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Case Series

Pathology Section

Diagnostic Challenges in Rare Head and Neck Tumours: A Series of Five Cases

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ABSTRACT

Meningiomas constitute a large group of tumours of the central nervous system with the prevalence of 24-30%. Extracranial localisation of meningioma is rare. By definition they are not associated with underlying meningioma of the neuraxis and extracranial extension of an intracranial tumour should always be excluded. A 65-year-old female patient with parotid swelling and 16-year-old male patient with mass in nasal cavity were admitted. Both cases came out to be an extracranial meningioma. Third case was a mass in paranasal sinus extending up to the brain of 12-year-old male. The case was diagnosed as pleomorphic Rhabdomyosarcoma (RMS). Pleomorphic RMS is a rare and aggressive tumour which has very poor prognosis, and the survival rate is less than one year. Fourth case was 66-year-old female presented with maxillary mass which was diagnosed as Intestinal Type of Primary Adenocarcinoma (ITAC) of maxillary sinus. Last and fifth case was diagnosed as leiomyosarcoma which was presented as lymph-nodal mass in neck in 60-year-old female. The site is very unusual and this tumour is a rare, aggressive as well. All cases were confirmed by Immunohistochemistry (IHC) study. The diagnosis of head and neck cancers is notoriously challenging, often resulting in advanced stage presentation and poor patient outcomes. The diagnostic difficulty stems from a combination of delayed patient presentation, symptoms that overlap with benign conditions, and high diversity of tumour subtypes.

Keywords: Immunohistochemical stain, Leiomyosarcoma, Meningioma, Pleomorphic rhabdomyosarcoma, Sinonasal intestinal type of adenocarcinoma

INTRODUCTION

Meningiomas are neoplasms arising from arachnoidal cells and majority cases behave benign in nature. It accounts for 24-30% of all intracranial tumours [1]. Ectopic Meningioma (EM) is extremely rare entity, with an incidence rate of approximately 2% of all meningiomas [2]. Most common extracranial sites are of head and neck region including middle ear, temporal bone, oral cavity, orbit, sinonasal cavity, but parotid gland is not a usual site for EM. Histological features are similar to those of intracranial meningiomas [3]. These pose a diagnostic problem due to their rarity compared to other neoplasm of parotid gland. EM can occur in nasal cavity but due to its rare incidence as well as diagnostic dilemma with other haemangioma or polyp of nasal cavity makes difficulty in diagnosis [4]. Here, the authors depict two cases of EM, one is located in parotid gland and other is in nasal cavity. Sinonasal tumours represent less than 3% of head and neck cancers and 0.8% of all human cancers. The symptoms are identical to those of inflammatory diseases. Due to low incidence of these tumours, there are difficulties in definitive diagnosis and adequate treatment. Sinonasal RMS is exceedingly rare category of RMS. Overall annual incidence of this tumour is 0.034 cases per 100000 populations. Pleomorphic variant is rarer and highly aggressive tumour associated with poor prognosis. Usually it occurs under the age of 10 years with no significant sex predilection [5]. One such case is presented here due its rarity as well as poorest prognosis. The Primary adenocarcinoma of salivary glands is a very uncommon tumour and represents 0.13% of salivary gland tumours in the largest revision. ITAC occurs 20% in maxillary antrum [6]. One such rare case is presented here. Soft-tissue sarcomas of the head and neck are rare tumours and account for less than 10% of all soft-tissue sarcomas and less than 1% of all neoplasm of this region. Leiomyosarcoma is the malignant smooth muscle tumour accounting for only 4% of the head and neck sarcomas [7]. One such a unique case has depicted here. For a period of 10 months these unusual tumours of head and neck region were studied.

CASE SERIES

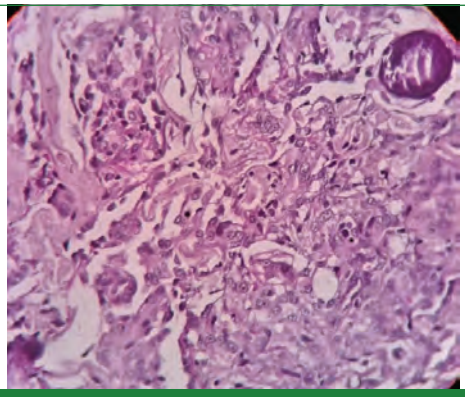
Case 1

A 65-year-old female attended in outpatient department of surgery with a slow growing, painless mass in the right parotid region for last six years. The swelling was located in front of the right ear, below the earlobe. It was non tender. Clinically it was diagnosed as parotid tumour. Radiological examination by Ultrasonography (USG) revealed parotid neoplasm. Fine Needle Aspiration Cytology (FNAC) could not be done due to the patient's apprehension. Computed Tomography (CT) scan of brain revealed normal study. However, complete resection of the tumour was done in the Department of Surgery and the specimen of a parotid tumour sent to the pathology department for histopathological diagnosis. Grossly, the tissue was globular with maximum diameter of 3 cm. After processing the tumour showed histological features are same as intracranial meningothelial meningioma. Tumour showed nests and lobules with meningothelial whorl formation. Psammomatous calcification was also noted focally [Table/Fig-1]. The IHC was done to confirm the diagnosis. The tumour showed positive stain for Epithelial Membrane Antigen (EMA) [Table/Fig-2] and progesterone [Table/Fig-3]. The diagnosis of extracranial meningioma was established. She had an uneventful recovery. Patient is now doing well. No complaint of recurrence is documented till now.

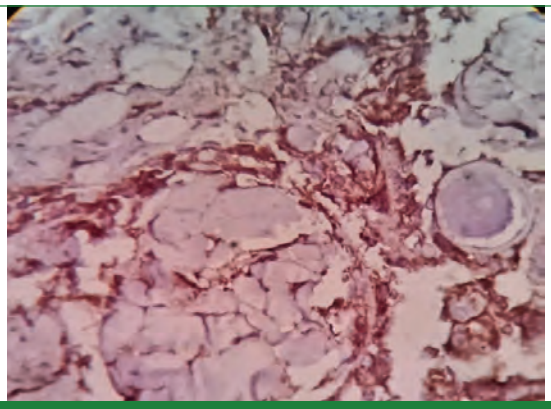
Case 2

A total of 16-year-old male patient presented with left-sided nasal blockage due to nasal mass for last one year. As blockage was progressing he came to Outpatient Department of ENT. Initially clinical diagnosis was nasal polyp. Resection of the mass was done and tissue sent for histopathological examination. Grossly, grayish white multiple tissue pieces were received. Largest tissue piece was 4 cm in maximum dimension. On microscopic examination, the tumour showed nests and lobules with meningothelial whorl formation and syncytial cells with indistinct cell membranes. Psammomatous calcification was also noted focally [Table/

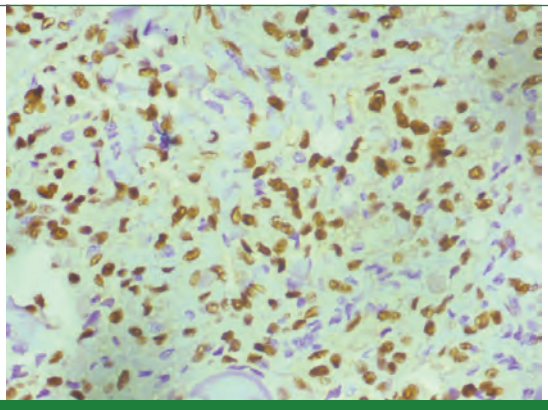
Fig-4]. Tumour was diagnosed histopathologically as extracranial meningothelial meningioma. The tumour showed positive stain for progesterone and EMA in immunohistochemical study [Table/Fig-5]. The diagnosis of extracranial meningioma was established. He had an uneventful recovery. But he was eventually lost to follow-up.



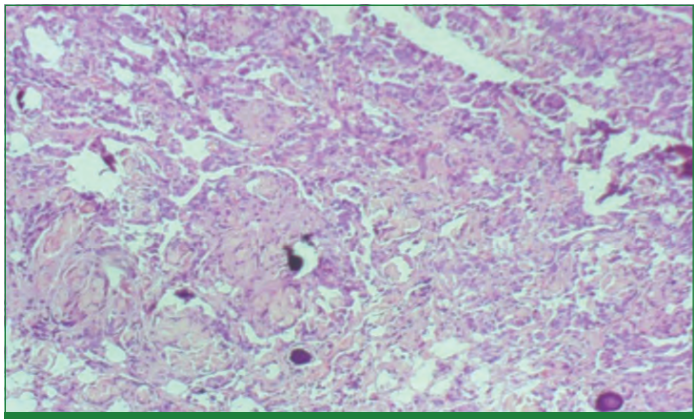
[Table/Fig-1]: Photomicrograph of meningioma showing syncytial growth pattern and psammoma body. (H&E, 400X magnification).
H&E: Haematoxylin and Eosin



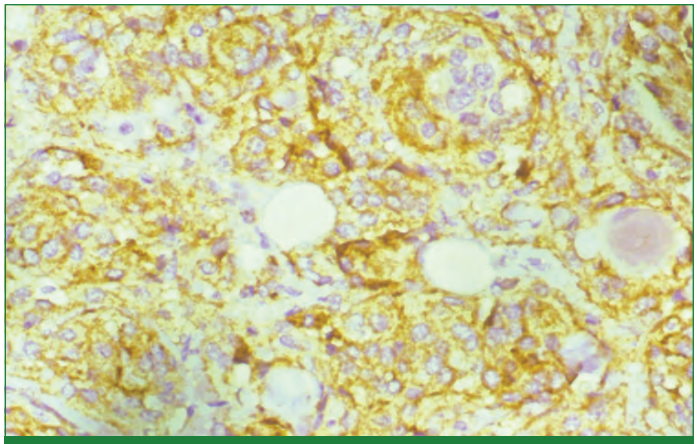
[Table/Fig-2]: Photomicrograph of meningioma showing strong membranous positivity in EMA. (IHC, 400X)



[Table/Fig-3]: Photomicrograph of meningioma showing nuclear positivity in Progesterone stain (IHC, 400X).



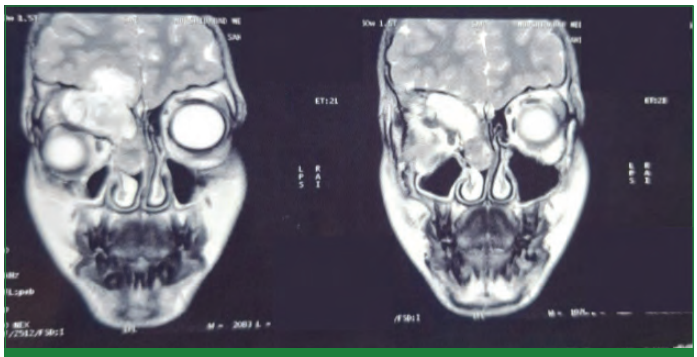
[Table/Fig-4]: Photomicrograph of meningioma sncytial growth pattern and psammoma body. (H&E, 100X).



[Table/Fig-5]: Photomicrograph of Meningioma showing strong membranous positivity in EMA. (IHC, 400X)

Case 3

Patient was 12-year-old boy suffering for difficulty in vision and headache for last three years. He had treated in Nepal for vision problem. But unfortunately vision was deteriorated. For last six months he was suffering from proptosis of right eye and severe headache. He was admitted for severe headache and loss of vision. Magnetic Resonance Imaging of the Paranasal Sinuses (MRI-PNS) revealed that lobulated altered signal intensity lesion at right fronto-ethmoidal air cells with significant mass effect and proptosis right eye-Mucocele/Polypoidal mass. The Contrast-Enhanced Computed Tomography of the Paranasal Sinuses (CECT-PNS) scan revealed that a fairly large heterogeneously enhancing mass arising from right ethmoidal-frontal sinuses with mass effect pushing the right orbit and extending up to anterior cranial fossa [Table/Fig-6]. After surgery we received fragmented whitish tissue pieces which were en bloc embedded for histopathological examination. On microscopical examination we found spindle cells arranged in fascicles with nuclear pleomorphism. Large tumour giant cells having Rhabdomyoblastic appearance along with inflammation were also present. Our histopathological diagnosis was pleomorphic RMS [Table/Fig-7]. The case was confirmed by immunohistochemical study. The spindle cells were Vimentin strongly positive [Table/Fig-8] and SMA positive [Table/Fig-9]. Large cells were Desmin positive [Table/Fig-10]. Spindle cells and large cells were negative for S100 and Cluster of Differentiation 34 (CD34), Cytokeratin and melan-A. The diagnosis of Pleomorphic RMS was established. Postoperative period was uneventful. He was treated with postoperative radiation therapy followed by chemotherapy by doxorubicin. Patient is now under treatment of chemoradiation therapy.

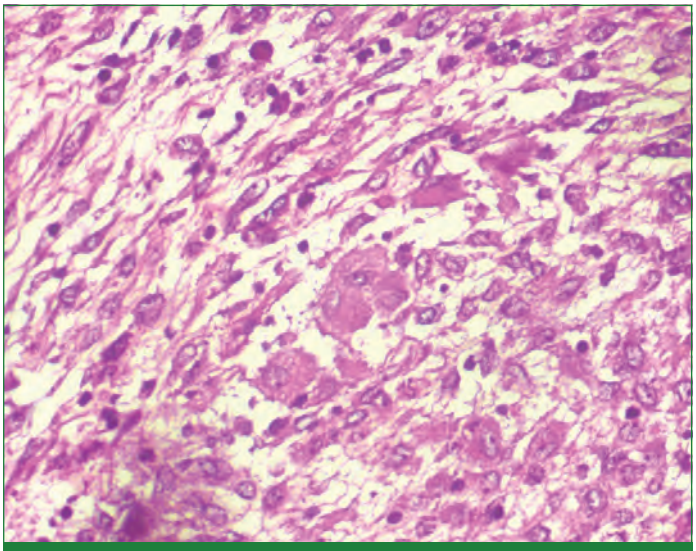


[Table/Fig-6]: CECT (contrast-enhanced) showing fairly large heterogeneously enhancing mass arising from right ethmoidal-frontal sinuses with mass effect pushing the right orbit and extending up to anterior cranial fossa in coronal view.

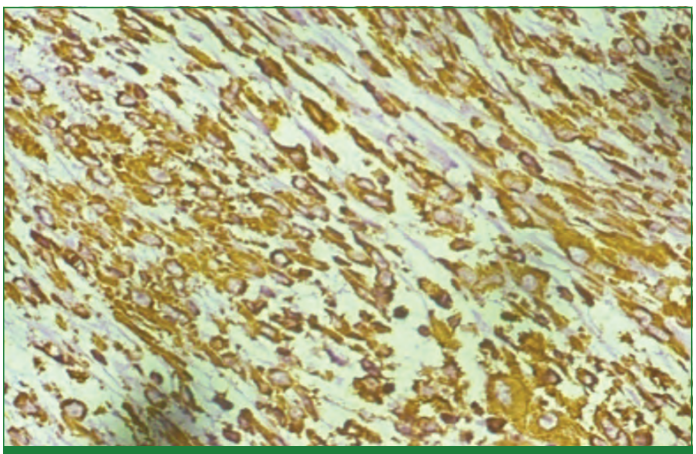
Case 4

A 66-year-old female patient was presented in outpatient department of surgery with painless swelling on maxillary area for last six months. Patient got admitted in Surgery Department. CT scan showed irregular heterogeneous mass involving maxillary antral cavity. Total maxillectomy was done and we received specimen of mass in the

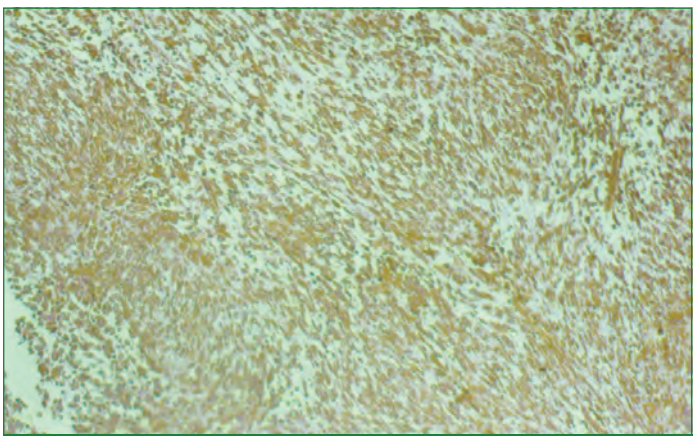
maxillary antral cavity. On gross examination, the tumour was grayish white in colour, 7 cm×5 cm×3 cm and completely filled maxillary cavity [Table/Fig-11]. Histopathological examination showed the tumour cells were arranged in nests and glandular patterns in fibrocollagenous stroma. Individual cells had a moderate amount of eosinophilic cytoplasm and hyperchromatic nuclei. Moderately differentiated adenocarcinoma was diagnosed [Table/Fig-12]. Then IHC study was done. IHC showed the tumour cells strongly positive for Cytokeratin (CK) 20 [Table/Fig-13] and focal positive for CK7. CK10 and S100 immunostains were negative. By clinical, histopathological and IHC study, the case was confirmed as ITAC of maxillary sinus (sinonasal ITAC). The recovery was uneventful, and the patient was referred to radiotherapy at a later date.



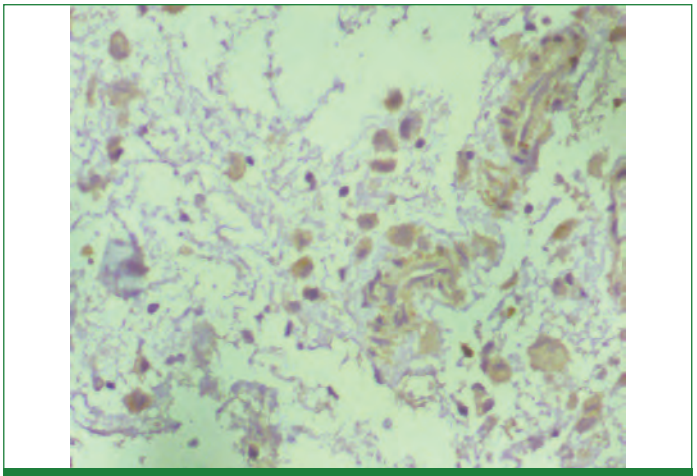
[Table/Fig-7]: Photomicrograph of Pleomorphic Rhabdomyosarcoma (RMS) showing spindle cells arranged in fascicles with nuclear pleomorphism. Large tumour giant cells having Rhabdomyoblastic appearances along with inflammation, (H&E, 400X).



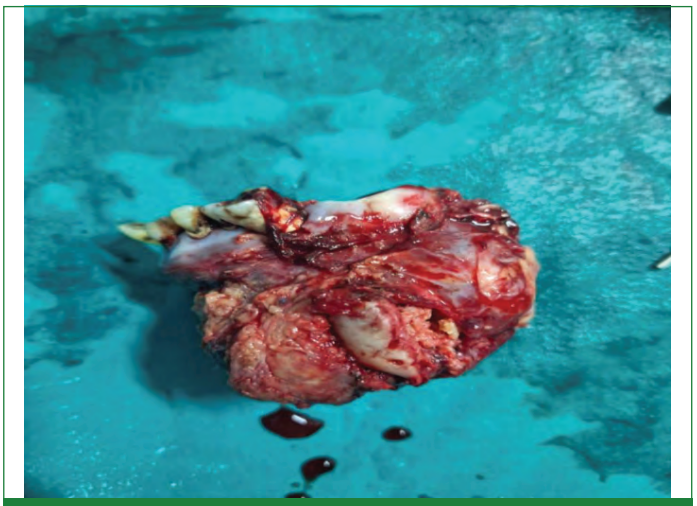
[Table/Fig-8]: Photomicrograph of Pleomorphic Rhabdomyosarcoma (RMS) showing spindle cells, showing strong cytoplasmic positivity (Vimentin IHC staining, 400X).



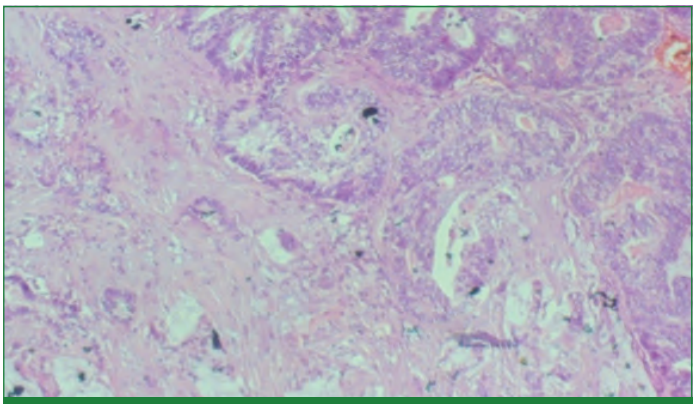
[Table/Fig-9]: Photomicrograph of pleomorphic Rhabdomyosarcoma (RMS) showing cytoplasmic stain (SMA, IHC, 400X).



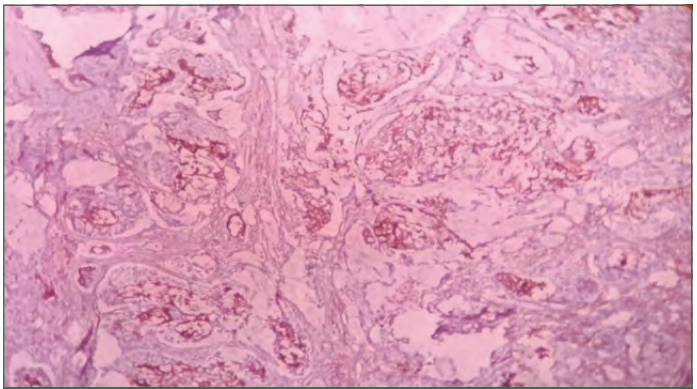
[Table/Fig-10]: Photomicrograph of Pleomorphic Rhabdomyosarcoma (RMS) showing large cells with strong cytoplasmic positivity (Desmin, IHC staining, 400X).



[Table/Fig-11]: Gross specimen of the tumour showing greyish-white area with haemorrhage.



[Table/Fig-12]: Microscopic section showing tumour cells arranged in glandular pattern, glands are lined by malignant cells and invades stroma (H&E, 100X magnification).

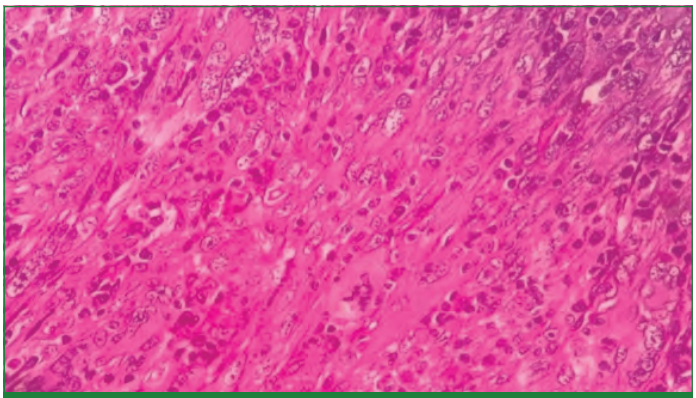


[Table/Fig-13]: Immunohistochemical staining for CK20 showing membranous positivity of malignant cells, (IHC stain, 100X).

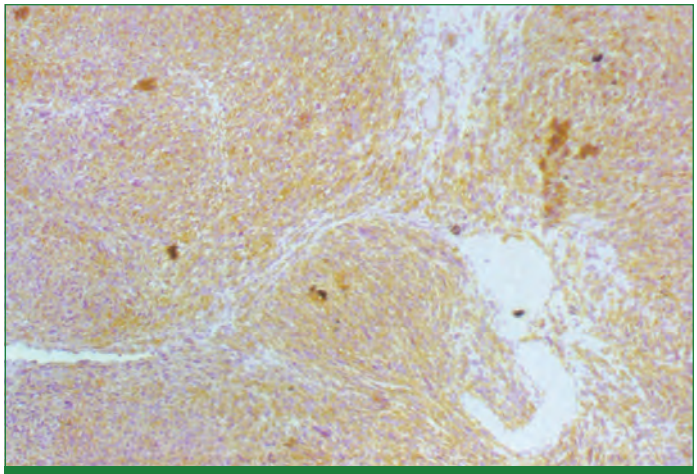
Case 5

A 60-year-old female was admitted in Medicine Department due to fever and swelling at neck region for 3 months. The swelling was located at upper part of posterior triangle of neck. It was around 5×3 cm and firm in consistency. Clinical diagnosis was tuberculosis. But FNAC revealed spindle cell neoplasm with nuclear atypia. After that patient was undergone surgery and complete resection of mass was done. Grossly, the mass was greyish white in colour, firm in consistency with irregular surface. The mass was 4.5×3 cm in dimension. Cut section had grayish colour and focal haemorrhage [Table/Fig-14]. On histopathological examination the mass was diagnosed as leiomyosarcoma as it showed spindle shaped highly pleomorphic cells arranged in intersecting fascicles. Areas of necrosis and high mitotic count were present [Table/Fig-15]. IHC studies were done to exclude differential diagnosis like malignant peripheral nerve sheath tumour, monophasic synovial sarcoma and undifferentiated pleomorphic sarcoma. Smooth Muscle Actin (SMA) was strongly positive [Table/Fig-16,17]; vimentin was positive and ki-67 was more than 20%. S100 was negative. Therefore the mass was reported as a case of leiomyosarcoma. Her postoperative period was uneventful, and she was referred to radiotherapy at a later date. She was eventually lost to follow-up.

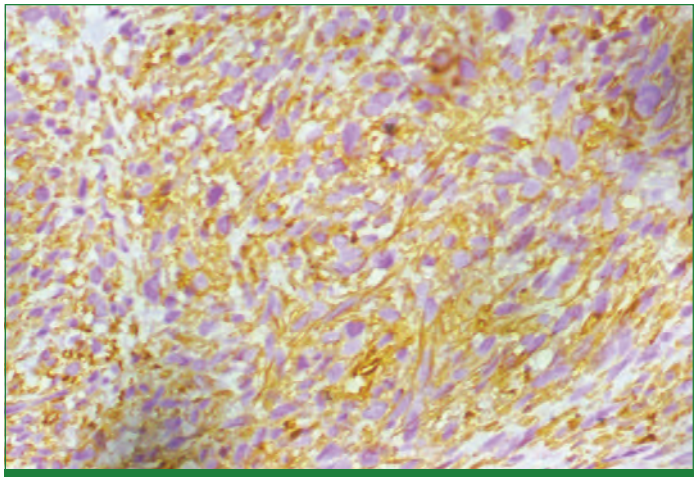
[Table/Fig-14]: Cut surface of the tumour showing greyish-white area with haemorrhagic foci.



[Table/Fig-15]: Photomicrograph of leiomyosarcoma showing spindle cells arranged in fascicles with nuclear pleomorphism and high mitotic figures (H&E, 400 X).



[Table/Fig-16]: Immunohistochemical staining for SMA showing strong positive stain of malignant cells, (IHC,200×).



[Table/Fig-17]: Immunohistochemical staining for SMA showing strong positivity in malignant cells (IHC stain, 400×).

DISCUSSION

Meningiomas are benign tumours that originate from meningothelial cells of the arachnoid. The prognosis of meningiomas is determined by the size of the tumour, its location and grade of the tumour. EM is extremely rare. Incidence of EM is 2% of all meningiomas [1]. Commonly it occurs in 5th to 7th decade of life and also in 2nd decade. EM may be associated with Neurofibromatosis type 2 (NF2) [8]. Though rare, extracranial meningiomas are well recognised in literature with some large case series without any obvious sex predilection in contrast with intracranial meningiomas which are female predominant [1]. EM are categorised in four types according to their location and extension or pathogenesis. The presented case was possibly under type C as it was arising from embryonic rest in parotid. Type C involves extracranial growth from embryonic rests of arachnoid without any apparent connection to the foramina of skull or cranial nerves. They can occur anywhere in the body [9]. EM is commonly misdiagnosed, resulting in inappropriate clinical management [10]. Extracranial meningioma in parotid gland is a diagnostic challenge due its clinical presentation and radiological study reflects parotid neoplasm. Sometimes cytology study misleads the diagnosis. Differential diagnosis of mixed parotid tumour, schwannoma, paraganglioma, other salivary adenoma and carcinoma confuse the diagnosis. So, proper histopathological examination and immunohistochemical study with EMA stain can confirm the diagnosis of EM [11].

Among soft-tissue sarcoma RMS is representing 5% of all childhood cancer. It is accounting for <1% of all malignancies and accounting for 3% of all soft-tissue sarcomas [12,13]. The most frequent site of involvement of pleomorphic RMS is the extremities and least common site is head-neck region [14]. Diagnosing RMS is difficult with histology alone. Immunostaining is one of the most important methods that can lead to a specific diagnosis [15]. Treatment of RMS is based on risk stratification at the time of diagnosis. Surgical removal of the tumour and chemotherapy or combination of both is the treatment of choice. As morphology of the present case showed spindle cells with pleomorphic features, differential diagnoses were undifferentiated carcinoma, pleomorphic sarcoma, and malignant melanoma.

The IHC for pancytokeratin, S-100 Melan-A and CD34 negativity in tumours has excluded the differential diagnoses. Pleomorphic RMS is very rare as well as aggressive sarcoma. So early diagnosis by histopathological and IHC study is crucial for improving patient prognosis. The Summary of all five cases are given in [Table/Fig-18].

S. no.	Age	Gender	Chief complaints	Duration	Investigations	Differential diagnosis	Histopathological diagnosis	IHC/Ancillary studies	Treatment	Follow-up
1.	65 years	Female	Painless swelling at parotid region	6 years	USG-Right parotid neplasm, CT brain: NAD	Benign parotid neoplasm	Meningothelial Meningioma (EM)	EMA and Progesterone - positive	Wide surgical resection	Patient is doing well
2.	16 years	Male	Nasal blockage	1 year	Not done	1. Inflammatory polyp 2.angiofibroma	Meningothelial Meningioma (EM)	EMA and Progesterone - positive	Wide surgical resection	Eventually lost to follow-up
3.	12 years	Male	Difficulty in vision, headache, proptosis	3 years	CECT- fairly large heterogeneously enhancing mass arising from right ethmoidal -frontal sinuses with mass effect pushing the right orbit and extending up to anterior cranial fossa.	1.Undifferentiated carcinoma, 2.Pleomorphic sarcoma, 3.Malignant melanoma	Pleomorphic Rhabdomyosarcoma (RMS)	Vimentin strongly positive SMA positive Large cells were Desmin positive Spindle cells and large cells negative S100 and CD34, Cytokeratin and melan-A.	Surgical resection followed by radiation therapy and chemo therapy with doxorubicin.	Patient is now under treatment of chemoradiarion.
4.	66 years	Female	Painless swelling at maxillary region	6 months	CECT scan irregular heterogenic mass involving maxillary antral cavity.	Sinonasal carcinoma	Sinonasal Adenocarcinoma (ITAC)	Strongly positive for CK20 and focal positive for CK7. CK10 and S 100 negative	Total maxillectomy followed by radiotherapy	Follow-up in radiotherapy dept every 3 months
5.	60 years	Female	Fever with swelling at neck region	3 months	Not avalilable	Soft-tissue sarcoma	Leiomyosarcoma	SMA strongly positive vimentin positive ki-67 >20%. S 100 negative	Surgical resection, refer to radiotherapy dept.	Eventually lost to follow-up

[Table/Fig-18]: Summary of all five cases.

Salivary gland tumours are infrequent lesions. They represent 6% of malignant tumours of head and neck and just 0.3% of all malignant tumours of the body [16]. The World Health Organisation (WHO) defines mucinous adenocarcinoma as a malignant tumour composed of epithelial clusters within large pools of extracellular mucin [17]. Sinonasal Adenocarcinoma (SNAC) may originate from respiratory epithelium or the underlying seromucinous glands. Histologically the tumour resembles adenocarcinoma that arises at other body location. ITAC is most common type, it localised 20% in maxillary antrum. It is thought to develop from metaplasia of sinonasal epithelium. ITAC has poor prognosis where as non ITAC has favourable outcome. High grade non ITAC and signet ring cell morphology has poor prognosis. In ITAC Epidermal Growth Factor Receptor (EGFR) mutation frequently observed [18]. Metastatic carcinomas are rare. In present case, to exclude metastatic disease, comprehensive physical and radiological (CT scan of the head, neck, chest, abdomen and pelvis) examinations were performed and no evidence of the disease was found elsewhere.

Leiomyosarcoma of soft-tissue falls into four main groups from the clinical point of view, though they share broadly the same histologic features. They are intra-abdominal leiomyosarcoma, subcutaneous or deep soft-tissue leiomyosarcomas, cutaneous leiomyosarcomas and vascular leiomyosarcomas. Most common (40-45%) leiomyosarcoma falls under intra-abdominal type. Subcutaneous or deep soft-tissue leiomyosarcomas occur 30% to 35% of cases and are found in the limbs. All types of leiomyosarcoma can metastasize. Deep soft-tissue type have 5-year survival rate of 60% to 65%. Leiomyosarcomas of the neck occur in adults and seem to arise from vascular structures as there is lack of smooth muscle in the sinonasal region [19]. Leiomyosarcoma is the malignant smooth muscle tumour accounting for only 4% of the head and neck sarcomas. This reflects the paucity of smooth muscle found in this region [20]. The majority of leiomyosarcoma of the head and neck arise in the oral cavity, superficial soft-tissues like scalp, paranasal sinuses and jaws [21]. In present case, neck is quite uncommon site for leiomyosarcoma. Higher incidence is supposed to occur among the middle age or elderly [22]. Based on a large review of leiomyosarcoma of the superficial soft-tissues, the lesions of soft-tissue origin 2.5 cm or larger are more likely malignant [23]. In this case tumour was 4.5 cm×3 cm. The differential diagnosis of this rare tumour may be problematic. The physical appearance can be deceptively benign and may be mistaken for non malignant conditions [24]. Therefore, the diagnosis was supported by histopathological examination and immunohistochemical study. Soft-tissue sarcomas of the head and neck are rare tumours. They tend to be intermediate or high grade and aggressive [25]. Considering these it is vital that the clinician be familiar with this lesion, anticipate the possible presence of this disease. As early diagnosis and aggressive initial management remains the mainstay of treatment. Further studies for early diagnosis and evaluation will improve the future management and survival of leiomyosarcoma in the head and neck.

CONCLUSION(S)

From the present case series it can be concluded that it should be kept in mind about the unusual site and presentation of meningioma, pleomorphic RMS, maxillary adenocarcinoma and leiomyosarcoma. These tumours are rare and represent a significant burden due to their unusual presentation, diagnostic dilemmas and aggressive nature. Pleomorphic RMS and leiomyosarcoma are rare high-grade sarcoma. They are very aggressive sarcoma too. Immunohistochemical study plays an important role in confirmation of the diagnosis. This study has enlightened the awareness as well as guide for future research among clinicians, radiologist and pathologist. For early and accurate diagnosis of such cases, multidisciplinary approach including clinical, radiological, histopathological and immunohistochemical study is needed for patient betterment. Early detection and treatment of such rare entities with unusual presentation will ultimately improving the overall quality of care for patients.

Authors' contributions: NB and SN contributed to the conceptualization of the study. The manuscript was written by SN and NB. Data collection was carried out by SN, AR, NB and AM.

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