

# A Clinicopathological and Immunohistochemical Analysis to Study Extragenadal Malignant Germ Cell Tumors

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## ABSTRACT

**Introduction:** Only 2-5% of the malignant germ cell tumours are primary extragonadal germ cell tumours. They are generally midline in location in the whole body starting from pineal gland to coccyx like retroperitonium, central nervous system and mediastinum. The present study was aimed at establishing the biological feature of extragonadal malignant gonadal germ cell tumours and to determine the usefulness of markers like OCT3/4, CD117, CD30, PLAP, AFP and  $\beta$ -HCG for diagnosis of these tumours.

**Material and methods:** The present study was conducted in the department of pathology AIIMS, New Delhi during the period of two years. The study included 80 cases of extragonadal malignant germ cell tumours. A semi quantitative scoring system was used for grading of immunohistochemical expression which was based on percent positivity ranging from 0 to 100%. In this negative expression was considered as 0%, weak expression as < 50% and  $\geq$ 50% was strong expression. <sup>7</sup> All the data thus obtained was arranged in a tabulated form and analysed using SPSS software.

**Results:** In the present study there were 19 males and 14 females having CNS germ cell tumours, 16 males had mediastinal germ cell tumours and 11 male had retroperitoneal germ cell tumour. PLAP was detected in more than 80% gerinomas and 100% cases of mixed germ cell tumors. 90% cases of germinomas had CD117 and 100% mixed germ cell tumor had this.

**Conclusion:** An accurate and correct diagnosis of extragonadal germ cell tumours is critical for patient management. Immunohistochemistry is an important tool in the diagnosis and differentiating its different histological types.

**Keywords:** Extragenadal, Immunohistochemistry, Germ Cell

## INTRODUCTION

Only 2-5% of the malignant germ cell tumours are primary extragonadal germ cell tumours. They are generally midline in location in the whole body starting from pineal gland to coccyx like retroperitonium, central nervous system and mediastinum. Approximately 50%-70% of these tumours occur at mediastinum. Out of these approximately 70%-75% of these are mature teratomas. There are only 25%-30% of these tumours that are malignant. Based on the histology, cytology and cytological characteristics, they are similar to gonadal tumours i.e. those occurring at testis and ovary. But studies have shown that their clinical and biological characteristics are quite different from the gonadal tumors. It is very necessary that accurate diagnosis is established so that adequate clinical therapy is initiated and prognosis is established. Their diagnosis cannot be solely based on

haematoxylin and eosin (H&E) staining but also requires immunohistochemical studies. Because of their different clinical line of treatment and prognosis, it is very necessary for the clinicians to make accurate differential diagnosis between gonadal and non gonadal tumours as well as germinomas and non-germinomatous tumors.<sup>1-4</sup>

For the diagnosis of gonadal germ cell tumours, immunohistochemical verification is required. The various routinely used immunohistochemical markers for diagnosis of gonadal germ cell tumours include PLAP, CD117, AFP and  $\beta$ -HCG. The present study was aimed at establishing the biological feature of extragonadal malignant gonadal germ cell tumours and to determine the usefulness of markers like OCT3/4, CD117, CD30, PLAP, AFP and  $\beta$ -HCG for diagnosis of these tumours.<sup>5,6</sup>

## MATERIAL AND METHODS

The present study was conducted in the department of pathology AIIMS, New Delhi during the period of two years. The study included 80 cases of extragonadal malignant germ cell tumours. Ethical committee clearance was obtained from the Institute's ethical board. All the subjects were informed about the study and a written consent was obtained from all of them in their vernacular language. All the specimens were fixed using 10% formalin and then embedded in paraffin. H and E staining was done of 4  $\mu$ m cut sections. Another set of 4  $\mu$ m sections were removed of paraffin with xylene and rehydration of the were done using ethanol. Intubstion of these sections was done using 3% H<sub>2</sub>O<sub>2</sub> for inhibition of endogenous peroxidise, this was followed by digestion for antigen retrieval using trypsin. Intubation was done in a humid chamber at a temperature of 4°C overnight after the addition of primary antibodies. This was followed by rinsing with PBS and 2<sup>nd</sup> set of antibodies were added. Intubation was done at room temperature for 30 minutes. After that coloring was done with DAB for 15 minutes and couterstaining was done with Heatoxylin. Using placental tissue, GIT stromal tumor a positive control staining was prepared. For negative controls blocking serum was used instead of primary antibody. A semi quantitative scoring system was used for grading of immunohistochemical expression which was

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Characteristics	CNS	Mediastinum	Retroperitonium
Gender			
Male	19	16	11
Female	14	10	10
Age			
<10	6	5	6
10-20	12	7	5
21-30	8	8	5
>30	5	8	5
Size	0.6-5.5 cm	7-20 cm	8-17cm
Histological type			
Germinoma	15	7	4
Immature teratoma	4	4	4
Yolk sac tumor	3	4	3
Embryonal carcinoma	4	3	3
Choriocarcinoma	3	3	4
Mixed germ cell tumors	4	4	4

**Table-1:** Clinical features of the tumours

HISTOLOGY	Plap	CD117	OCT3/4	HCG	AFP	CD30	CK AE1/3	EMA
Germinoma	+	+	+	-	-	-	+/-	+
Immature teratoma	-	-	-	-	-	-	+	+
Yolk sac tumor	-/+	-/+	-	-	+	-	+	+
Mixed germ cell tumor	+	+	-	-	+/-	+	+	+

**Table-2:** Expression of immunohistochemical markers

based on percent positivity ranging from 0 to 100%. In this negative expression was considered as 0%, weak expression as < 50% and ≥50% was strong expression. <sup>7</sup>

### STATISTICAL ANALYSIS

All the data thus obtained was arranged in a tabulated form and analysed using SPSS software.

### RESULTS

The present study included a total of 80 subjects. The mean age of the subjects was 24.56 +/- 8.65 years. Table 1 shows the clinical features of tumors. In the present study there were 19 males and 14 females having CNS germ cell tumours, 16 males had mediastinal germ cell tumours and 11 male had retroperitoneal germ cell tumour. There were 17 patients younger than 10 years of age. Majority of subjects (n=24) were between 10- 20 years of age. There were 21 subjects between 21-30 years of age. There were 8 subjects having mediastinal germ cell tumours were more than 30 years of age. The size range of subjects having CNS germ cell tumours was 0.6-5.5 cm and of mediastinal germ cell tumours was 7-20 cm. The mean size of retroperitoneal tumours was 8-17 cm. On the basis of histology there were 15 cases of germinoma, 4 cases of immature teratoma, 3 case of yolk sac tumour and 4 cases of mixed germ cell tumours.

The immunohistological results are illustrated in table 2. PLAP was detected in more than 80% gerinomas and 100% cases of mixed germ cell tumors. 90% cases of germinomas had CD117 and 100% mixed germ cell tumor had this. EMA staining was seen in all yolk sac tumors and mixed germ cell tumors. All the controls were negative for PLAP, CD117 and OCT3/4. Yolk sac tumors were also positive for AFP but

Germinoma and immature teratome didn't had this marker.

### DISCUSSION

Germ cell tumors are frequently found in testes and ovary but they are hardly found in extragonadal locations like mediastinum, CNS and retroperitoneal locations. The most common location for primary extragonadal germ cell tumor is mediastinum which is followed by CNS and retroperitoneal region.<sup>8</sup> There are also variation in the clinical characteristics as per the age, gender and histological type. Majority of cases of CNS extragonadal germ cell tumors occur in children and adolescents especially during 10-20 years of age.<sup>9</sup> Patients having retroperitoneal teratoma are generally younger than 10 years of age.<sup>10</sup> In our study, there were 9 males and 4 females having CNS germ cell tumours, 6 males had mediastinal germ cell tumours and 1 male had retroperitoneal germ cell tumour. There were 2 patients younger than 10 years of age. Majority of subjects (n=9) were between 10-20 years of age. There were 6 subjects between 21-30 years of age. There were 3 subjects having 3 mediastinal germ cell tumours and were more than 30 years of age. The size range of subjects having CNS germ cell tumours was 0.6-5.5 cm and of mediastinal germ cell tumours was 7-20 cm. The mean size of retroperitoneal tumours was 8-17 cm. On the basis of histology there were 14 cases of germinoma, 3 cases of immature teratoma, 1 case of yolk sac tumour and 2 cases of mixed germ cell tumours. These tumors are also more common amongst males compared to females. According to a study, the male to female ratio ranges from 1.5 to 3:1 in CNS germ cell tumors.<sup>11</sup> The clinical signs and symptoms include abdominal mass, pain, hemoptysis, fever, cough and dyspnea. However there are also certain asymptomatic

cases. In our study, PLAP was detected in more than 80% gerinomas and 100% cases of mixed germ cell tumors. 90% cases of germinomas had CD117 and 100% mixed germ cell tumor had this. EMA staining was seen in all yolk sac tumors and mixed germ cell tumors. All the controls were negative for PLAP, CD117 and OCT3/4. Yolk sac tumors were also positive for AFP but Germinoma and immature teratome didn't have this marker. The most common diagnostic marker employed for diagnosis of germinoma is PLAP and CD117.<sup>12,13</sup> In a study conducted by Hattab, Oct3/4 was also found to be highly sensitive for germinoma.<sup>14</sup>

## CONCLUSION

Extragonadal malignant germ cell tumors are rare and generally arise in midline structures, like mediastinum retroperitoneum and coccygeal region. It has been seen that Seminomas/germinomas have better prognosis as compared to malignant tumors. An accurate and correct diagnosis of extragonadal germ cell tumours is critical for patient management. Immunohistochemistry is an important tool in the diagnosis and differentiating its different histological types.

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