 39 months for ACC (Table 6 & 7). The period of follow up ranged from 11 to

192 months in case of pheochromocytoma (Table 8), from 16 to 52 months for NB and from 10 to 45 months for GNB patients (Table 9). The GN patients were followed in the outpatient clinic for a period ranged from 23 to 121 months (Table 10).

All patients with adenoma and GN are alive but in case of ACC 3 patients from 12 were alive while nine patients with a percentage of 66.7 % were died from distant metastases. In case of pheochromocytoma, 32/39 patients were alive during the follow up period while 7 cases were died. Moreover, 2/13 patients with NB and 4/12 cases with GNB are still alive after adrenalectomy. The patients of this study were examined clinically to determine the body weight, hypertension, monitoring blood pressure. Moreover, radiological investigations were carried out for local or distant metastases in malignant cases.

II- Histological Observations:

A. Adrenal cortical Tumor (ACT)

1- Adrenal cortical adenoma (ACA)

The most common architectural patterns of ACA are cells grouped in a nesting or alveolar pattern. These cells have compact eosinophilic cytoplasm. Their nuclei are deeply stained and vesicular with central to eccentric nucleoli (Fig. 2). In addition, an organoid architectural is observed in most of the studied ACA (Fig. 3). In all cases of ACA, there are neither mitotic figures nor tumor necrosis.

In the present study, the tumor tissues of all cases were stained by PAS reaction and by Gordon technique to demonstrate the total hyaline globules and Reticulin fibers, respectively. The results of staining are recorded in table (11). This table showed that the PAS Positive intracytoplasmic hyaline globules (Fig. 4) were detected in 13 cases only

from the studied (ACA) 28 cases. The other 15 cases revealed negative reactivity to the PAS reaction.

Moreover, most of the ACA, (23/28) stained by Gordon technique were highly rich in the reticular fibers (Fig. 5). Moderately staining reactivity for reticular fibers was observed in 5 cases only. The reticular fibers surround the individual cells.

2- Adrenal Cortical carcinoma (ACC):

The tumor has a diffuse or solid pattern of irregular-pleomorphic cells. Most tumor cells have moderate to abundant eosinophillic compact cytoplasm. Mitotic figures were numerous with many atypical forms (Fig. 6). Sections of tumors were stained with PAS and Gordon technique for reticulin stain. The result of staining is recorded in table (11). From this table, it can be observed that the PAS positive intracytoplasmic hyaline globules were detected in eight cases of ACC (Fig. 7), while the other four cases showed negative staining. Most of the ACC tumors studied (10/12) showed a relative deficiency of the reticular fibers (Fig. 8). Two cases only of ACC gave negative results with reticulin stain.

B- Adrenal medullary tumors:

1- Pheochromocytoma:

The pheochromocytoma showed the typical cell nests (Zellballen pattern) of the chief parenchymal cells in 35 cases of the studied 39 cases (Fig. 9). Whereas, four cases only of the studied tumors showed spindling of the chief parenchyma cells. Generally, the cytoplasm of the tumor cells is often lightly eosinophillic and finely granular (Fig. 10). The nuclei were also lightly basophilic and possessed spherical shape with prominent nucleoli. Two cases of composite pheochromocytoma were studied (Fig. 11). Spindle cell schwannian stroma admixed with

pheochromocytoma. The sections of tumor were stained with PAS and reticulin stains. The results of staining are recorded in table (11). This table showed that the PAS positive intracytoplasmic hyaline globules were detected in most cases (28/39) of pheochromocytoma (Fig. 12). No hyaline globules were demonstrated in 11 cases of pheochromocytoma. Most cases of tumor were rich in reticular fibers (Fig. 13). Moreover, the results of reticulin staining showed highly rich stain ability (33/39), moderately rich (4/39) and weak stain ability (2/39) for the reticular fibers.

2- Neuroblastoma and ganglioneuroblastoma:

Neuroblastoma shows accentuation of fibro vascular stroma and tumor nodules formed of monotonous primitive cells (Fig. 14). Some areas suggest the formation of homer Wight pseudo rosettes. These rosettes appear as pale zones with fibrillar matrix corresponding to neuritic cell processes (Fig. 15). Sometimes, there are areas with a more diffuse or solid pattern with patches of calcification (Fig. 16).

Ganglioneuroblastoma showed patchy nodules of immature neuroblasts set within a full-grown Ganglioneuromatous stroma (Fig. 17).

From table (11) it can be observed that there is no intracytoplasmic hyaline globules were detected in all cases of neuroblastoma and ganglioneuroblastoma (Fig. 18 and 19). Moreover, both NB and GNB were rich in reticular fibers (Fig. 27 and 21). These figures showed that the reticular fibers are more abundant in case of Neuroblastoma.

3-Ganglioneuroma:

Microscopically, it can be observed that two distinct cell groups were identified. The first is ganglionic cells and the second is Schwannian

cells placed in an eosinophillic matrix (Fig. 22). From table (11) it can be observed that there is no intracytoplasmic hyaline globules were detected in all cases of tumor (Fig. 23). Positive PAS reaction is observed in the stroma of ganglioneuroma. All cases of tumors are rich in reticular fibers (Fig. 24). The abundant reticular fibers are observed in between the tumor cells of GN.

III- Immunohistochemical observations:

1- Adrenal cortical tumors (ACT):

The immunohistochemical reactivity was studied using paraffin sections of the studied tumors. The immunoreactivity of both cytokeratin and vimentin were documented in this study for ACA, and ACC tumors. Generally, the immunohistochemical reactions appear as granular brown deposits precipitated in the cytoplasm of tumor cells. Meanwhile, the expression of cytokeratin and vimentin in the ACA and ACC are summarized in Table (12).

Expression of cytokeratin in the adrenal cortical adenoma and carcinoma (ACA & ACC):-

From table (12), it can be noticed that most of the studied ACA cases (21/28) showed relative expression of cytokeratin with different grades of intensity. However, a wide range of expression is noticed. The staining was observed to be focal and the nuclei stained blue with prominent nucleoli (Fig. 25). Seven cases showed strong staining pattern and five cases showed weak staining pattern. Moreover, the last seven cases of ACA gave negative immunoreactive staining pattern for cytokeratin.

In the adrenal cortical carcinoma (ACC), cytokeratin expression was seen in all cases of tumors. However, a wide range of expression was

noticed, 3 cases demonstrated strong staining pattern and 9 cases showed moderate staining pattern (Fig. 26).

Expression of vimentin in ACT:

1- Adrenal cortical adenoma (ACA):

ACA exhibited a wide range of expression with vimentin. Some tumors showed immunostaining reactivity mainly in stromal elements, while others showed strong expression of vimentin in the neoplastic cells (Fig.27). Vimentin expression was observed in 20 cases of adrenal cortical adenomas. The staining was generally strong in eight cases, moderately in also eight cases and four cases gave weakly staining. While the other 8 cases of tumor were negative for the staining reactivity (Table12).

2- Adrenal cortical carcinoma ACC:

While in ACC, vimentin is seen in the cytoplasm of the tumor cells and its expression was observed in (10/12) ACC cases (Fig. 28). The staining was generally strong in three cases, moderately in five cases and weak immunoreactive in two cases. The last two cases were negative for the staining immunoreactivity.

b- Adrenal medullary tumors :

Table (13) shows the immunoreactivity of the adrenal medullary tumors with Cg A, NSE and S-100 protein.

I- Expression of Cg A :

a- Pheochromocytoma :

Chromogranin A showed diffuse cytoplasmic staining in all chromaffine cells (Fig. 29). Cg A staining was consistently intense in most tumors, 34 cases of tumor showing intense staining pattern and 5 cases of tumor show

moderate staining pattern. The two cases of composite pheochromocytoma (pheochromocytoma and ganglioneuroma) showed intense immunoreactivity for Cg A in pheochromocyte components (Fig.30), whereas the other components for ganglioneuroma were negative for Cg A immunoreactivity (Table 13).

b- Neuroblastoma (NB):

In five cases of 13 Neuroblastoma Cg A expression was observed. It revealed intense immunoreactivity in one case of 13 neuroblastoma and the other four cases being moderately immunoreactive for Cg A. The other eight cases were completely negative for Cg A. The immunoreactivity of Cg A is detected as brown deposits in the fibrillar areas with overlapping inter twisting neuritic processes (Fig. 31).

C- Ganglioneuroblastoma (GNB):

The immunoreactivity of Cg A revealed intense cytoplasm staining in the large neuroblasts and immunostaining in neuritic processes in five cases of tumors (Fig. 32). Two cases only give weak immunoreactivity. The other five cases were completely negative for Cg A (Table 13).

d- Ganglioneuroma (GN):

The immunoreactivity of Cg A is noticed in the cytoplasm of the ganglionic cells that gave an intense reaction in five cases of tumors (Fig. 33). The other four cases not expressed for Cg A giving negative results.

II- Expression of NSE:

a- Pheochromocytoma:

All pheochromocytoma were immunoreactive for NSE with different degree of staining as follow; 37 cases of tumors being intense, 2 cases showed moderate staining. The other two cases were negative for

NSE immunoreactivity. The reactions appear as brown color and diffuse in the cytoplasm of the chief cells of tumor (Fig. 34).

b- Neuroblastoma (NB):

Expression of NSE has been observed in almost all the cell of NB. An intense reaction is seen in the cytoplasm of theses cells, whereas the stroma is unstained. It also can be observed in abundance in the neuritic process (Fig. 35). The staining was intense in 5 cases, moderate in also five cases and the other three cases being slight immunoreactivite for NSE.

C- Ganglioneuroblastoma (GNB):

Expression of NSE immunostaining was observed in abundant stromal septa. In addition, the cytoplasm of cell bodies is intensely positive all cases of ganglioneuroblastoma (GNB) were intensely reactive for NSE (Fig. 36).

d- Ganglioneuroma (GN):

The immunoreactivity of NSE is observed in the ganglionic cells and Schwann cells of GN. These cells showed a wide range of immuno-reactivity. In addition, the stroma of GN stained blue color by haematoxylene as a counter stain (Fig.37). Six cases of tumor showed intense immunostaining reactivity and the other three cases gave negative immunoreactions (Table 13).

III- Expression of S-100 protein:

a- Pheochromocytoma:

S-100 protein was absent in chromaffin cells but was present in the cytoplasm and nuclei of sustentacular cells surrounding chromaffin cells (Fig. 38). S-100 protein stained moderately too intensely in all cases. 27 cases were intense staining five cases show moderate staining. The

other seven malignant pheochromocytoma were negative for the immunoreactivity of S-100 protein.

b- Neuroblastoma:

The immunoreactions of S-100 protein are seen adjacent to the vascular septa. The cells of NB are consistent with Schwann or sustentacular cells that gave intense reaction. However, S-100 protein expression was observed in all cases of Neuroblastoma (Fig. 39). The staining was generally strong in 7 cases and the other 6 cases of tumor showed moderate immunoreactivity cells.

c-Ganglioneuroblastoma (GNB):

In GNB, the cells are in contact with ganglionic cells. These cells showed intense immunoreactive S-100 protein. They are in the typical location of satellite cells. All 12 GNB stained positively for S-100 protein (Fig. 40) and the other three cases of tumor showed moderate immunoreactivity for S-100 protein.

d- Ganglioneuroma (GN):

S-100 protein expression revealed a brown staining in the cytoplasm of the ganglionic cells. In addition, an intense S-100 protein immuno reactivity is observed in the Schwann cells as well as the matrix of GN. All a GN stained positively with S-100 protein, immunoreactivity was consistently present in nerve fibrils. All case of tumors demonstrates a strong staining pattern for S-100 protein (Fig. 41).

Table (5): The histopathology of 113 patients with adrenal gland tumors.

Pathology		No. of patients (%)	Male	Female
Adrenal Cortical Tumors (40, 35.3%)	ACA	28 (24.7%)	12	16
	ACC	12 (10.6%)	5	7
Adrenal medullary Tumors (73, 54.7%)	Pheo.	39 (34.5%)	15	24
	NB	13 (11.5%)	7	6
	GNB	12 (10.6%)	6	6
	GN	9 (7.9%)	6	3

Table (6): Clinical data of the patients with adrenal cortical adenoma.

Case No.	Sex	Age (Year)	Size (cm.)	Follow up (month)	Status
1	F	30	7	168	S
2	M	22	7	120	S
3	F	53	8	124	S
4	F	56	5	84	S
5	F	30	8	120	S
6	M	53	8	82	S
7	F	35	5	78	S
8	M	46	4	72	S
9	F	58	8	68	S
10	M	59	7	60	S
11	F	54	7	62	S
12	M	56	5	48	S
13	F	51	8	36	S
14	M	43	3	35	S
15	M	53	6	32	S
16	F	27	4	28	S
17	F	60	7	26	S
18	F	53	5	24	S
19	M	58	8	20	S
20	F	57	6	12	S
21	F	35	10	26	S
22	F	54	9	32	S
23	F	37	8	48	S
24	M	34	4	32	S
25	M	50	6	24	S
26	M	52	3	30	S
27	F	37	5	27	S
28	M	60	2	18	S

Table (6a): Age distribution in patients with adrenal cortical adenoma.

Age group	No. of patients	Percentages %
First decade (1-10)	0	0%
Second decade (11-20)	0	0%
Third decade (21-30)	4	14.2%
Fourth decade (31-40)	5	17.8%
Fifth decade (41-50)	3	10.7%
Sixth decade (51-60)	16	57.1%
Total	28	100.0 %

Table (6b): Sex distribution in patients with adrenal cortical adenoma.

Sex	No. of patients	Percentages %
Male	12	42.8%
female	16	57.2%
Total	28	100.0%

Table (6c): Tumor size in patients with adrenal cortical adenoma.

Size group (cm)	No. of patients	%
0-5	11	39.28%
6-10	17	60.72%
Total	28	100.0

Table (7): The clinical presentation of Adrenal Cortical Carcinoma.

Case	sex	Age (years)	Size (cm)	Followup (months)	Status
1	M	45	12	36	D
2	M	42	10	11	D
3	F	46	10	16	D
4	M	10	13	24	D
5	F	46	15	24	D
6	M	43	11	37	D
7	F	32	16	38	D
8	M	24	18	27	D
9	M	36	13	24	S
10	M	53	10	39	D
11	M	44	11	36	S
12	F	42	14	23	S

D=Died, S=Survival, M= male, F= female.

Table (8): The clinical data of patients with pheochromocytoma

Case	Sex	Age (year)	Size (cm)	Follow up (months)	Status
1	F	36	5	192	S
2	F	43	7	120	S
3	M	35	8	96	S
4	F	58	8	82	S
5	F	21	10	94	S
6	M	19	8	86	S
7	F	30	10	81	S
8	F	36	11	78	S
9	F	43	13	72	S
10	F	40	14	66	S
11	M	28	7	58	S
12	F	60	5	58	D
13	M	53	4	55	D
14	F	45	4	71	S
15	F	52	7	51	S
16	M	41	6	49	S
17	F	35	6	47	S
18	M	46	7	44	S
19	M	46	5	42	S
20	F	54	13	38	D
21	M	36	10	37	S
22	F	24	11	32	S
23	F	34	8	30	S
24	M	61	7	28	D
25	M	20	11	26	S
26	F	25	13	24	S
27	F	35	7	24	S
28	F	24	6	21	S
29	F	19	9	20	S
30	F	42	11	19	S
31	M	44	4	17	D
32	F	19	7	15	S
33	M	44	6	14	S
34	F	20	5	13	S
35	M	42	12	11	S
36	F	34	14	24	S
37	F	54	12	58	D
38	F	30	11	36	S
39	F	37	12	48	S

Table (8a): Age distribution in patients with pheochromocytoma.

Age group	No. of patients	Percentage %
1-10	0	0%
11-20	5	12.8%
21-30	8	20.51%
31-40	10	25.64%
41-50	9	23.07%
51-60	6	15.38
Over 60	1	2.5%
Total	39	100.0

Table (8b): Sex distribution in the patients with Pheochromocytoma.

Sex	No. of patients	%
Male	15	38.46%
Female	24	61.54%
Total	39	100.0

Table (8c): The tumor sizes in 39 patients with pheochromocytoma.

Tumor size (cm)	No. of patients	%
0-5	6	17.1%
6-10	17	48.6%
11-15	16	34.3%
Total	39	100.0

Table (9): Clinical data of patients with neuroblastoma and ganglioneuroblastoma (25 cases)

Tumors	Case	Sex	Age	Size	Follow up	Status
I-Neuroblastoma	1	F	4 m	10	30	D
	2	M	3 y	9.5	23	D
	3	M	4 y	17	19	D
	4	M	7 m	17	20	D
	5	M	10 m	10	18	D
	6	M	3 y	13	24	S
	7	M	7 m	17	26	D
	8	M	3 y	12	52	D
	9	F	6 m	17	16	S
	10	F	11 m	20	22	D
	11	F	1 y	13	60	D
	12	F	9 m	10	96	D
	13	F	5 y	12.5	20	D
Ganglioneuroblastoma	14	F	4 y	14	23	D
	15	M	44 y	16	20	D
	16	M	3 y	10	30	D
	17	M	10 m	11	16	S
	18	F	8 m	18	24	D
	19	M	43 y	12	45	D
	20	M	5 y	13	24	D
	21	F	2 y	15	12	S
	22	F	16 y	10	10	S
	23	F	3 y	17	17	D
	24	M	1 y	20	24	D
	25	F	4 y	18	17	S

y= Year m=Months, S= survival, D= died

Table (9a): Age distribution in patients with neuroblastoma and ganglioneuroblastoma.

Age group	No. of patients	%
1 month- 11 m	9	36%
1 y-10 y	13	52%
11 y-20 y	1	4%
21 y-30 y	0	0
31 y-40 y	0	0
41 y-50 y	2	8%
Total	25	100%

Table (9b): Sex distribution in (25) patients with neuroblastoma and ganglioneuroblastoma

Age sex	No. of patients	%
Male	13	52%
Female	12	48%
Total	25	100.0%

Table (9c): Tumor size in (25) patients with neuroblastoma and ganglioneuroblastoma.

Tumor size	No. of patients	%
0.5	0	0
6-10	6	20%
11-15	9	36%
16-20	10	40%
Total	25	100.0

Table (10): Clinical data of 10 patients with ganglioneuroma.

Case	Sex	Age (years)	Size (Cm)	Follow up (Months)	Status
1	F	20	13	30	S
2	M	19	14	23	S
3	M	31	8	23	S
4	M	35	13	31	S
5	M	17	10	18	S
6	F	24	12	121	S
7	F	28	15	46	S
8	M	15	11	52	S
9	M	20	10	36	S

Table (11): The results of PAS and Reticulin stain for adrenal cortical and medullary tumors (ACT & AMT).

Stain / Tumor	PAS		Reticulin stain		
	+ve	-ve	high +2	low +1	-ve -
Adrenal cortical tumor					
- ACA	13/28	15/28	23/28	15/28	-
- ACC	8/12	4/12	-	10/12	2/12
Adrenal medullary tumor					
- Pheo.	28/39	11/39	33/39	6/39	-
- NB	-	13/13	13/13	-	-
- GNB	-	12/12	12/12	-	-
- GN	-	9/9	9/9	-	-

+ve Positive **-ve Negative**

Table (12): Immunohistochemical expression of cytokeratin and vimentin in adrenal cortical tumors (ACA & ACC).

Immunostaining / Tumor	Expression of Cytokeratin				Expression of Vimentin			
	+3	+2	+1	0	+3	+2	+1	0
Adrenal cortical tumor								
- ACA	7/28	9/28	5/28	7/28	8/28	8/28	4/28	8/28
- ACC	3/12	9/12	-	-	3/12	5/12	2/12	2/12

+3 intense immunoreactivity. +2 moderate immunoreactivity.

+1 weak immunoreactivity. -ve negative immunoreactivity.

Table (13): The immunoreactivity of AMT with Chromogranin A (Cg A), Neuron-specific enolase (NSE) and S-100 protein.

Stain / AMT	Intensity for Cg A				Intensity for NSE				Intensity for S-100			
	+3	+2	+1	-ve	+3	+2	+1	-ve	+3	+2	+1	-ve
- Pheo.	34/39	5/39	-	-	37/39	2/39	-	-	27/39	5/39	-	7/39
- NB	1/13	4/13	-	8/13	5/13	5/13	3/13	-	7/13	6/13	-	-
- GNB	5/12	-	2/12	5/12	12/12	-	-	-	9/12	3/12	-	-
- GN	5/9	-	-	4/9	6/6	3/9	-	-	9/9	-	-	-

+ 3 intense immunoreactivity. + 2 moderate immunoreactivity.

+ 1 weak immunoreactivity. - ve negative immunoreactivity.

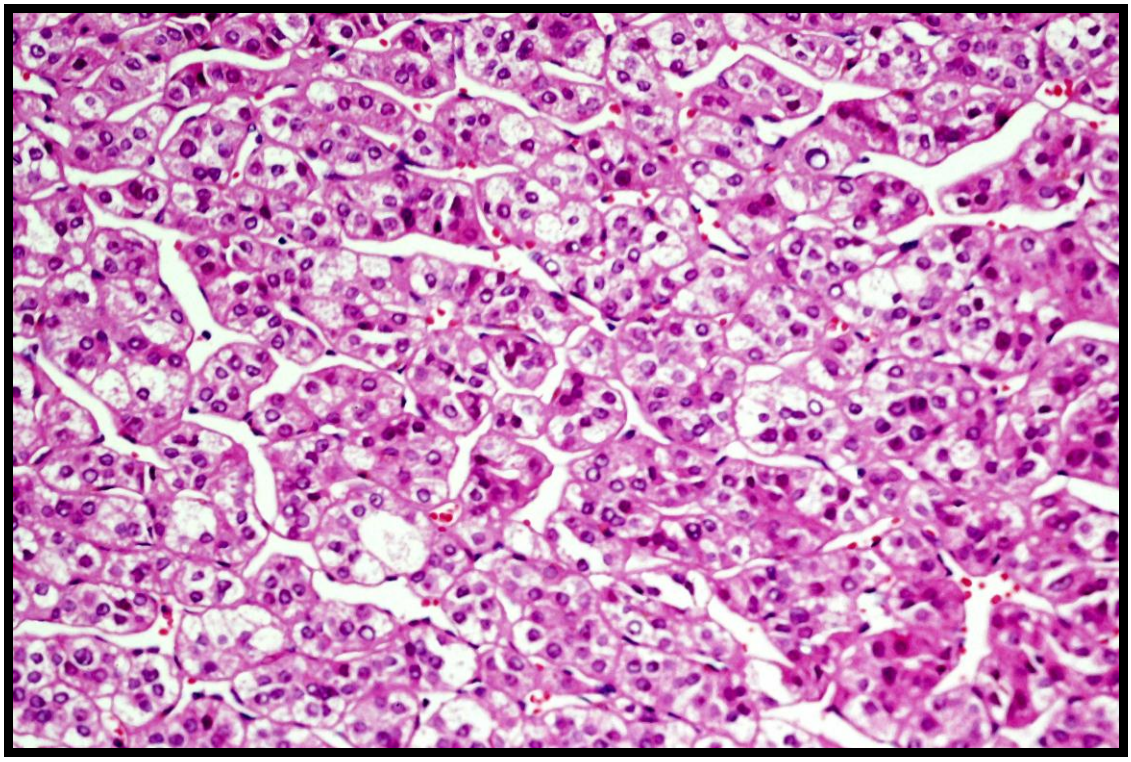

Fig. (2): Photomicrograph of adrenal cortical adenoma showing alveolar or nesting pattern, cells have compact eosinophilic cytoplasm. (Hx & E x 200).

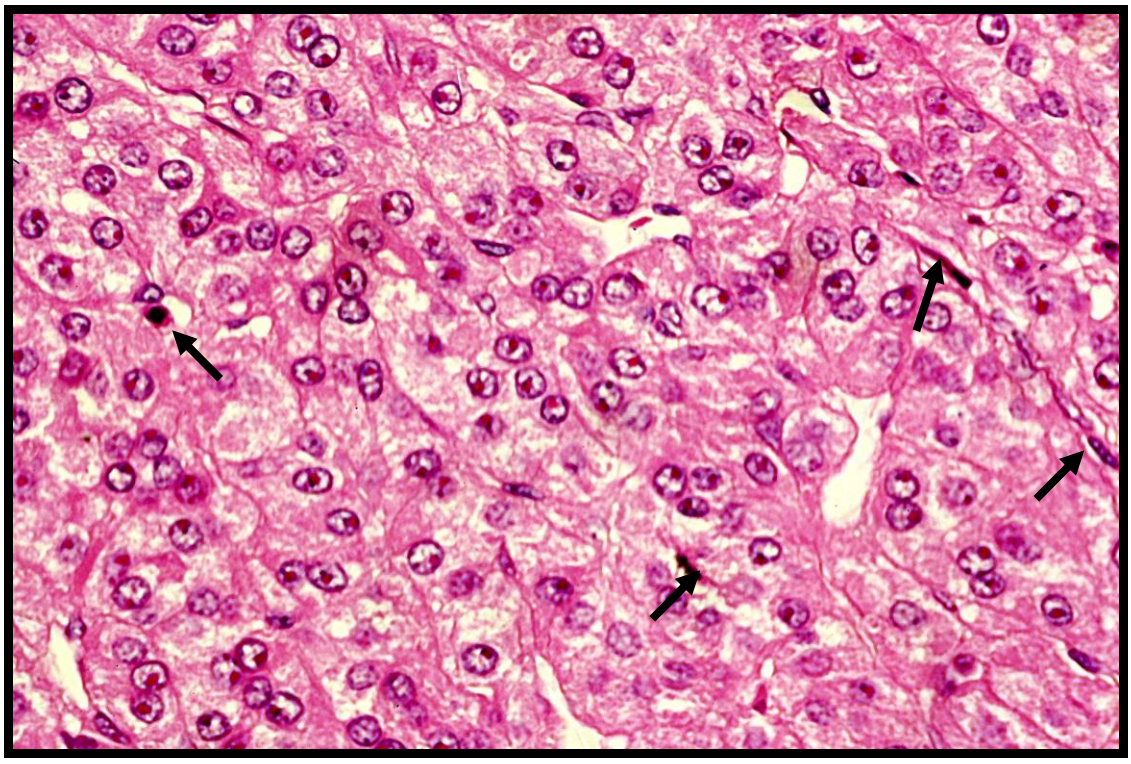

Fig. (3): Photomicrograph of adrenal cortical adenoma showing organoid arciticure (arrows) . No mitotic figures are present, nuclei are vesicular with central to erchntric nucleoli. (Hx & E x 400).

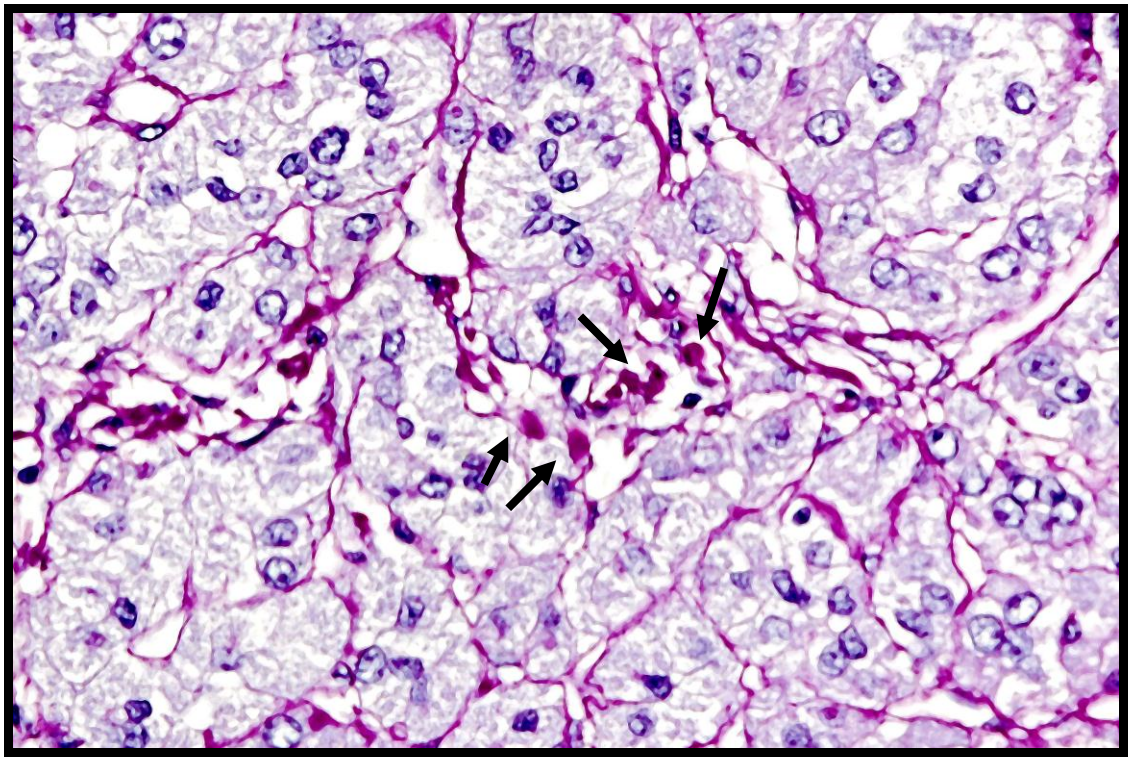

Fig.(4): Photomicrograph of adrenal cortical adenoma showing intra-cytoplasmic hyaline PAS positive globules, (arrows).(PAS X 400).

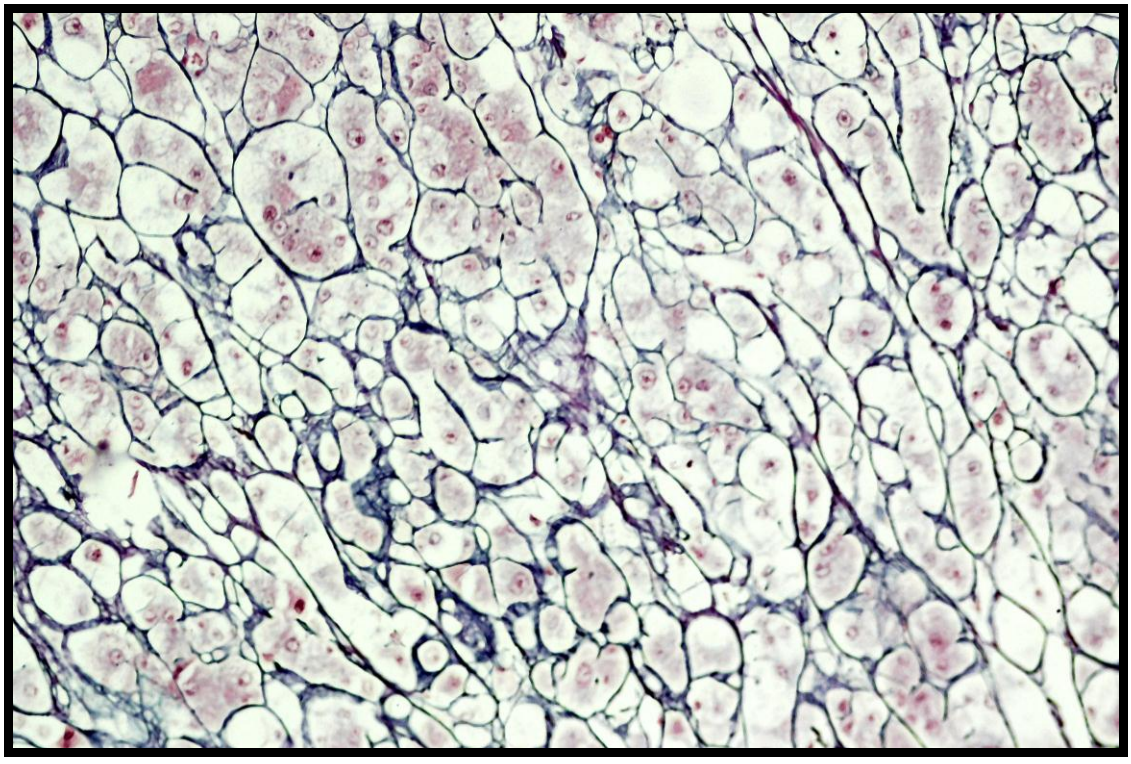

Fig. (5): Photomicrograph of adrenal cortical adenoma showing abundant reticular fibers.(Gordon stain X200).

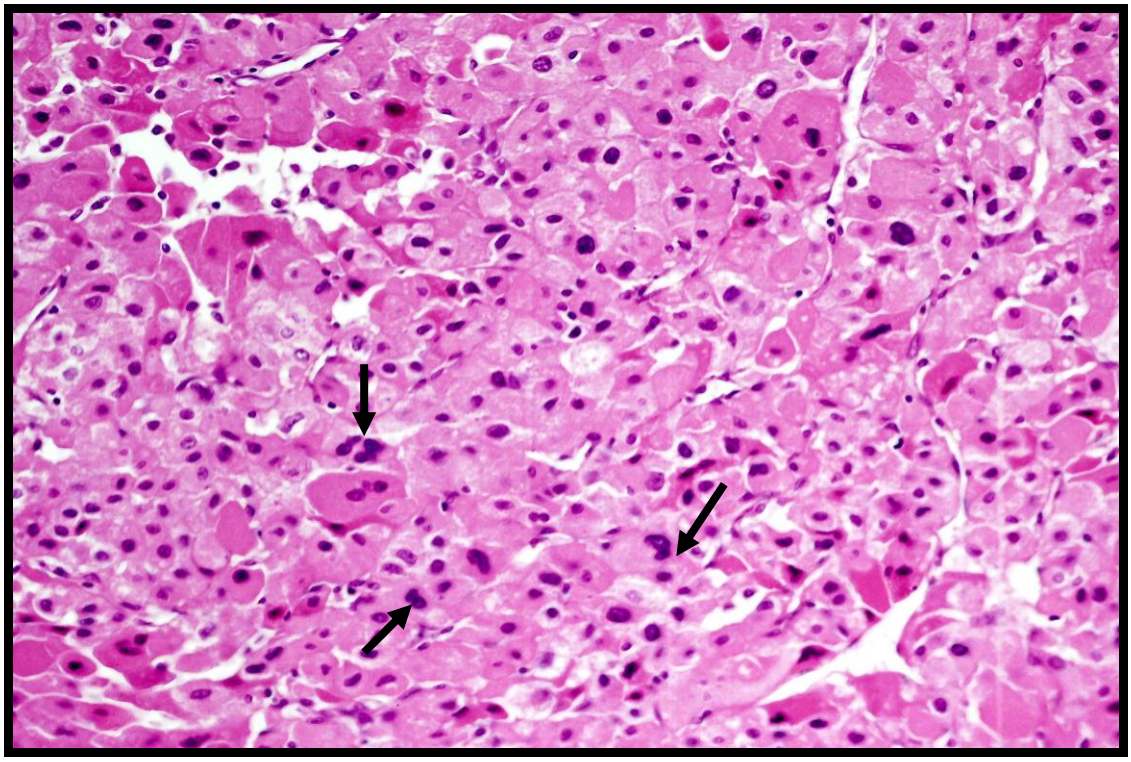

Fig. (6): Photomicrograph of adrenal cortical carcinoma showing diffuse pattern of irregular pleomorphic tumour cells. Most tumour cells have moderate to abundant eosinophilic compact cytoplasm. Mitotic figures were numerous with many atypical forms. (Hx & E x200).

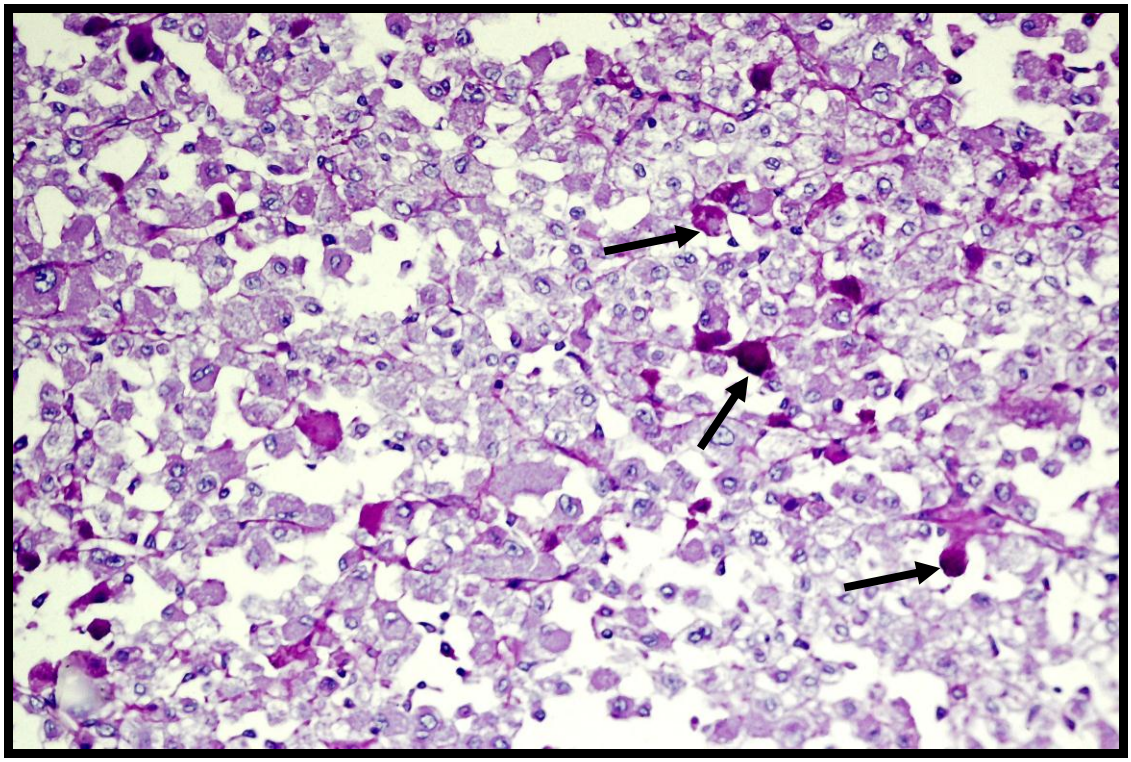

Fig. (7): Photomicrograph of adrenal cortical carcinoma showing intracytoplamic hyaline globules (arrows).(PAS x100).

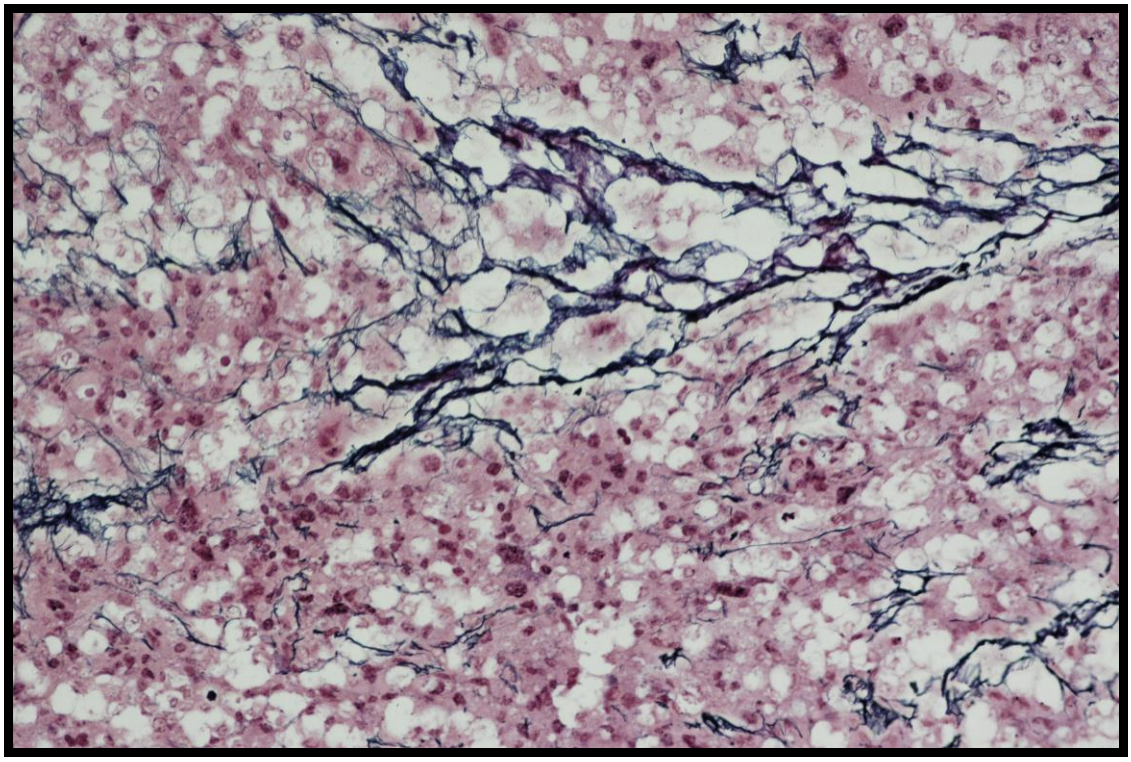

Fig. (8): Photomicrograph of adrenal cortical carcinoma showing deficient reticular fibers. (Gordon stain X 200).

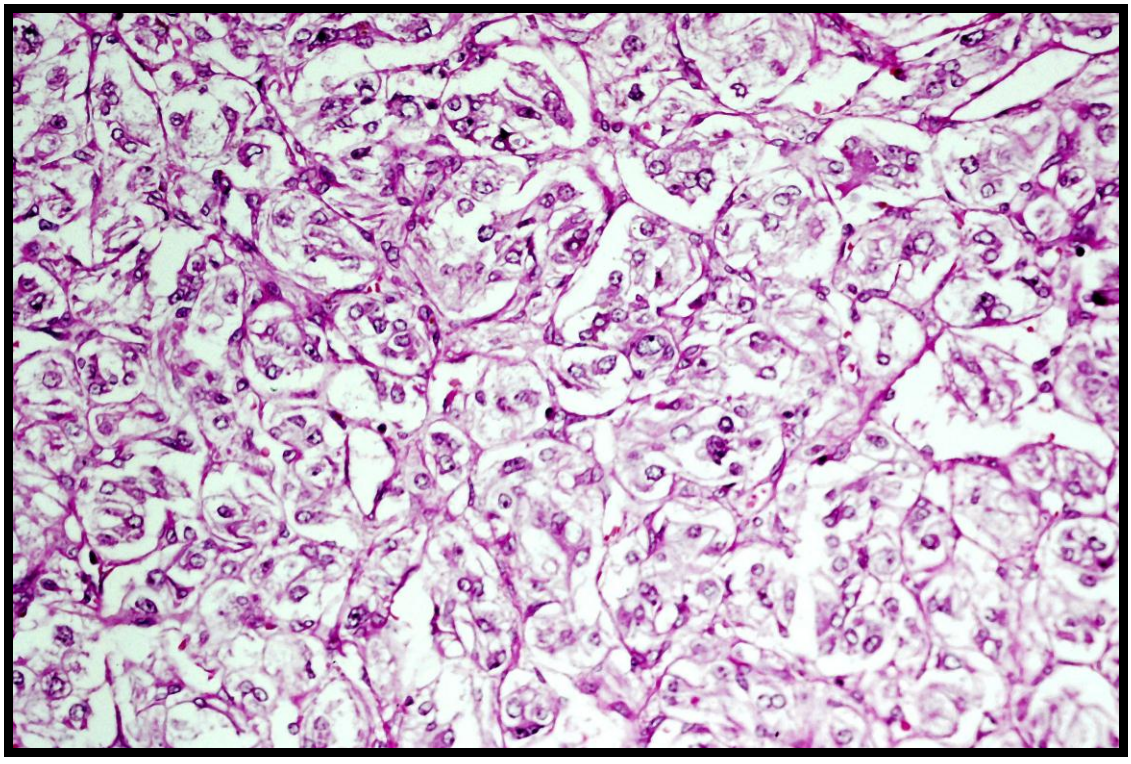

Fig. (9): Photomicrograph of adrenal pheochromocytoma showing the typical nesting pattern (Zellballen appearance). (Hx & E X 200).

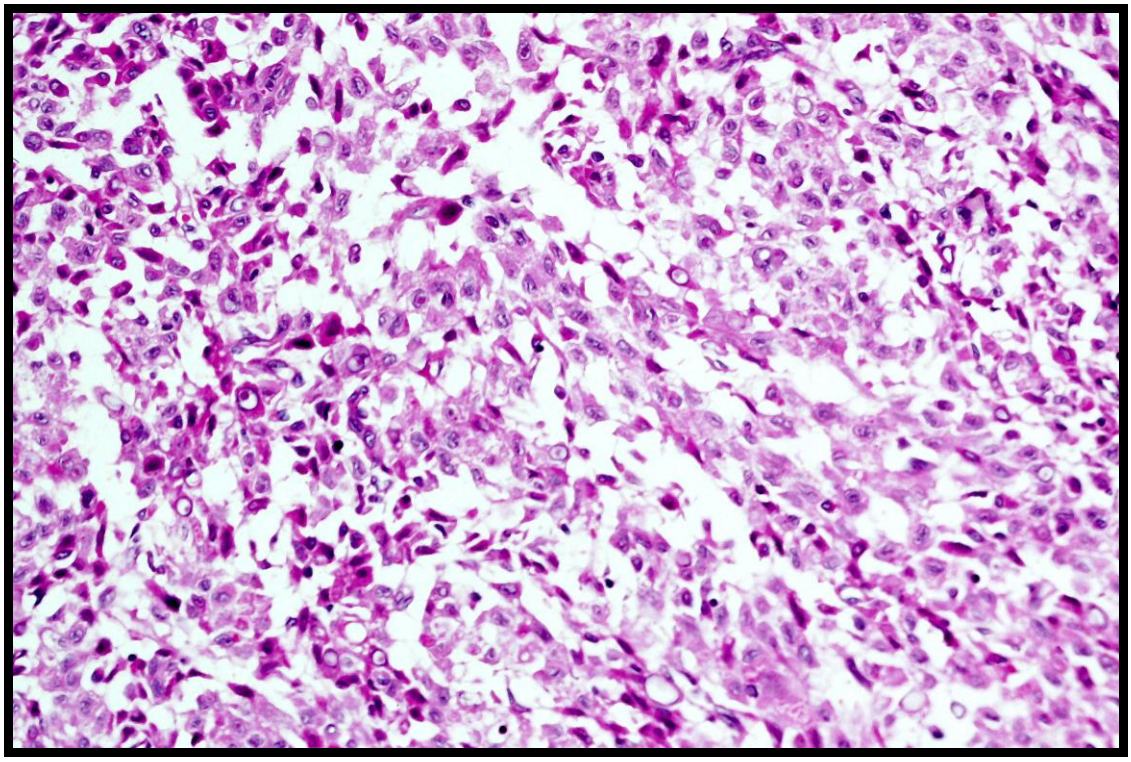

Fig. (10): Photomicrograph of adrenal pheochromocytoma, spindle cell pattern. (Hx & E X200).

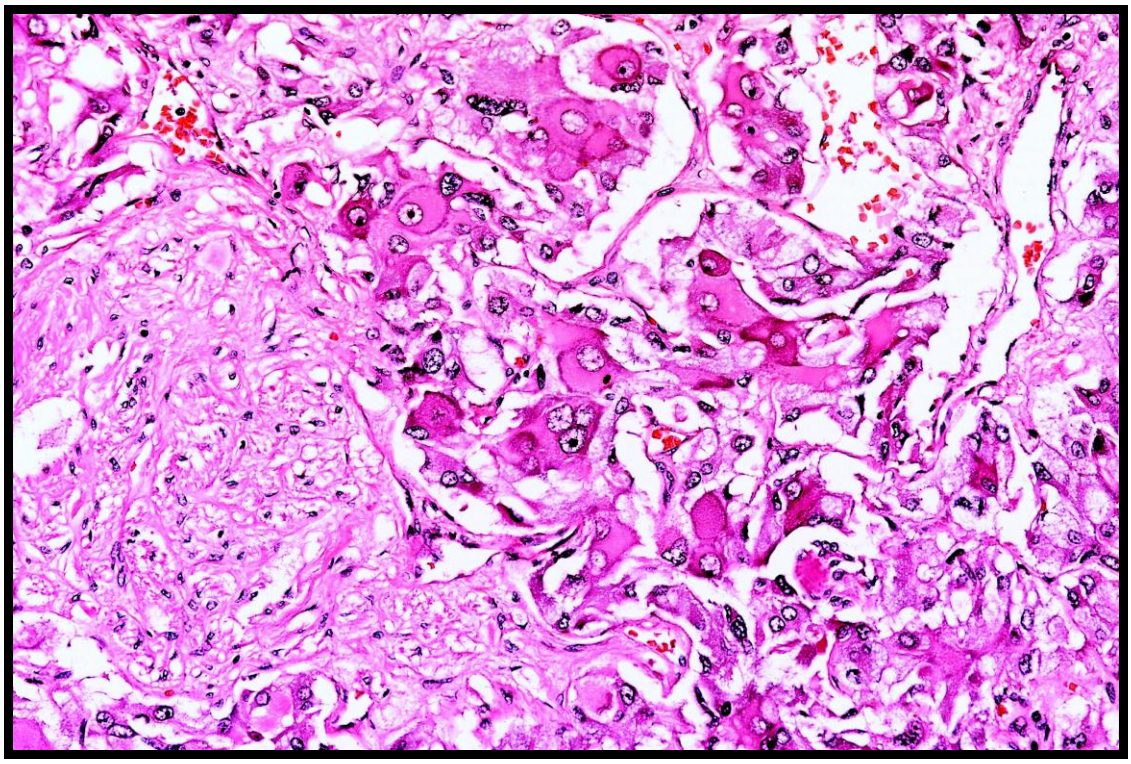

Fig. (11): Photomicrograph of composite pheochromocytoma showing spindle cell schwannian stroma admixed with pheochromocytoma. (Hx & E X 200).

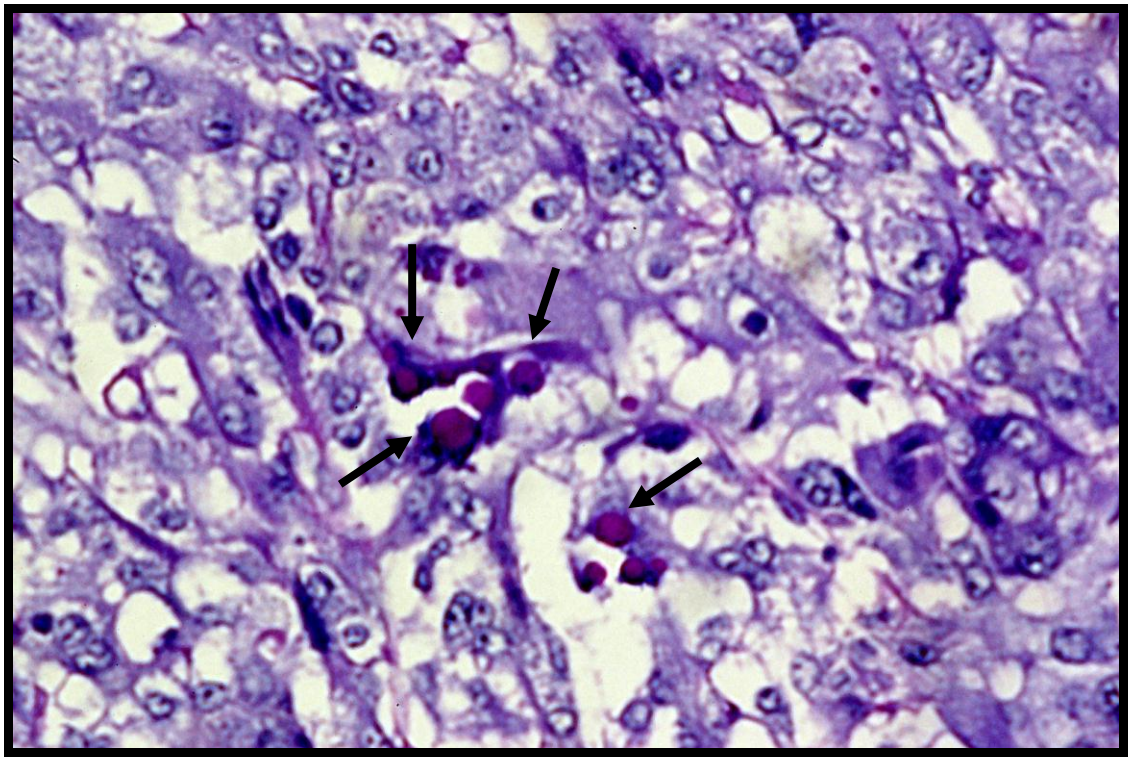

Fig. (12): Photomicrograph of pheochromocytoma showing intra-cytoplasmic hyaline globules (arrows). (PAS x400).

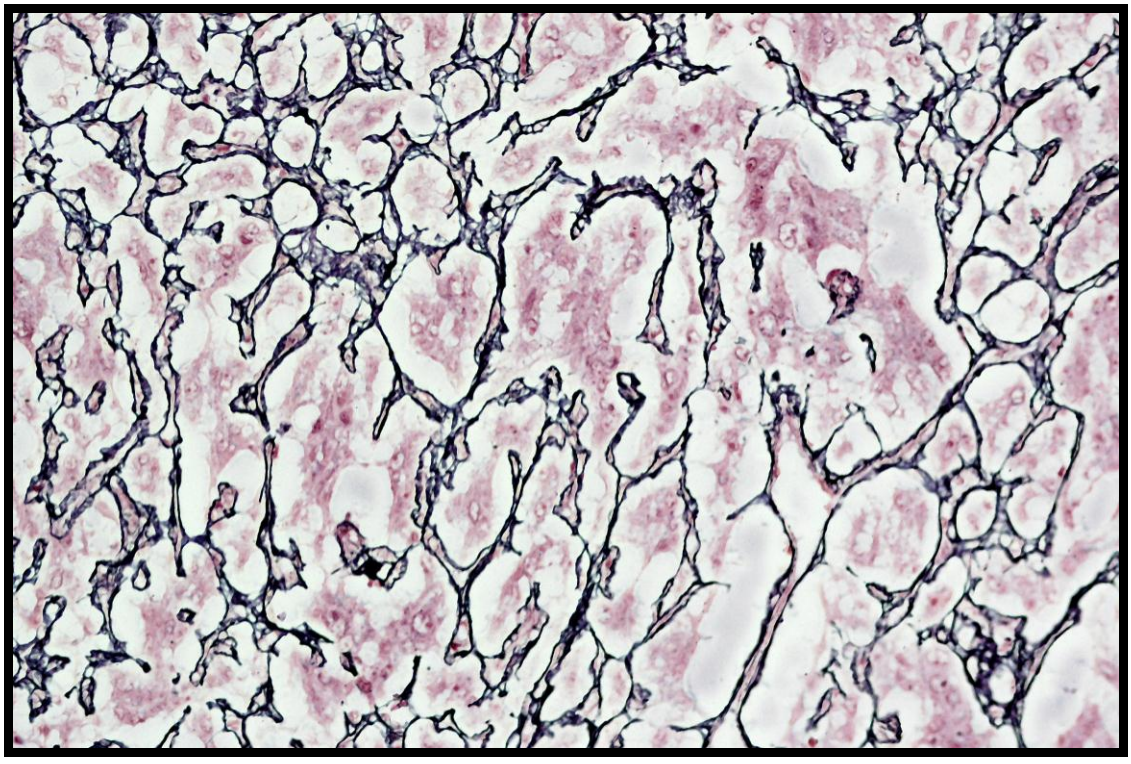

Fig. (13): Photomicrograph of pheochromocytoma showing accentuated alveolar pattern bounded by condensation of reticular fibers.(Gordon stain X 200).

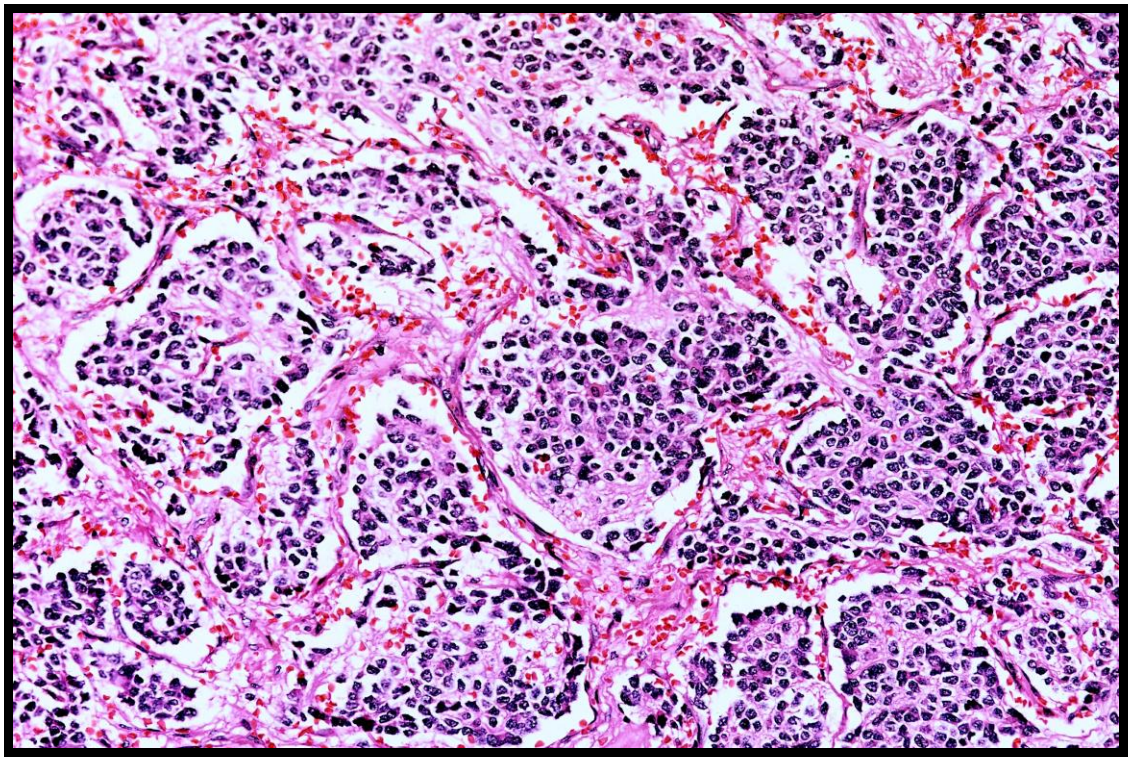

Fig. (14): Photomicrograph of neuroblastoma showing accentuation of fobrovascular stroma and tumour nodules formed of monotonous primitive cells. (H x & E X 200).

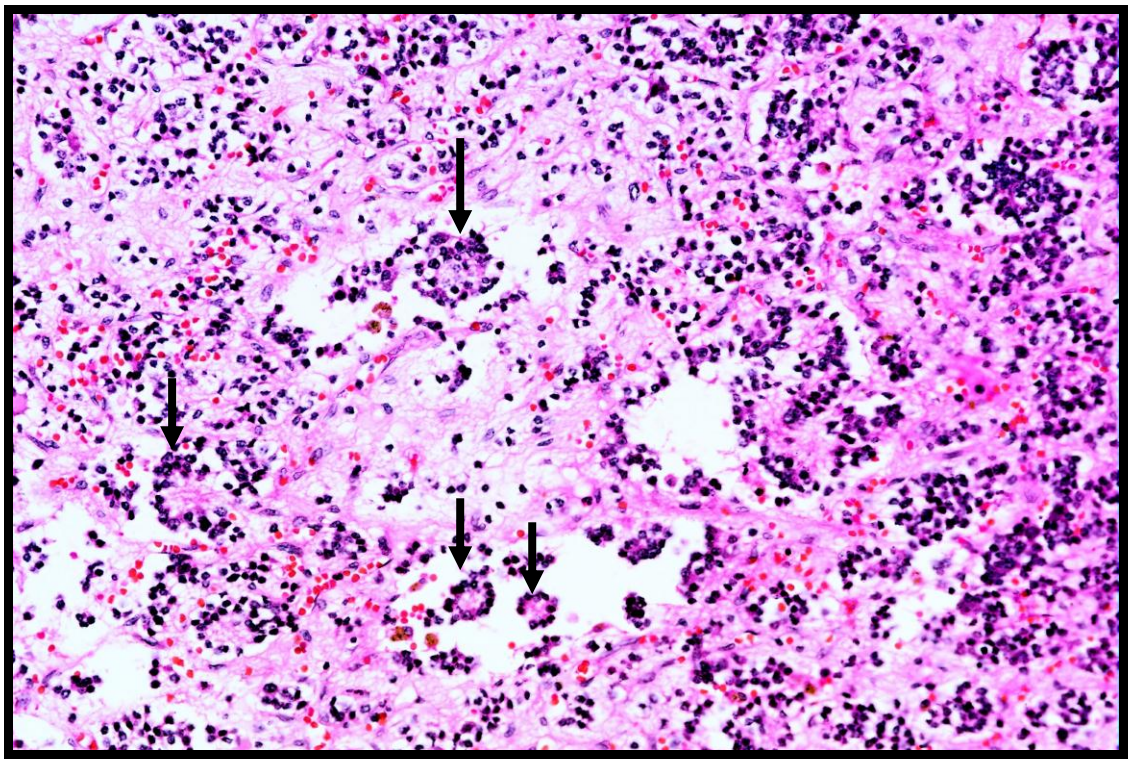

Fig. (15): Photomicrograph of neuroblastoma showing numerous Homer Wright rosettes. (H x & E X 200).

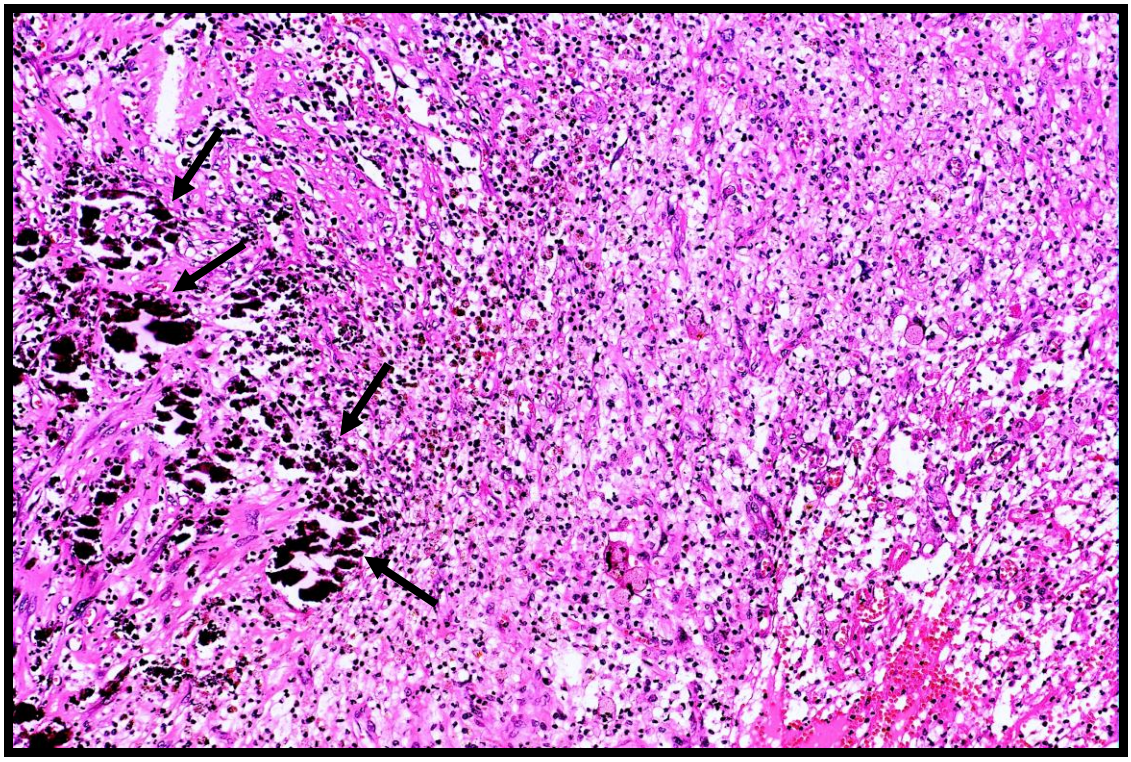

Fig. (16): Photomicrograph of neuroblastoma showing patches of calcification. (Hx & E X 100).

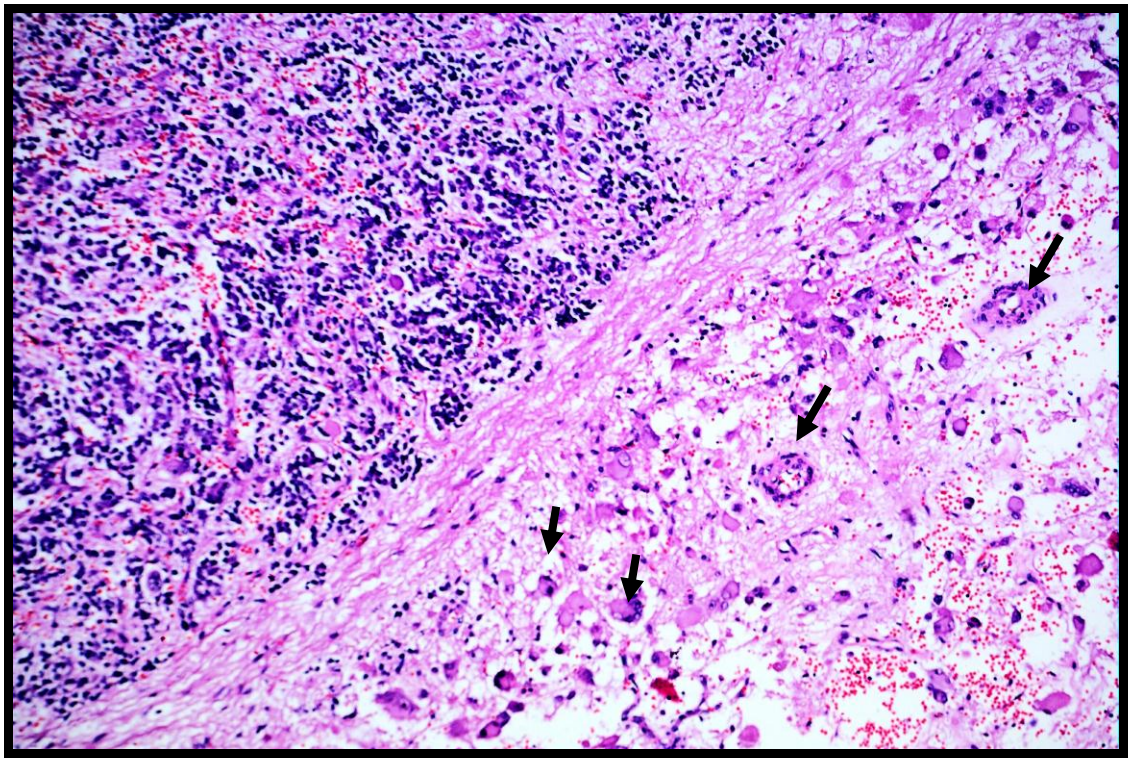

Fig. (17): Photomicrograph of ganglioneuroblastoma showing patchy nodules of immature neuroblasts set within a mature ganglioneuromatous stroma arrows.(Hx& E X100).

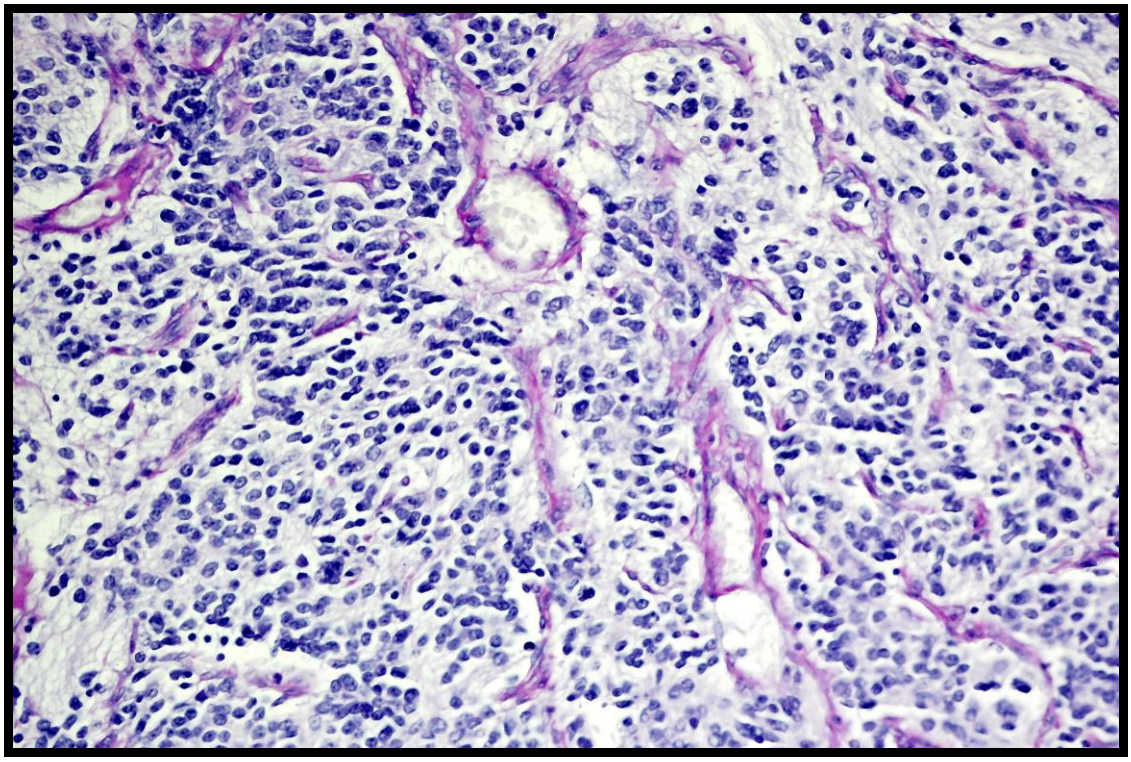

Fig. (18): Photomicrograph of neuroblastoma showing no intracytoplasmic hyaline globules. (PAS stain X 200).

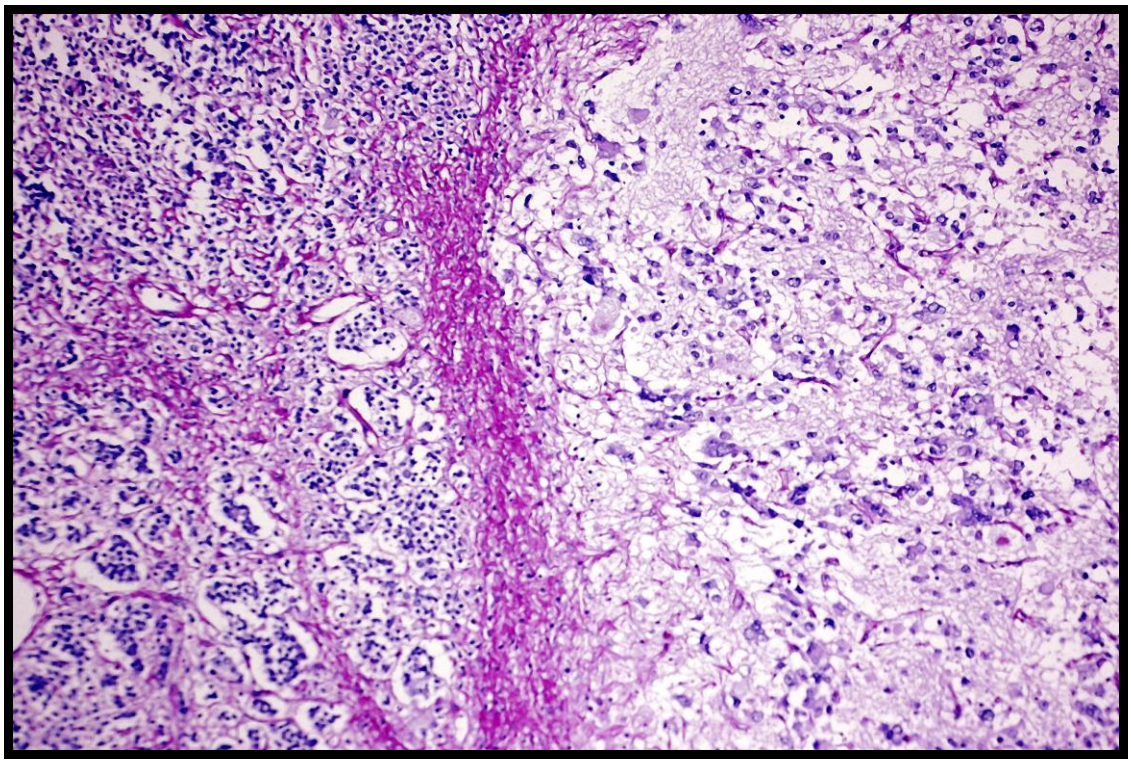

Fig. (19): Photomicrograph of ganglioneuroblastoma showing no intracytoplasmic hyaline globules. (PAS stain X 100).

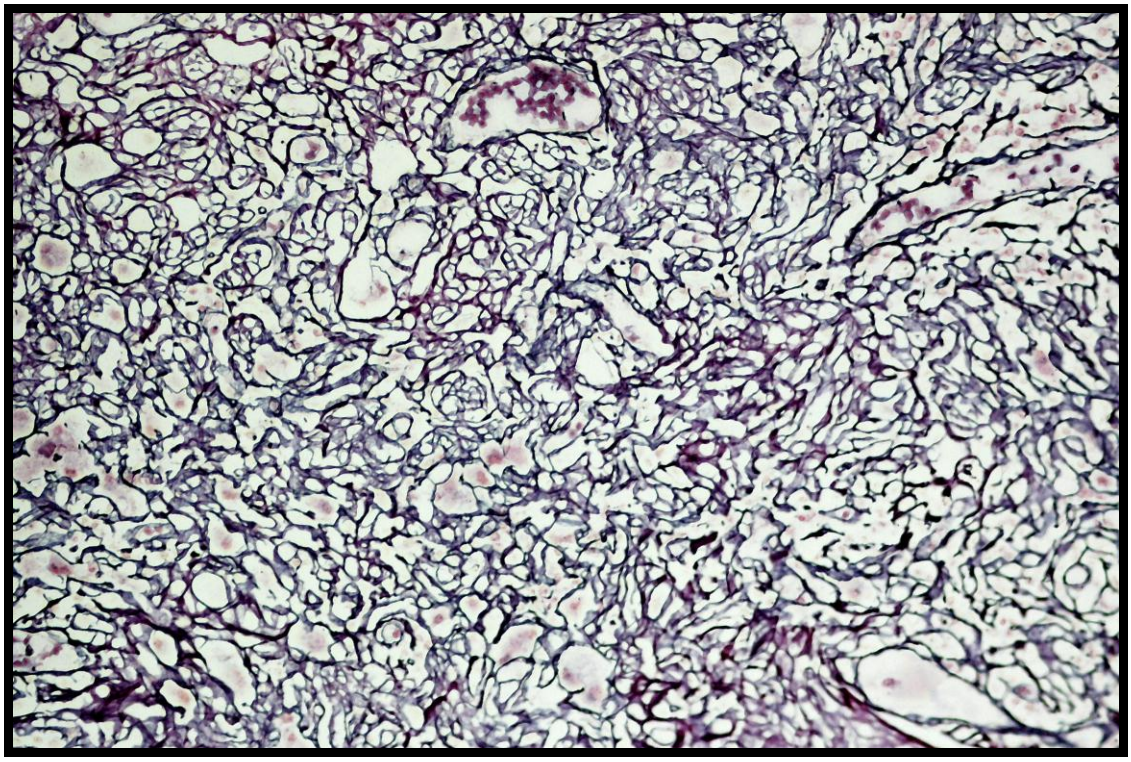

Fig. (20): Photomicrograph of neuroblastoma showing abundant reticular fibers in tumour cells. (Gordon stain X 200).

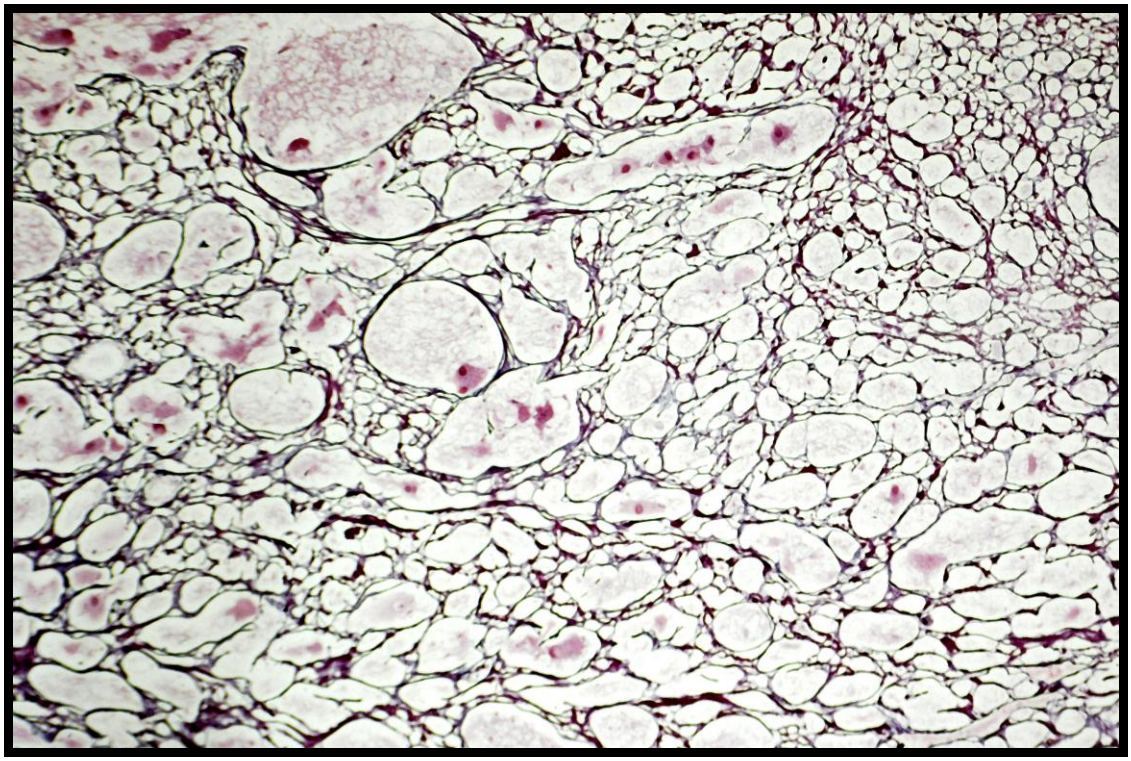

Fig. (21): Photomicrograph of ganglioneuroblastoma showing abundant reticular fibers in tumour cells. (Gordon stain X 200).

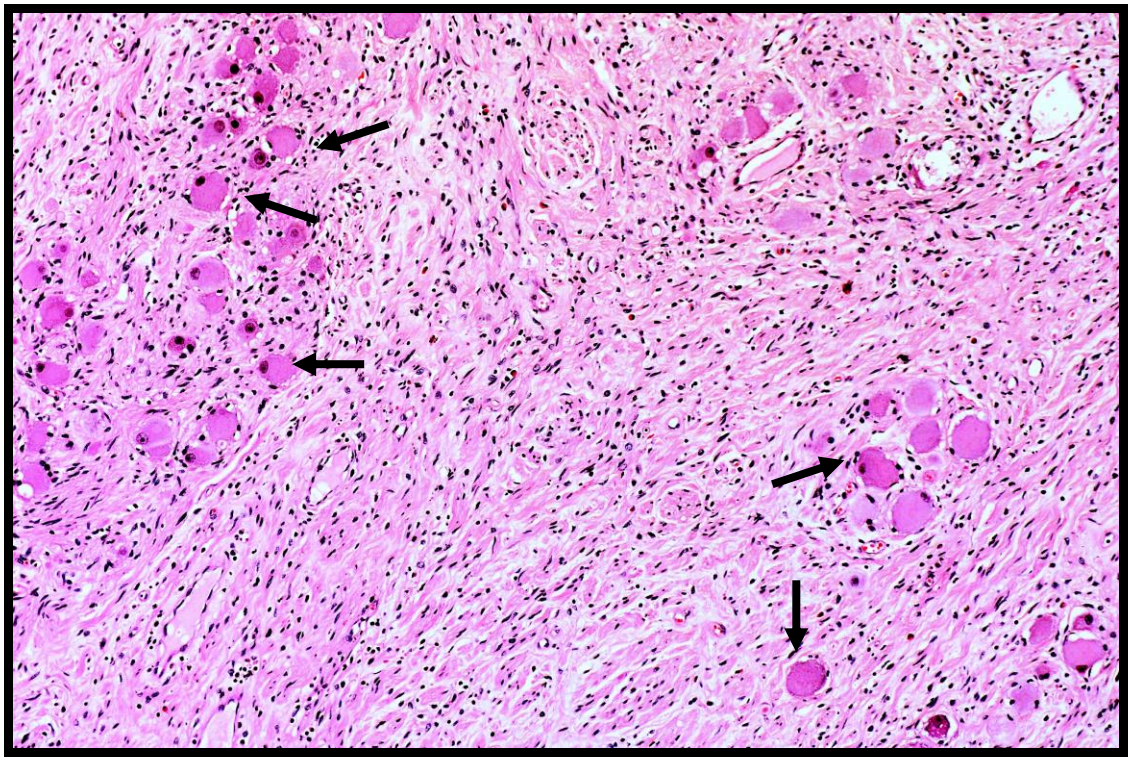

Fig. (22): Photomicrograph of ganglioneuroma showing mature ganglion cells (arrows) in schwannian cell dominant stroma.(Hx & E X200).

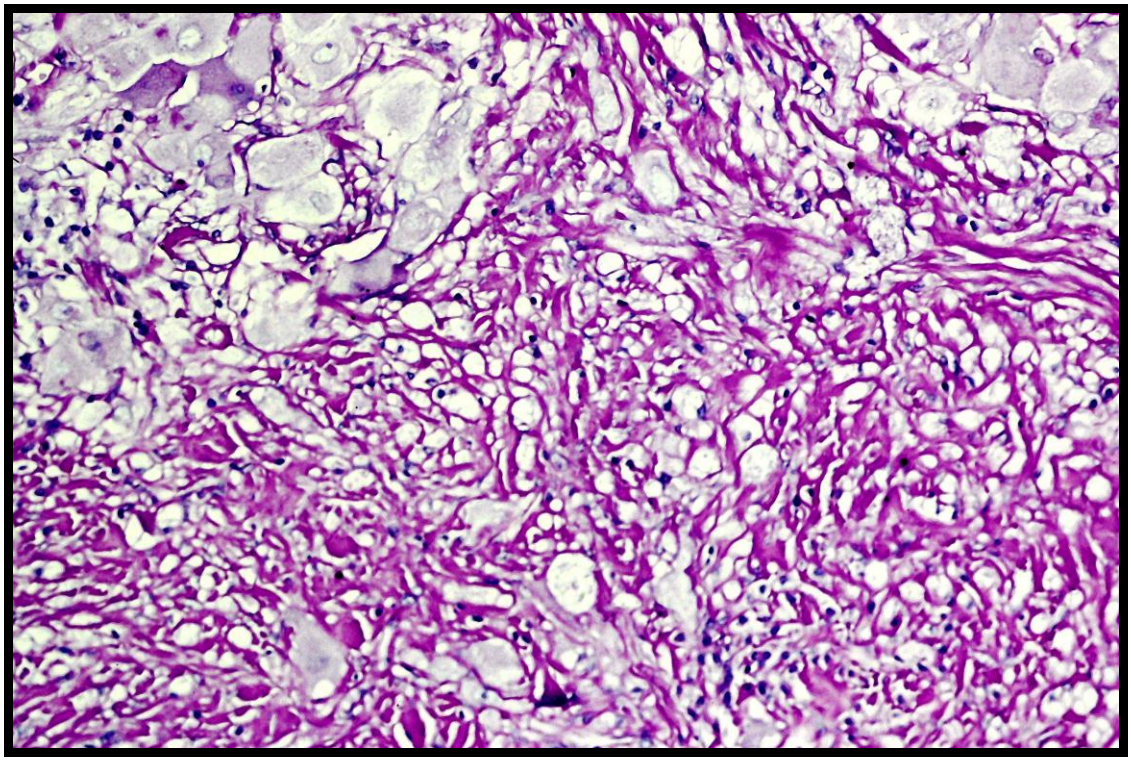

Fig. (23): Photomicrograph of ganglioneuroma. Note the intracytoplasmic hyaline globules not detected in tumour cells.(PAS stain X 200).

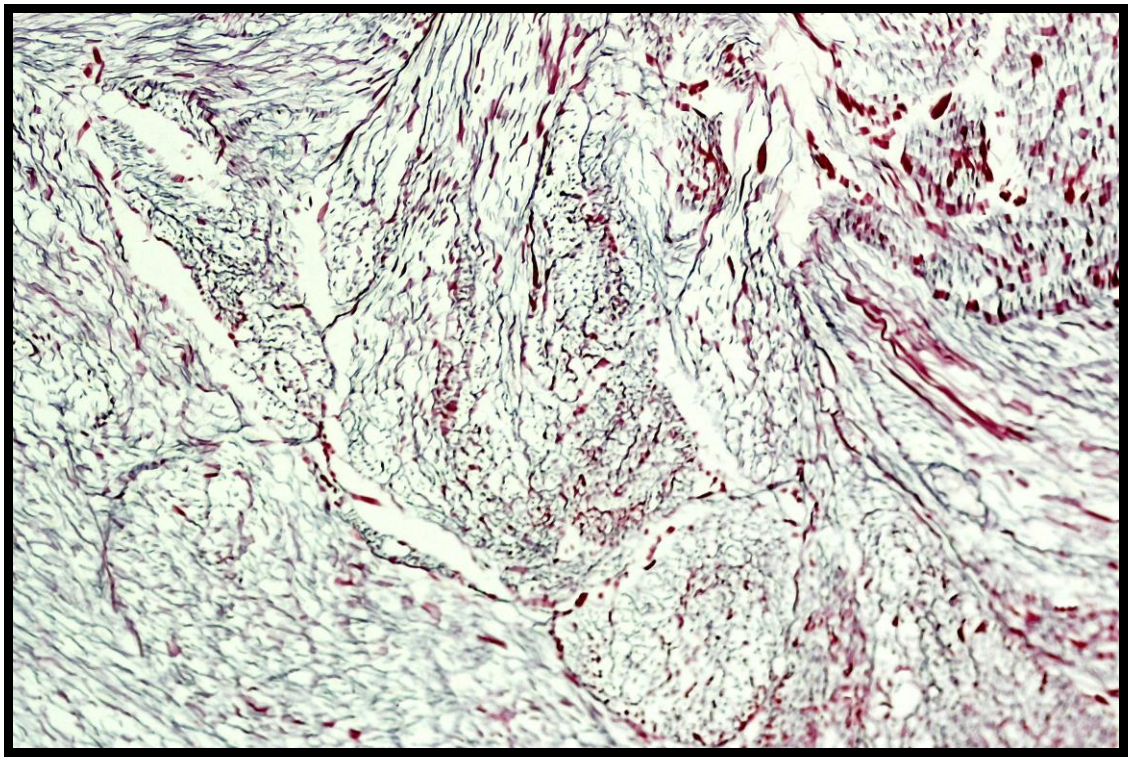

Fig. (24): Photomicrograph of ganglioneuroma showing abundant reticular fibers in tumour cells. (Gordon stain X 100).

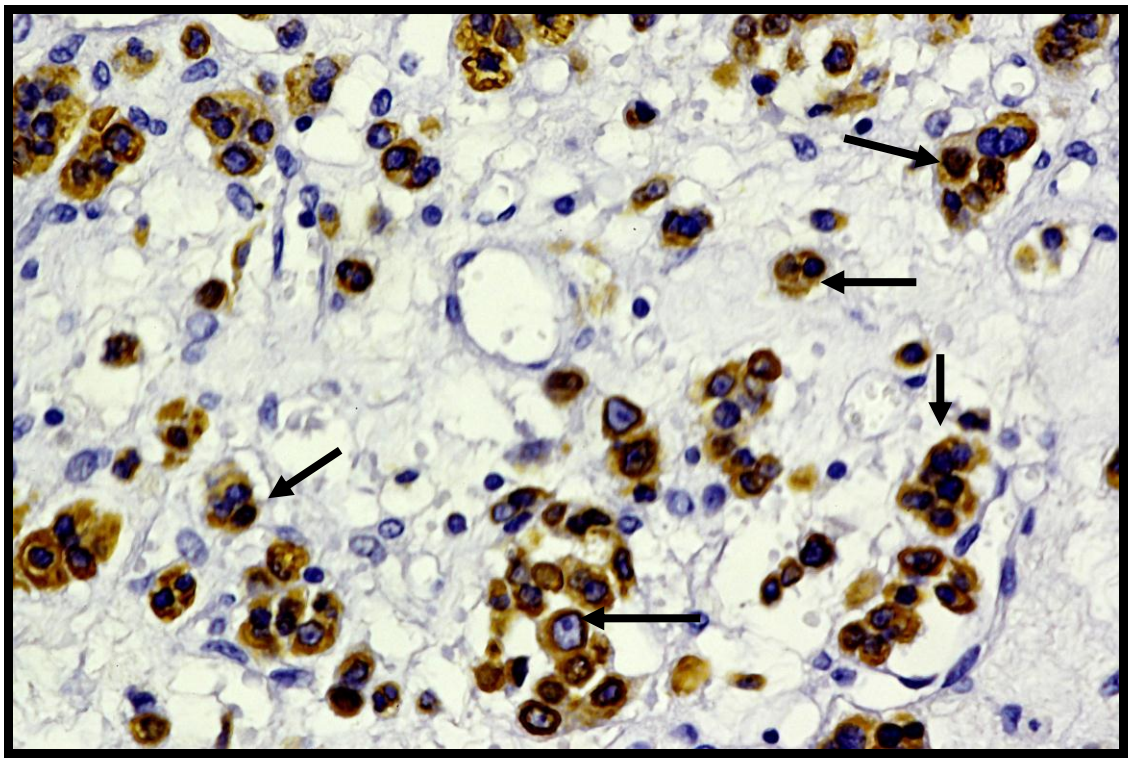

Fig. (25): Photomicrograph of adrenal cortical adenoma showing intense cytoplasmic immunoreactivity for Cytokeratine.(Immunoperoxidase X 400).

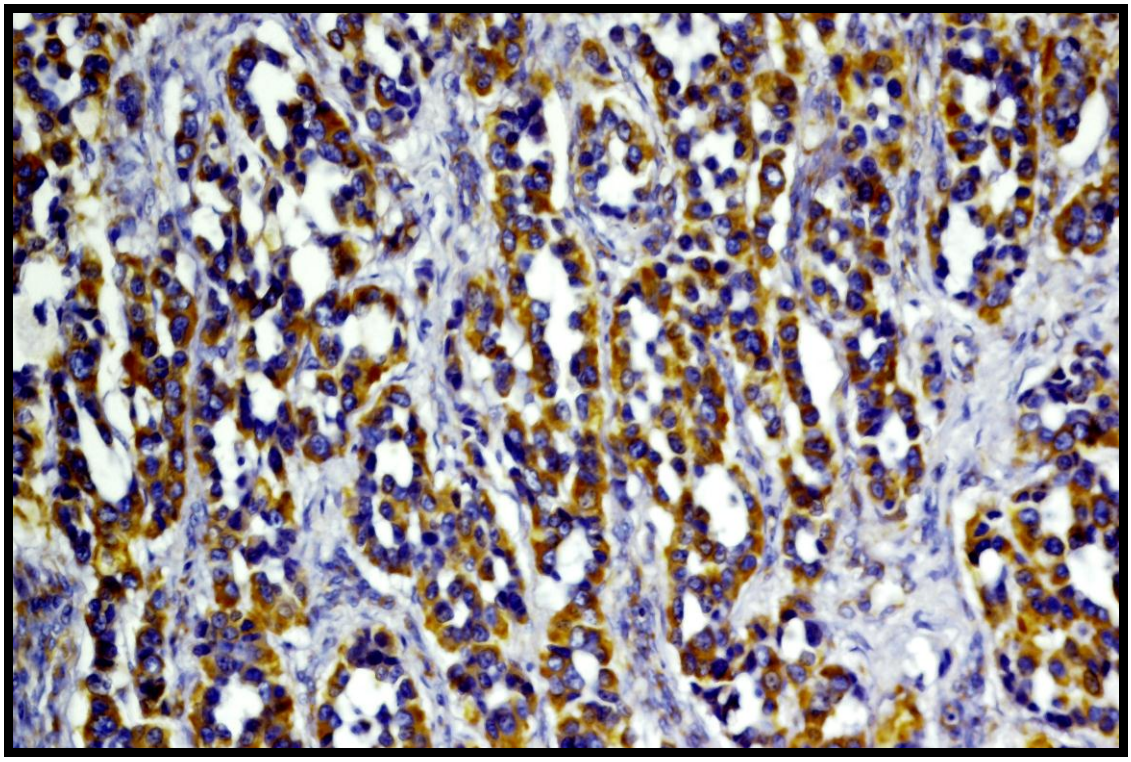

Fig. (26): Photomicrograph of adrenal cortical carcinoma showing intense cytoplasmic immunoreactivity for Cytokeratine (The brown color)(Immunoperoxidase X 200).

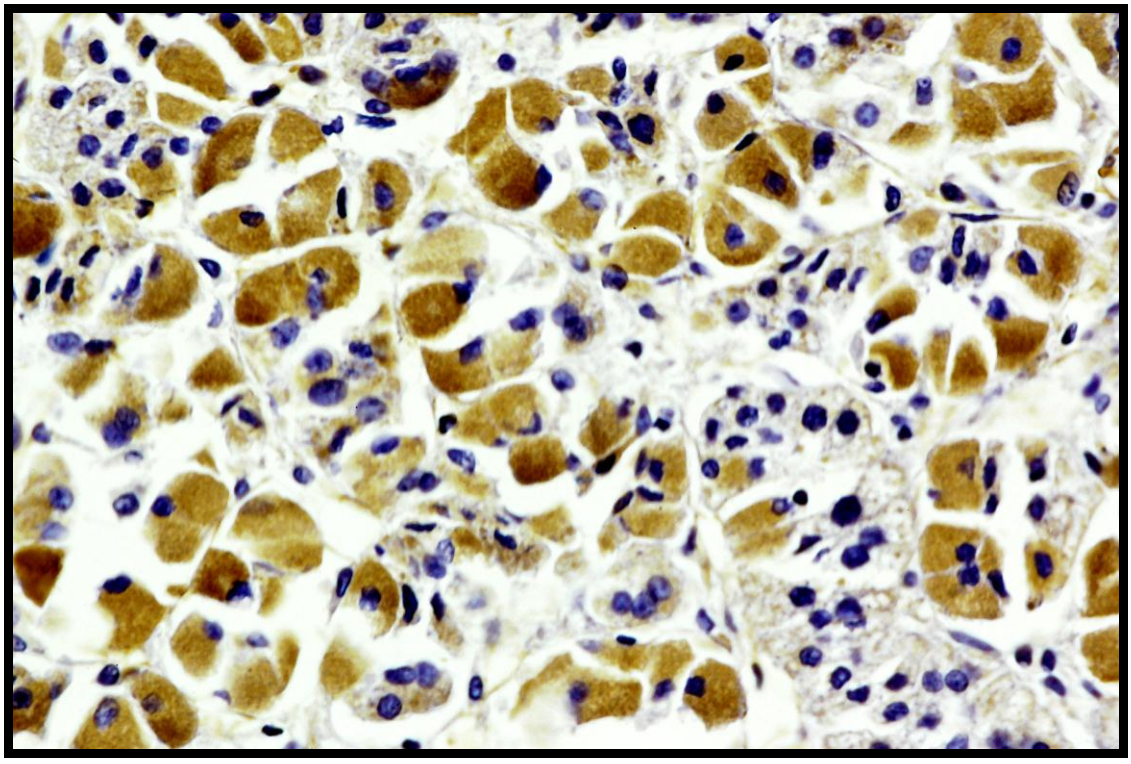

Fig. (27): Photomicrograph of adrenal cortical adenoma showing intense cytoplasmic immunoreactivity for Vimentine (The brown color) (Immunoperoxidase X 400).

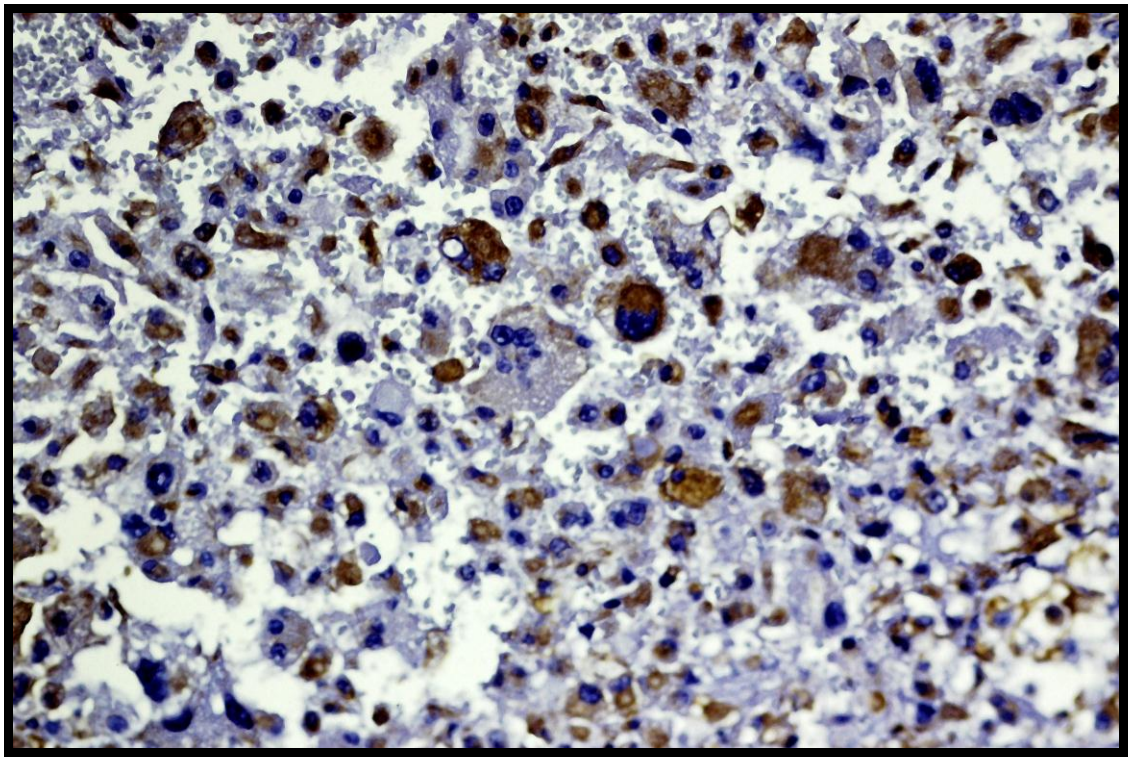

Fig. (28): Photomicrograph of adrenal cortical carcinoma showing intense cytoplasmic immunoreactivity for Vimentine(brown color) (Immunoperoxidase X 200).

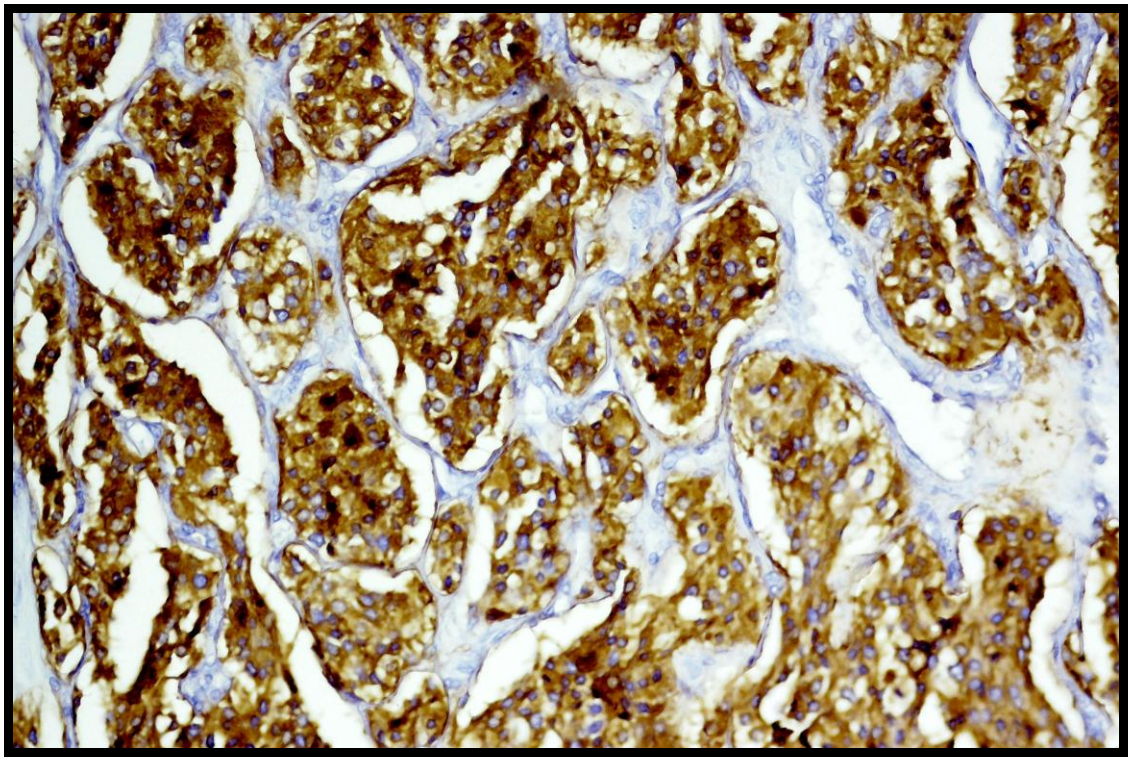

Fig. (29): Photomicrograph of pheochromocytoma showing intense cytoplasmic immunoreactivity of chromaffin cells for Chromogranine (The brown color) (Immunoperoxidase X 200).

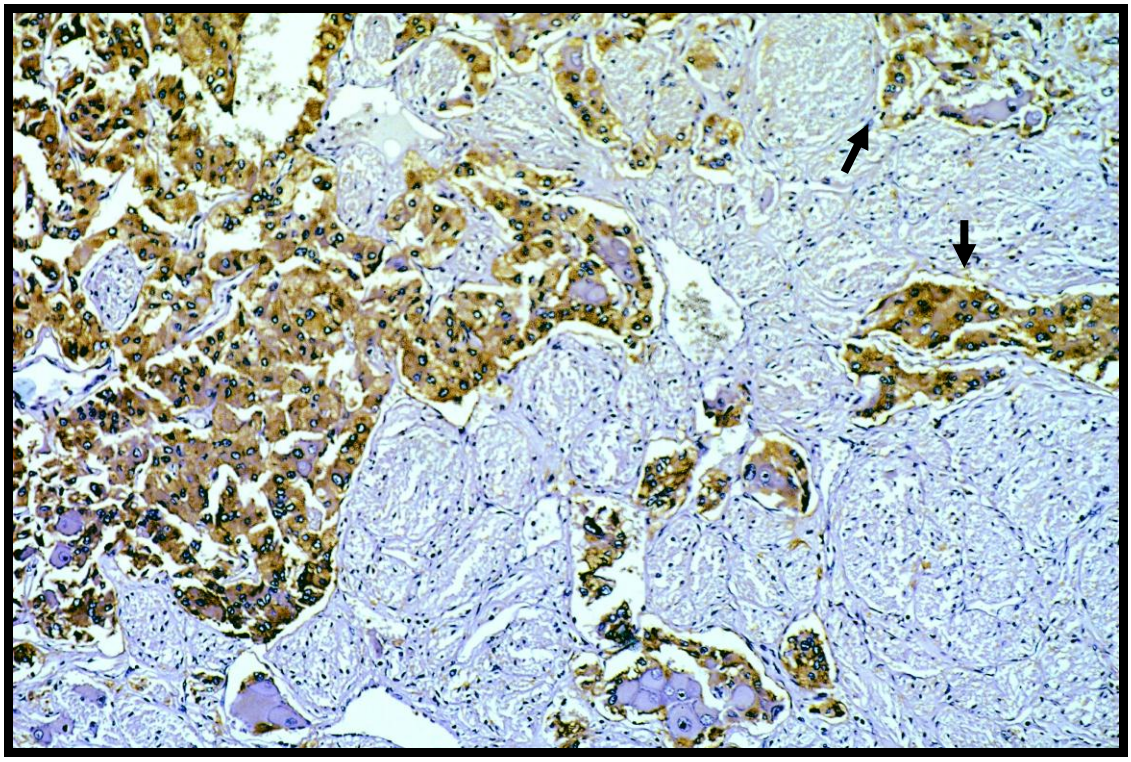

Fig. (30): Photomicrograph of composite pheochromocytoma showing intense cytoplasmic immunoreactivity for Chromogranine within the chromaffin cells (arrows). (Immunoperoxidase X 200).

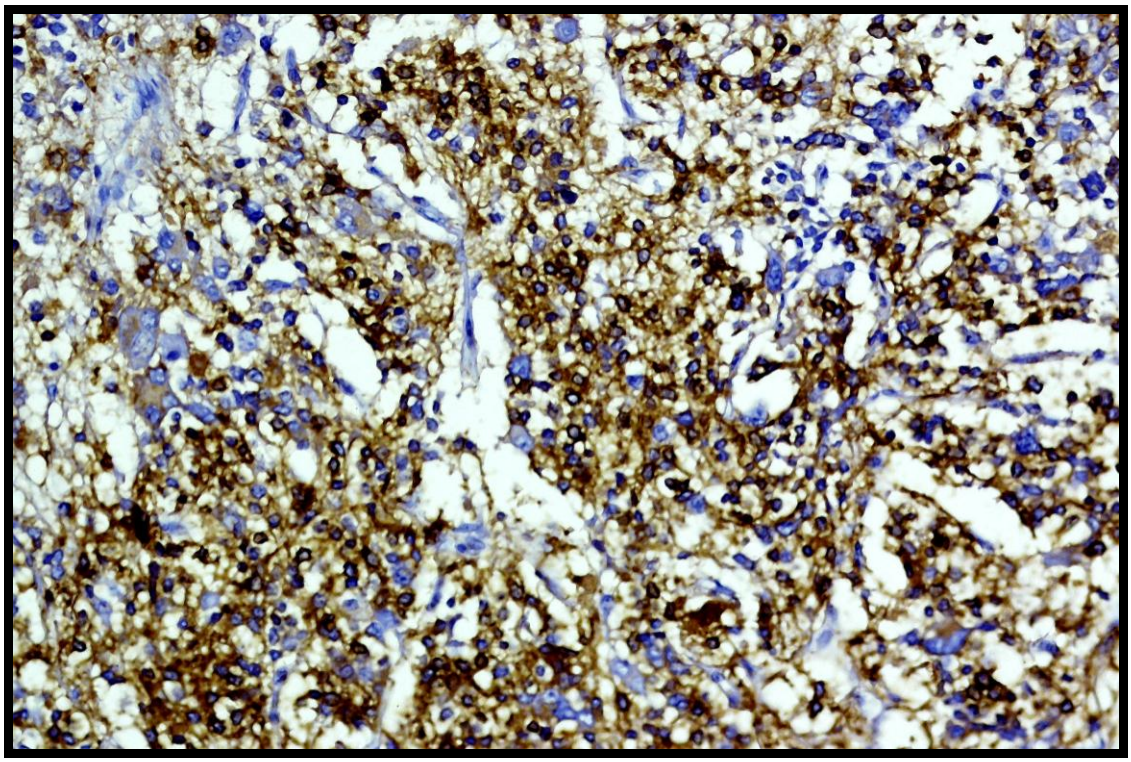

Fig. (31): Photomicrograph of neuroblastoma . immunoreactivity for chromogranin A was seen in brown fibrillar areas with overlapping interwining neuritic processes (brown color) (Immunoperoxidase X 200).

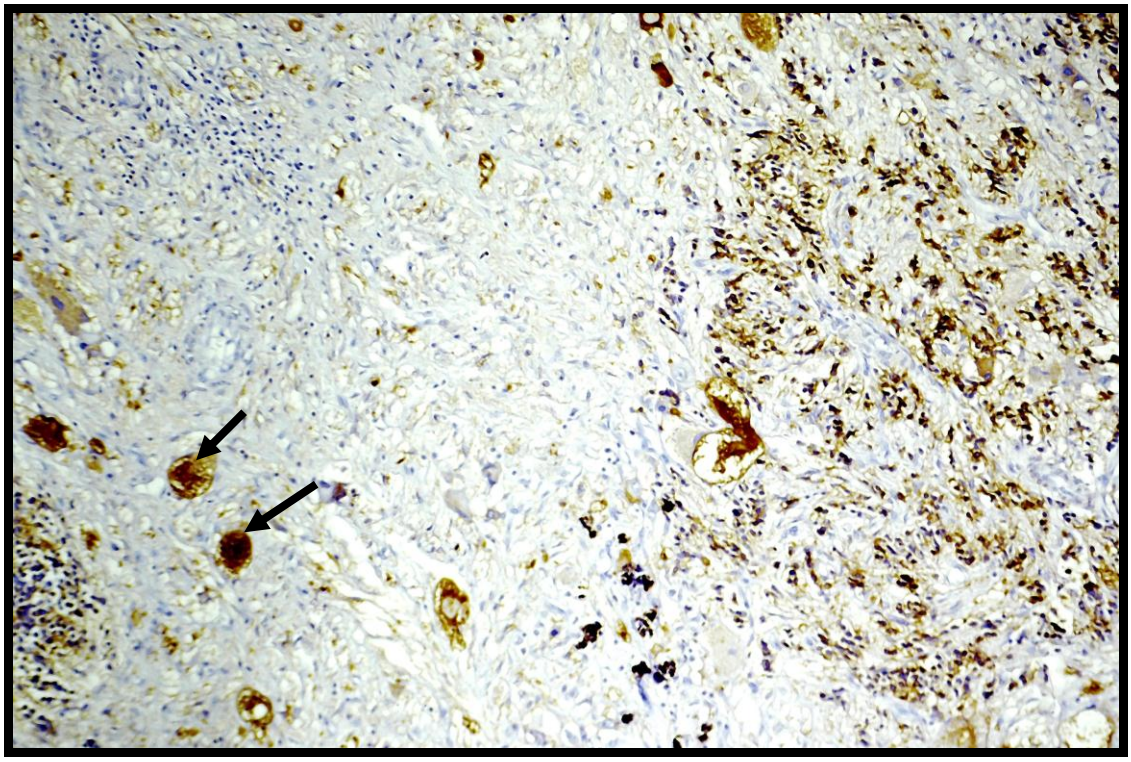

Fig. (32): Photomicrograph of ganglioneuroblastoma, Immunohistochemical analysis directed to chromogranin A. Note the large neuroblasts with intense cytoplasmic staining also staining in processes. (Immunoperoxidase X 100).

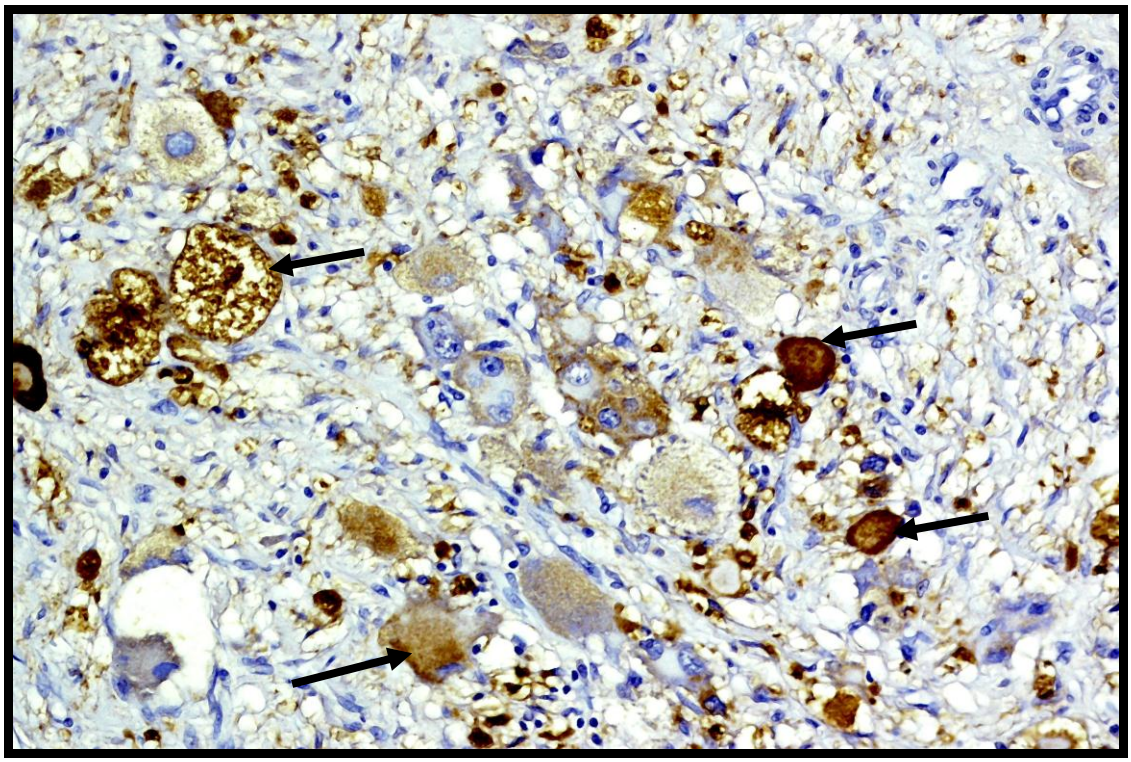

Fig. (33): Photomicrograph of ganglioneuroma showing immunoreactivity for chromogranin A. Note ganglion cells(arrows) are strongly stained. (Immunoperoxidase X 200).

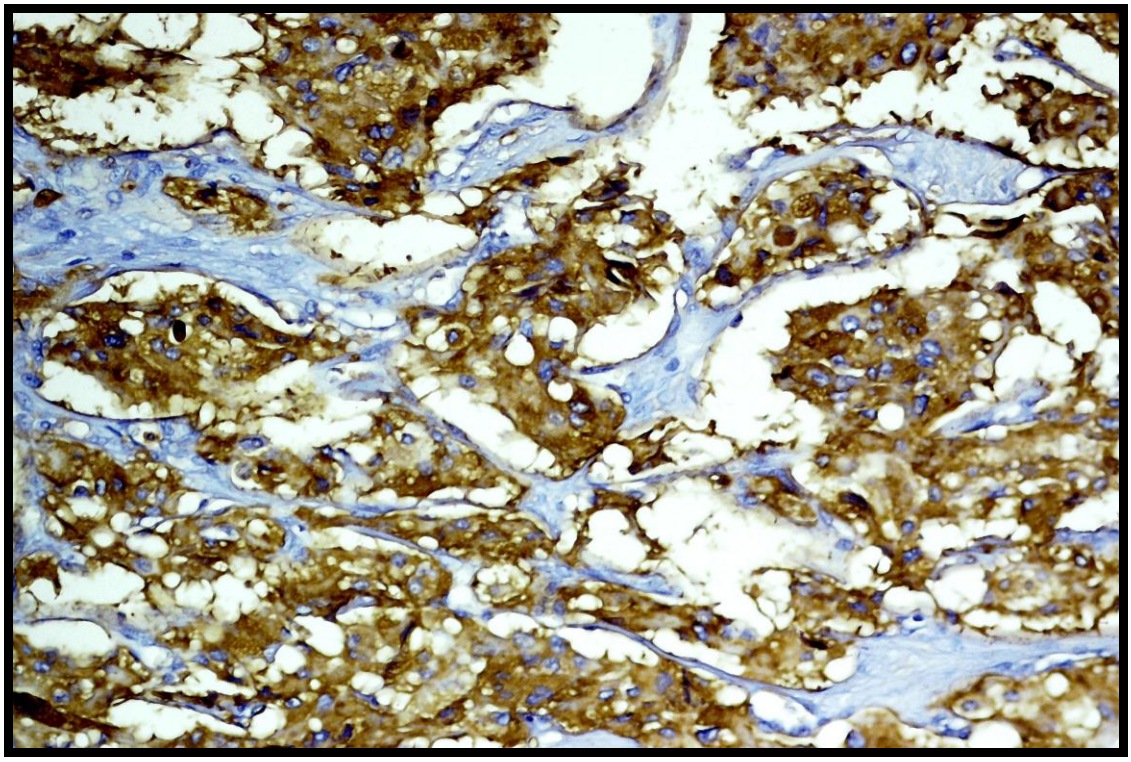

Fig. (34): Photomicrograph of pheochromocytoma showing immunoreactivity for neuron specific enulase, Note the diffusely strong staining within the cytoplasm of Chief cells. (Immunoperoxidase X 200).

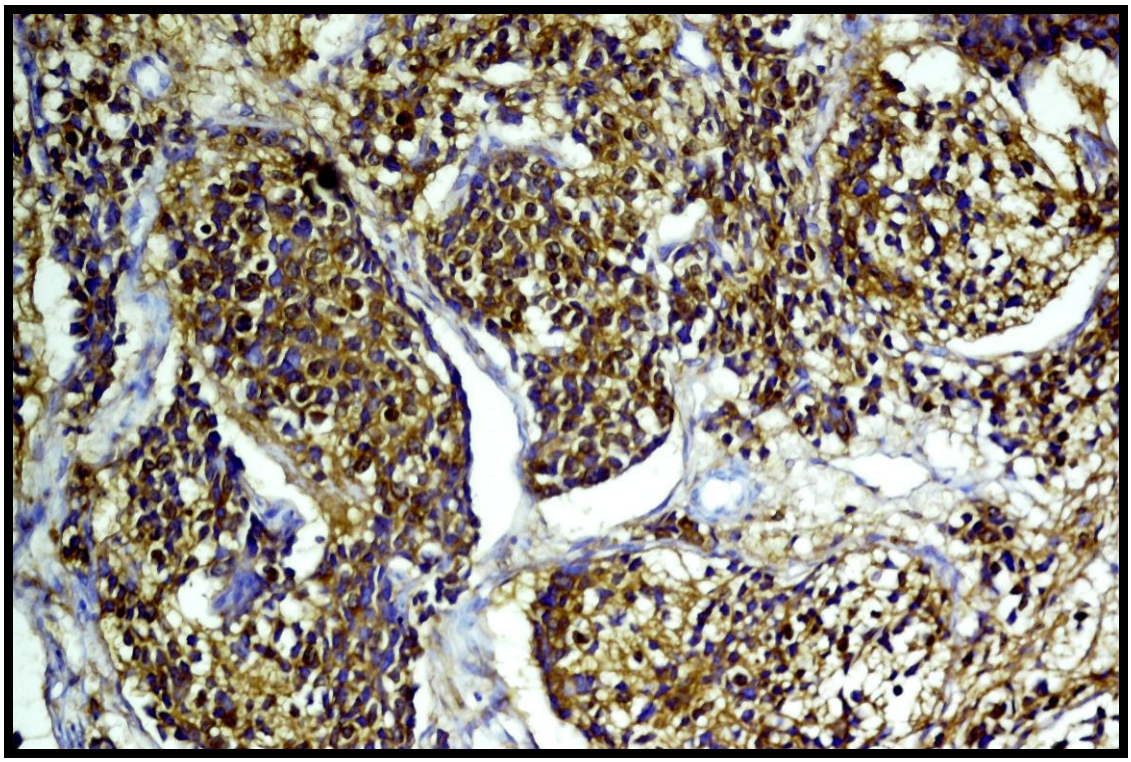

Fig. (35): Photomicrograph of neuroblastoma stained for neuron specific enulase. Almost all of the cells show a positive cytoplasmic reaction, whereas the stroma is unstained. (Immunoperoxidase X 200).

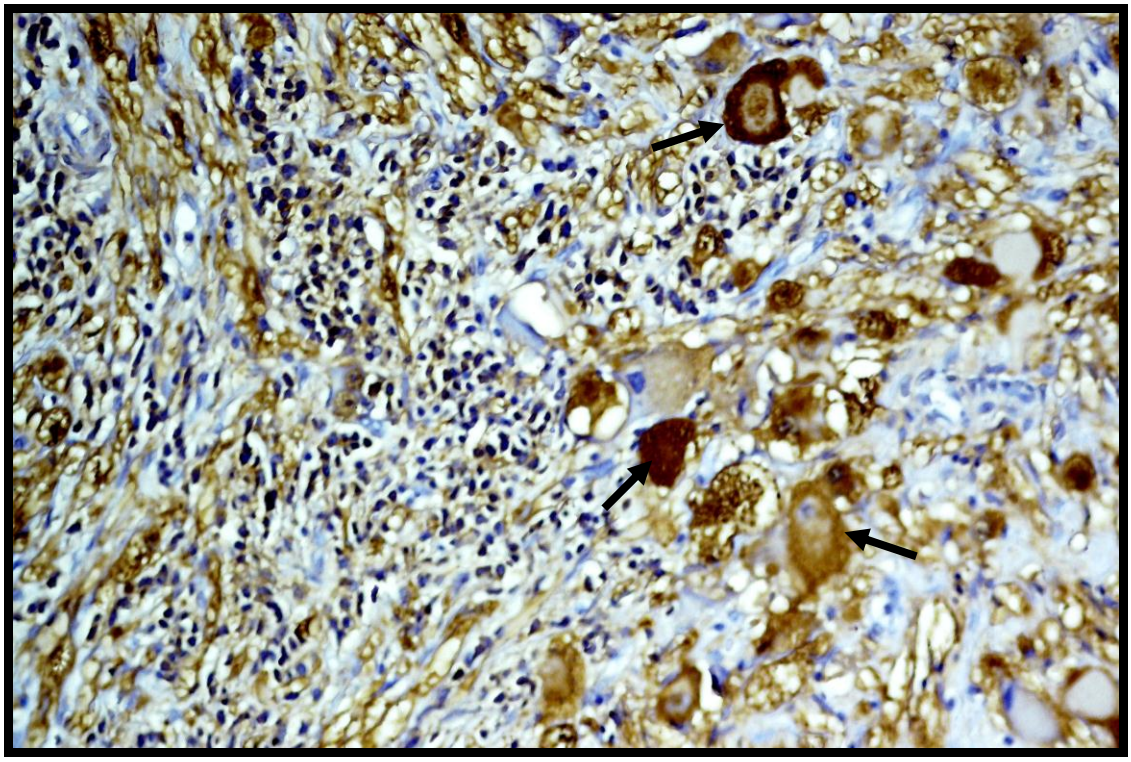

Fig. (36): Photomicrograph of ganglioneuroblastoma stained for neuron specific enolase, highlights abundant stromal septa. The cytoplasm of ganglion cells (arrows) is also intensely positive.(Immunoperoxidase X 200).

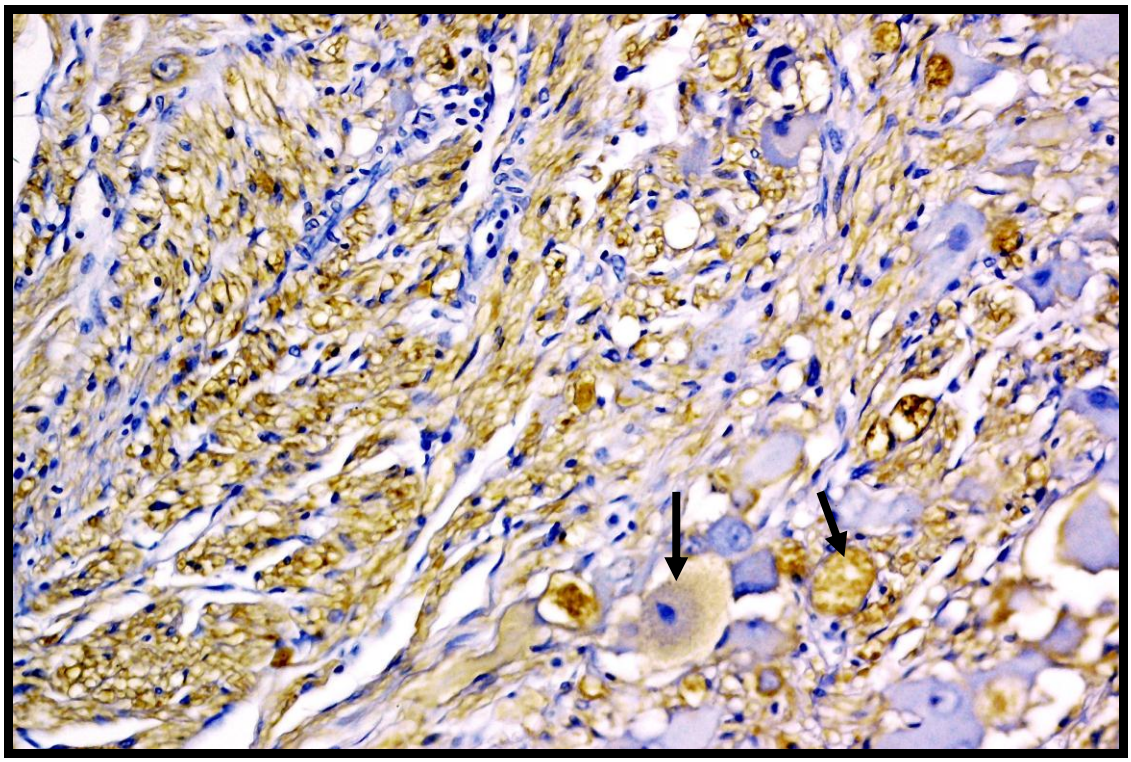

Fig. (37): Photomicrograph of ganglioneuroma showing immunoreactivity for NSE. Ganglion cells are strongly stained (arrows). Schwann cells also stained positively.
(Immunoperoxidase X 200).

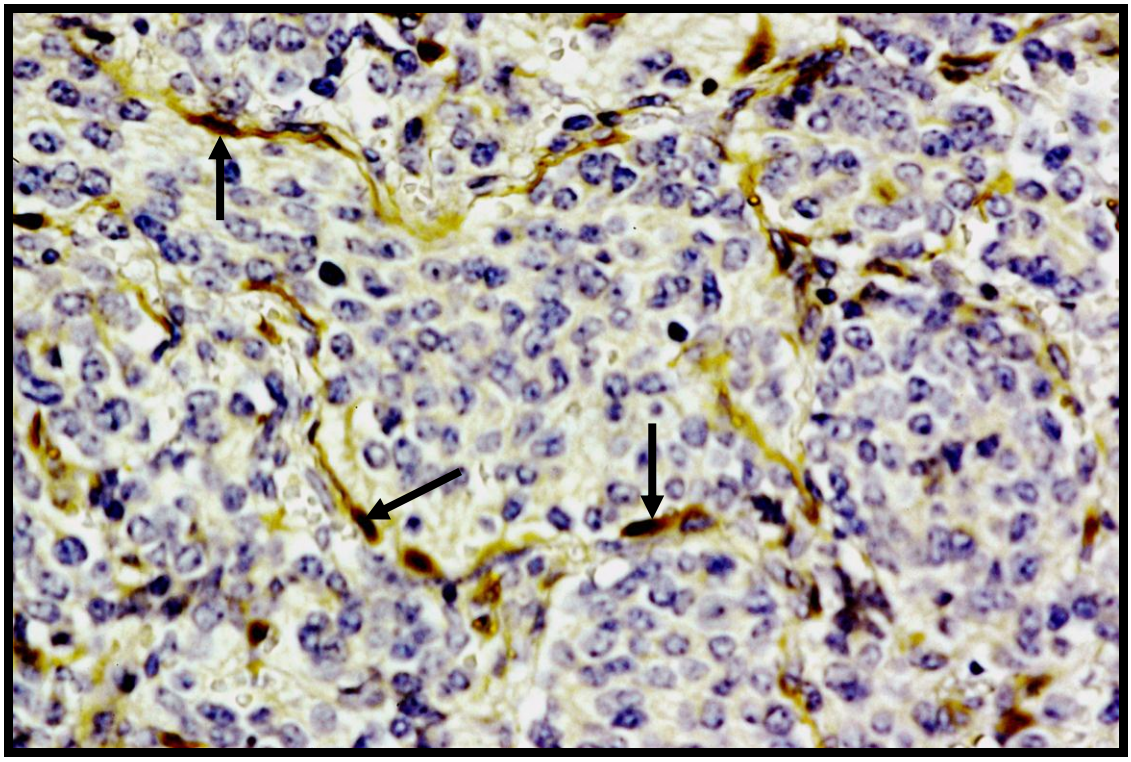

Fig. (38): Photomicrograph of pheochromocytoma showing immunoreactivity for S-100 protein in sustentacular cells (arrows) surrounding the chromaffin cells. (Immunoperoxidase X 200).

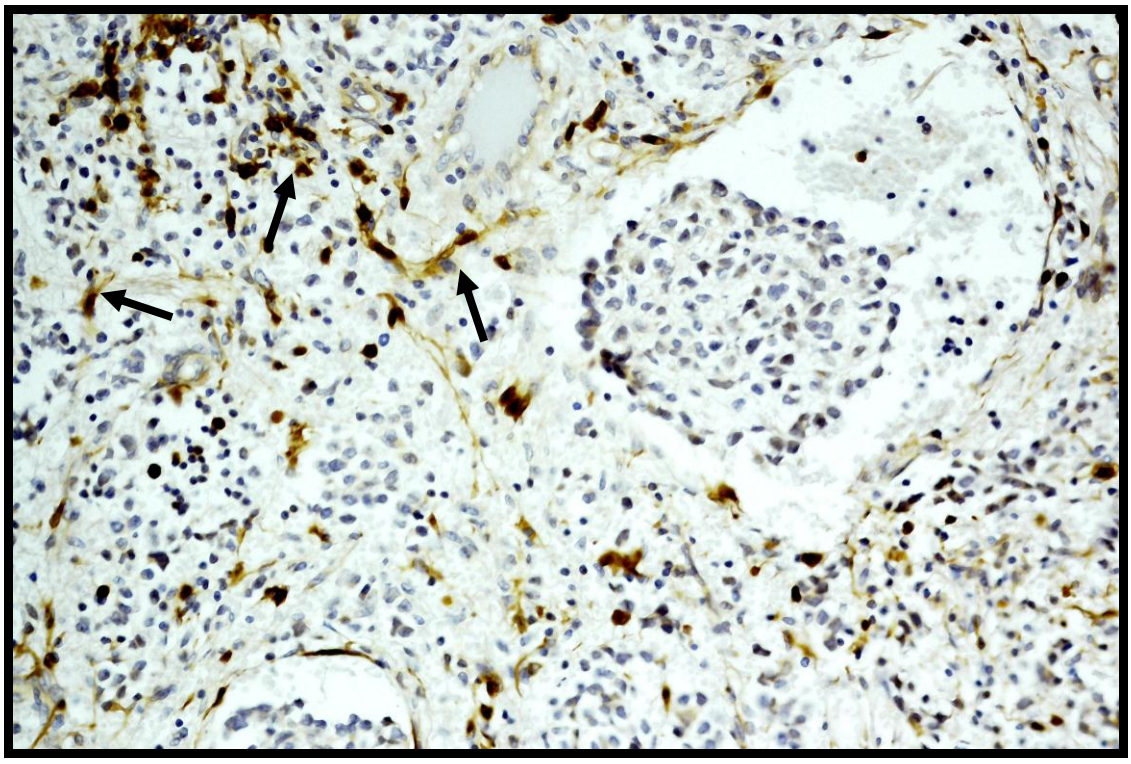

Fig. (39): Photomicrograph of neuroblastoma show satellite to dendritic cells immunoreactive for S-100 protien are adjacent to vascular septa (arrows). Cells are consistent with schownn or sustenticular cells. (Immunoperoxidase X 100).

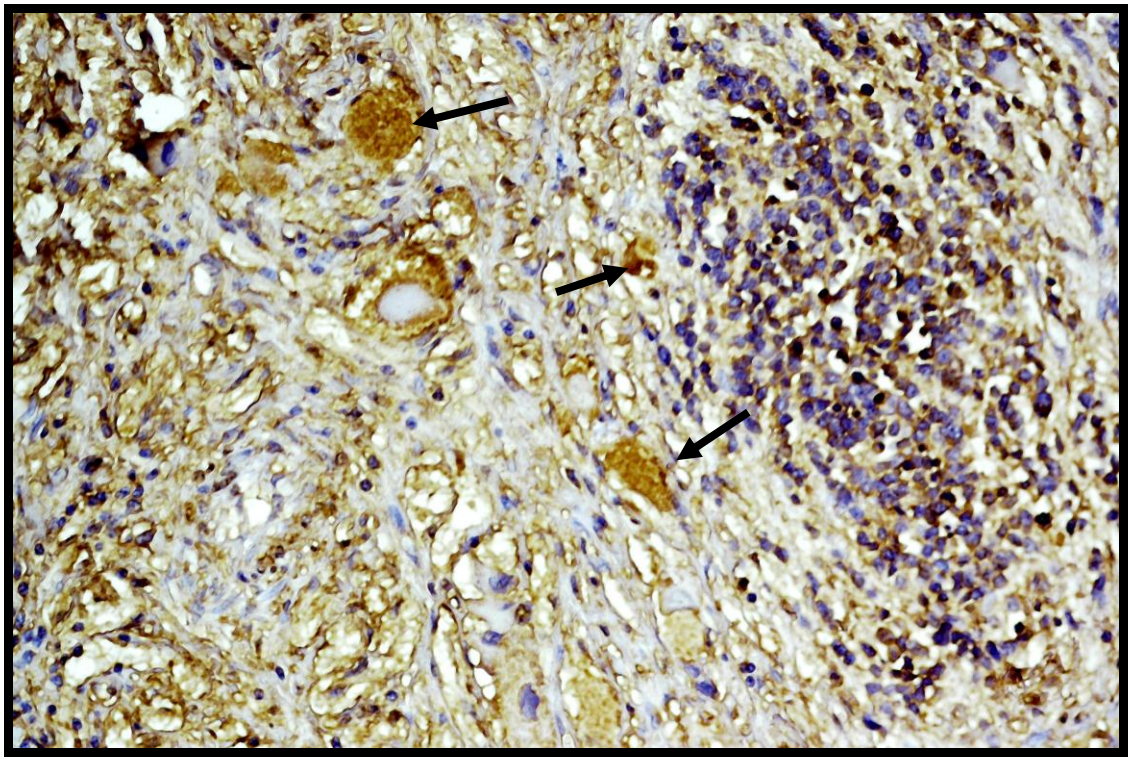

Fig. (40): Photomicrograph of ganglioneuroblastoma, immunostain for S-100 protein. Cells in intimate contact with ganglion cells show intense staining (arrows), and are in the typical location of satellite cells. (Immunoperoxidase X 100).