

## Gross and immunohistochemical studies on undifferentiated ethmoid carcinoma in an indigenous pig

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**PRAMOD, S., N. VIJAYAN, N. D. NAIR, A. P. USHA, R. GOPALAKRISHNA, V. TIRUPATHI, C. R. LALITHAKUNJAMMA: Gross and immunohistochemical studies on undifferentiated ethmoid carcinoma in an indigenous pig. Vet. arhiv 84, 97-102, 2014.**

### ABSTRACT

An undifferentiated ethmoid carcinoma with uncommon initial stage invasion into the brain parenchyma in an indigenous pig is reported. A nodular, fleshy tumor mass, located in the posterior part of the nasal sinus adjacent to the cribriform plate and pressing on the brain, was noticed on post mortem. Rarefaction of the cribriform plate was evident. The histological picture showed sheets of cells with nuclear atypia, anaplasia and hyperchromatic nuclei infiltrating into the brain parenchyma. Upon detailed examination, the neoplasm revealed a mixture of spindle, squamous and round tumor cells. The case was diagnosed as ethmoid carcinoma of undifferentiated type, as the epithelial origin of the neoplasm was proved by immunohistochemical positivity against an anti-pancytokeratin antibody.

**Key words:** brain, indigenous pig, undifferentiated ethmoid carcinoma

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### Introduction

An ethmoid carcinoma is a malignant neoplasm arising from the mucosa lining the ethmoturbinate bone. The growth results in compression of the surrounding structures, occlusion of the nasal passages, causing progressive dyspnoea and finally death. An

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ISSN 0372-5480  
Printed in Croatia

endemic form of ethmoid tumor in cattle was reported in the Scandinavian countries at the beginning of the past century (STENSTRÖM, 1915; MAGNUSSON, 1916). Ethmoid carcinoma was first recorded in cattle in Kerala state, India in 1960 (RAJAN et al., 1972). Thereafter, an increased rate of occurrence of such cases had been noticed for the past five decades. It is reported more among crossbred cattle in Kerala and has been found to have no species barrier, as it was encountered in all species including wildlife (RAJAN, 1987). The literature dealing with such conditions in pigs, especially indigenous breeds, which are more disease resistant than exotic porcine varieties, is however very rare.

### Materials and methods

A two year old male indigenous pig, maintained in the university pig farm, was reported to manifest symptoms such as: epistaxis, respiratory distress, ataxia, staggering gait and blindness. Nervous symptoms were more pronounced. There was moderate swelling near the left periorbital area. The pig was sacrificed humanely by the electrocution (head only) method and detailed postmortem examination was conducted at the Department of Pathology of the institute. Gross examination of the carcass was done in detail, and representative tissue samples were collected in 10% neutral buffered formalin for histopathology. Sections were made at four micrometer thickness and stained by Haematoxylin and Eosin staining technique (LUNA, 1972). Immunohistochemical differentiation of the neoplasm was performed using anti-pancytokeratin and anti-vimentin antibodies (Abcam plc, Cambridge Science Park, Cambridge, England) on paraffinized tumor tissue sections (RAMOS-VARA, 2005).

### Results

Sagittal sectioning of the head revealed a soft, reddish white, nodular and fleshy tumor mass of about 5×5 cm near the turbinates, projecting into the nasal sinus. The cribriform plate of the ethmoid bone separating the sinus and brain was almost completely rarefied, and the fleshy mass was seen to be firmly adhered to the adjacent brain tissue (Fig. 1). On histopathological examination, the tumor was found to be composed of sheets of neoplastic cells, varying in shape as spindle, oval, round and squamous (Fig. 2). The cells had scanty, faintly basophilic, granular cytoplasm. The nuclei showed marked hyperchromasia, vacuolation, prominent nucleoli and chromatin. The mitotic figures and the vascularity in the tumor mass were abundant. Remnants of rarefied cribriform plate could also be observed as bony spicules in between the tumor cells (Fig. 3). The stromal reaction was scanty.

The brain parenchyma was seen to be invaded by neoplastic cells, predominantly of the spindle type. Highly pleomorphic neoplastic cells with extensive nuclear vacuolation were seen, forming emboli within the cerebral vessels (Fig. 4). Clumps of necrotic tumor

cells with severe inflammatory reaction, as evidenced by a high degree of angiogenesis and mononuclear infiltration, were also within the tumor mass. Certain areas of the neoplasm showed round, oval and occasional squamous type tumor cells. The cytoplasmic and nuclear changes in these cells were similar to that observed in the tumorous spindle cells. The stromal reaction was negligible. None of the other organs revealed any changes both morphologically and histologically. On immunohistochemical evaluation, the type cells were intensively positive against anti-pancytokeratin and gave a negative reaction to anti-vimentin antibodies.

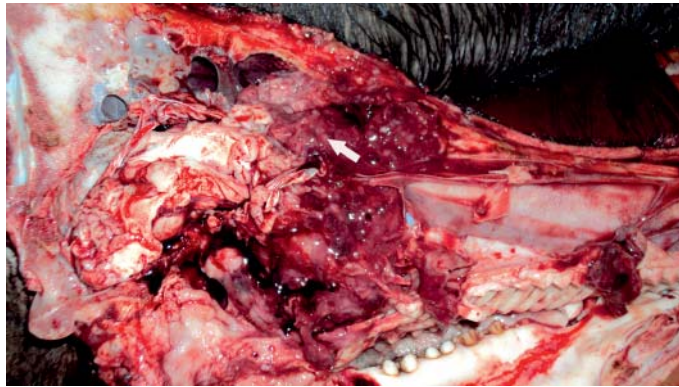


Fig. 1. Fleshy tumor mass (arrow) firmly adhering to the brain, with rarefaction of the cribriform plate

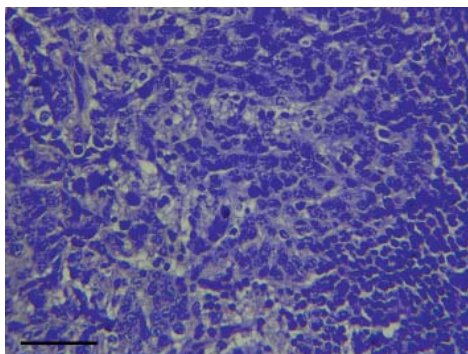


Fig. 2. Sheets of neoplastic cells varying in shape as spindle, oval, round and squamous. H&E; ×400; scale bar = 100  $\mu$ m.

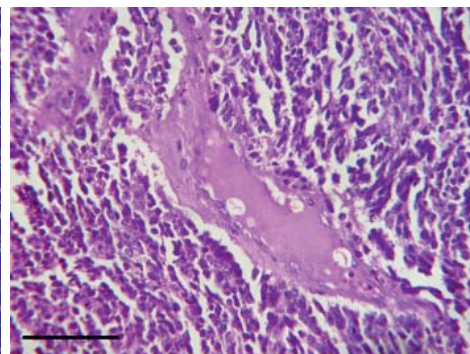


Fig. 3. Remnants of the rarified cribriform plate as bony spicules (arrow) in between the tumor cells. H&E; ×400; scale bar = 100  $\mu$ m.

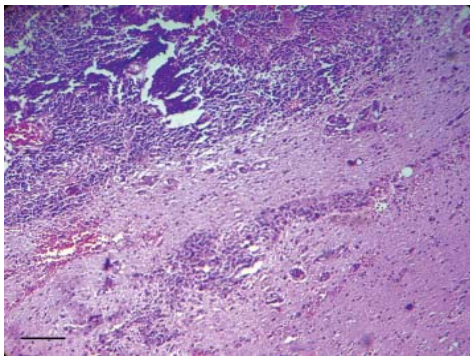


Fig. 4. Invasion of the brain parenchyma by the tumor. Pleomorphic neoplastic cells forming emboli within the cerebral vessels. H&E;  $\times 100$ ; scale bar = 200  $\mu\text{m}$ .

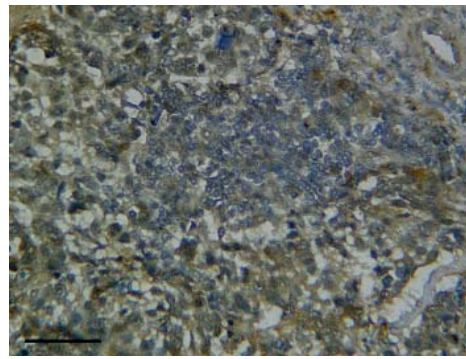


Fig. 5. Tumor cells showing strong immunohistochemical positivity to pancytokeratin. IHC - One step polymer HRPO technique;  $\times 400$ ; scale bar = 100  $\mu\text{m}$ .

### Discussion

Unlike most ethmoid tumors, which grow progressively into the sinus, this tumor infiltrated into the brain itself in the initial phase. Tumors usually only progress towards the brain in the advanced stages, after almost completely filling the nasal sinus, thereby creating severe respiratory distress and marked epistaxis. There will be protrusion of the eye ball and marked facial abnormalities, indicating the advanced stage of growth of the tumor and by this time period the brain is seen to be invaded, following rarefaction of the cribriform plate (RAJAN et al., 1972). Nervous symptoms start to be manifest at this point. However, in this case, the tumor invaded the brain very early in the phase of development, probably because of the aggressive growth pattern of the tumor. RAJAN et al. (1981) reported complete destruction of the ethmoturbinates and disappearance of the nasal septum in porcine ethmoid tumor cases. They also found that epistaxis was the most common symptom and exophthalmos was not a feature in porcine ethmoid carcinomas, unlike that of bovine. The etiology of these nasal tumors in animals remains unsolved. The rapid manifestation of the tumor is suggestive of viral involvement (RAJAN, 1987). DE LAS HERAS et al. (1991) observed budding and extracellular retrovirus-like particles ultrastructurally in enzootic intranasal tumors (EIT) in goats. However, in pigs there was a direct correlation between the incidence of the tumor and consumption of aflatoxin contaminated feed (RAJAN et al., 1981). Histologically, the site in the brain where the tumor exerted pressure showed diffuse neuronal degeneration, vacuolation, softening, gliosis and satellitosis, which accounted for the prominent nervous symptoms shown. Strong immunohistochemical positivity against anti- pancytokeratin antibodies confirmed that the type cells were of epithelial origin only (CHU et al., 2000). Cytokeratins are cytoskeletal

filament proteins specific to cells of epithelial origin. During the transformation of normal epithelial type cells into malignant cells, the cytokeratin patterns are usually maintained. (BARAK et al., 2004). The negative reaction shown against anti-vimentin antibodies excluded the possibility of any mesenchymal involvement.

### Conclusions

The cell types of the tumor were of various morphology with malignant features, without significant stromal and adenoid structure. In addition, the tumor cells gave immunohistochemical positivity against anti-pancytokeratin antibodies. Based on these histological and immunohistochemical observations, the tumor was classified as an undifferentiated ethmoid carcinoma. Sinus neoplasms are usually found in aged animals. In this case, the uncommon pattern of progression and the expression of nervous signs even after a short time strongly point to the chance of viral etiology, which is to be investigated further.

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Received: 19 October 2012  
Accepted: 30 September 2013

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**PRAMOD, S., N. VIJAYAN, N. D. NAIR, A. P. USHA, R. GOPALAKRISHNA, V. TIRUPATHI, C. R. LALITHAKUNJAMMA: Patoanatomski i imunohistokemijski nalaz neizdiferenciranog karcinoma sitaste kosti u domaće svinje - prikaz slučaja. Vet. arhiv 84, 97-102, 2014.**

**SAŽETAK**

Opisan je karcinom sitaste kosti u domaće svinje s rijetko viđenim početnim stupnjem širenja na parenhim mozga. Čvorasta, mesnata tumorska masa bila je smještena na stražnjoj strani nosnog sinusa tik uz sitastu ploču i pritiskala je na mozak. Uočena je prorijedenost sitaste ploče. Histološki je ustanovljena infiltracija moždanog parenhima sa stanicama s atipičnim, hiperkromatskim jezgrama i anaplazijom. Detaljnom pretragom dokazano je da se novotvorina sastojala od mješavine vretenastih, ljuskavih i kuglastih tumorskih stanica. Tumor je bio dijagnosticiran kao karcinom sitaste kosti neizdiferenciranog tipa s obzirom na to da je njegovo epitelno podrijetlo bilo dokazano imunohistokemijskim postupkom upotrebom antipancitokeratinskog protutijela.

**Ključne riječi:** mozak, domaća svinja, neizdiferenciran karcinom sitaste kosti

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