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Case Report

Pathology Section

Prominent Intracytoplasmic Crystals in Alveolar Soft Part Sarcoma (ASPS): An Aid in Cytological Diagnosis

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ABSTRACT

Alveolar soft part sarcoma (ASPS) is a rare neoplasm of unknown histogenesis with poor prognosis. Due to the epithelioid appearance of the neoplastic cells, ASPS may resemble many neoplastic conditions, such as metastatic epithelial cell tumours with clear cell change, metastatic renal cell carcinoma, granular cell tumour, epithelioid sarcoma, malignant melanoma and even paragangliomas. Presence of abundant, rod like crystals in the cytoplasm of tumour cells is an important finding characteristic of this tumour, which helps in differentiating it from the other entities. The case study highlights the importance of correlating cytological features that help in reaching the diagnosis such as the background, cell morphology and presence of characteristic rod shaped crystals as immunohistochemical studies are often non-conclusive. The case also is unique as it demonstrates presence of intra-cytoplamic crystals in such abundance.

Keywords: Intracytoplasmic crystals, Alveolar soft part sarcoma, Cytology

INTRODUCTION

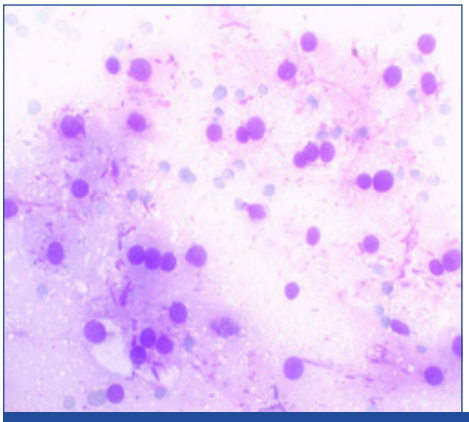
ASPS is a rare malignant soft tissue tumour that was first described and named by Christopherson and Stewart [1]. The credit for the discovery of intracytoplasmic crystals belongs to Dr. Masson, who, published a study on the ultrastructural appearance of these structures [2]. ASPS often represent a diagnostic challenge to the cytopathologist due to the presence of a number of morphological mimics.

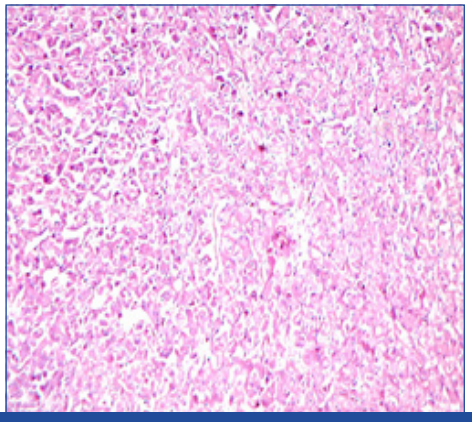
CASE REPORT

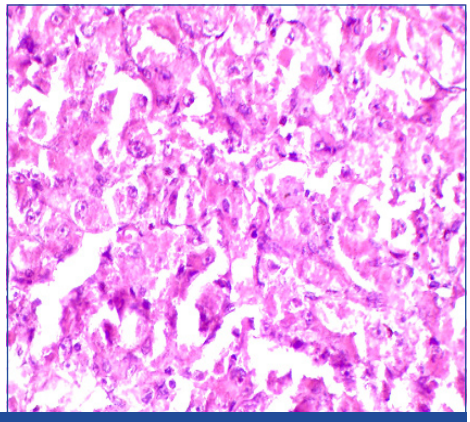
An 18-year-old female came to the surgery outpatient with complain of an ill-defined pain less swelling in the forearm for the past 4 years. The swelling had increased in size for the past 2 month. On examination a soft, ill-defined, non tender swelling 3 x 2 x 2 cm in size was palpated. The swelling was not associated with any elevation in temperature, change in colour or bruit. No regional lymph nodes were palpable. Fine needle aspiration (FNA) was planned to ascertain the nature of the swelling. The aspirates submitted for cytological examination were cellular and showed mainly singly scattered cells having round vesicular nuclei, prominent nucleoli and moderate to abundant amount of cytoplasm. Seen in the cytoplasm were large, purple rods like inclusions, forming faggot like clusters at places [Table/Fig-1]. These crystals were PAS positive. Few binucleate cells and many bare nuclei were also seen against a secretory and granular background.

Based on the age of the patient, the clinical presentation, and cytological findings, the possibility of ASPS was suggested and histopathological examination and extensive radiological work-up was advised as the ASPS is known to have pulmonary metastasizing potential and also to rule out clear cell renal cell carcinoma and other metastatic epithelial cell tumours which can present with clear cell change. The radiological work-up was primarily negative; with no lesion noted in lungs, breast, ovary, kidney or gastro-intestinal tract.

A wide excision of the swelling was done and sample was submitted for histopathological examination. The sections processed showed a pseudo alveolar arrangement of tumour cells [Table/Fig-2]. Individual cells were polygonal, with round vesicular nuclei, prominent nucleoli and abundant granular cytoplasm [Table/Fig-3]. Faint rod like crystals could be made out in some cells on Haematoxylin & Eosin (H&E) stain. The diagnosis of ASPS was confirmed. The patient was explained about the prognosis and referred to the oncology unit for radiotherapy.







[Table/Fig-1]: Intra-cytoplasmic purple rod like inclusions, forming faggot like clusters at places in the tumor cells. (MGG 400X) **[Table/Fig-2]:** Pseudo alveolar arrangements of tumor cells. (H&E 200X) **[Table/Fig-3]:** Individual polygonal tumor cells, with round vesicular nuclei, prominent nucleoli and abundant granular cytoplasm. (H&E 400X)

DISCUSSION

ASPS accounts for about 1% of all soft tissue sarcomas. Most ASPSs occur in adolescents and young adults between 15 and 35 years of age. There is a predilection for females especially during the first and second decades of life [3]. The majority of patients have metastatic disease at the time of diagnosis [4]. In adults, it most commonly involves the muscle and deep soft tissue of the extremities, trunk, head and neck, and retroperitoneum. In children and adolescents, this tumour most commonly occurs in the head and neck region [5]. Clinically, these tumours are highly aggressive, with early onset of local recurrence and distant metastases, primarily to the lungs.

Aspirates of ASPS are highly cellular, containing oval cells with eosinophilic granular cytoplasm and vesicular cytoplasm, with prominent nucleoli. Binucleated and multinucleated cells can also be present. The abundant cytoplasm is frequently disrupted during smearing, creating a secretary background. Typical crystalline material is noted within cell cytoplasm of the tumour cells [6].

The differential diagnosis on cytology include , metastatic epithelial tumours with clear cell change, metastatic renal cell carcinoma, malignant melanoma or even an epithelioid sarcoma and paragangliomas, all of which have polygonal cells with abundant cytoplasm [7]. But none of these is known to contain intracytoplasmic PAS positive rod shaped crystals in the cytoplasm. The characteristic secretory background, with numerous bare nuclei has also not been observed in any of these tumours.

It is well established that immunohistochemistry (IHC) is neither conclusive nor reliable in ASPS. The tumour cells of ASPS are non reactive to most of the IHC markers and hence IHC helps in diagnosing by exclusion. APSP tumour cells show negative expression for pan-cytokeratin (distinguishing epithelial tumours with clear cell change) and epithelial membrane antigen (distinguishing clear cell type renal cell carcinoma), S-100 protein (distinguishing giant cell tumour with clear foamy cells), S-100/HMB-45/melan-A (distinguishing melanoma and clear cell sarcoma) and neuroendocrine markers (distinguishing paraganglioma). ASPS express neuron-specific enolase and vimentin in 30-50% cases. Even the smooth and skeletal muscle markers such as actin and desmin are immunoreactive in only half of the cases- thus can not conclusively diagnose this entity. Due to these reasons the histopathology is considered diagnostic and confirmatory by most researchers [8].

Due to these reasons IHC was also not employed in the present case due to characteristic histological findings (cell morphology and presence of crystals) noted in the sections examined.

Recently much has come up in literature to explain the histogenesis of ASPS. It is now proposed that a specific unbalanced translocation, del (17) t (X: 17) (p11; p25), results in formation of ASPL-TFE3 fusion gene which causes aberrant activated transcription leading to tumorogenesis. It is thus now thought that IHC studies for TFE 3 can help in diagnosis of this entity [9].

Regarding the most unique and charachteristic finding to label a case as ASPS; the intercytopasmic PAS-positive, diastase resistant needle shaped crystals are present in only 80% of all cases of ASPS. Hence, absence of crystals does not rule out ASPS, but their presence on cytology smears is of great diagnostic importance.

It has also been demonstrated that the precrystalline cytoplasmic granules of ASPS contain monocarboxylate transporter 1 and CD147 [10]. On ultrastructure, the tumor cells have numerous mitochondria, prominent smooth endoplasmic reticulum, glycogen, and well-developed Golgi apparatus. The crystals highlighted on PAS stain have a characteristic rhomboid shape with regular lattice pattern [8].

What makes our case unique, is that, in our review of literature we have not come across any case of ASPS having rod like crystals in such abundance.

To conclude, the diagnosis of ASPS on FNAC, like other soft tissue tumours presents a formidable challenge, and the above mentioned findings may be extremely helpful to the cytopathologist.

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