



NOTE

Wildlife Science

A case of nerve sheath tumor followed by multicentric high-grade T-cell lymphoma in an African pygmy hedgehog (*Atelerix albiventris*)

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ABSTRACT. A 3-year-old intact male African pygmy hedgehog was presented at the Teaching Hospital of the Faculty of Veterinary Medicine, University of Belgrade, with a growth on the left side of its abdomen. After clinical examination, the mass was surgically removed, and histopathological findings indicated a nerve sheath tumor. The hedgehog fully recovered after surgery and was euthanized eight months later due to the appearance of multicentric changes in the internal organs. Further necropsy and macroscopic, cytologic, histopathologic, and immunohistochemical findings revealed that the tumor was a multicentric high-grade T-cell lymphoma. This is an unusual case of an African pygmy hedgehog with two different neoplasms—a nerve sheath tumor followed by lymphoma.

KEYWORDS: African pygmy hedgehog, nerve sheath tumor, T-cell lymphoma

The African pygmy hedgehog (*Atelerix albiventris*) has become an increasingly popular pet in many American, Asian and European countries [16]. This has allowed clinicians to gain many insights into the health and diseases of this species. Neoplastic processes have been recognized as one of the leading causes of mortality in captive African pygmy hedgehogs [5]. A recent study conducted on 100 African pygmy hedgehogs in Japan showed that 63 had neoplastic lesions, of which 47 were classified as malignant and 16 as benign neoplasms [14]. Consequently, a better understanding of neoplastic processes, their incidence, pathophysiological behavior, and diagnostics are needed for appropriate treatment planning and prognosis assessment.

Nerve sheath tumors (NST) derive from Schwann cells or pluripotent cells of the neural crest [1]. NSTs are considered relatively rare but are reported in cattle, horses, goats, sheep, cats, and dogs [7, 17, 19]. According to the available information, 27% of canine nervous system neoplasms were NSTs, most of which occurred in the extremities or head or neck, as well as in the lungs, liver, nasal cavity and spleen [2]. However, just one case of sarcoma involving the peripheral nerve sheath has been reported in African pygmy hedgehog [12]. Lymphomas are malignant proliferation of lymphocytes and lymphoid cells. They appear as solid tumors and/or acute or chronic leukemia [15]. According to some authors, they are one of the most common tumors in hedgehogs [14].

This report describes the successful removal of nerve sheath tumor and later development of high grade lymphoma in an African pygmy hedgehog. A 3-year-old intact male African pygmy hedgehog was presented at the Teaching Hospital of the Faculty of Veterinary Medicine, University of Belgrade, with a subcutaneous mass on the lateral abdominal wall. The owners first noticed the change two weeks before they brought the hedgehog. During that time, the size of the mass had approximately doubled. The owners reported no other clinical signs. Initial physical examination revealed the presence of a subcutaneous mass that measured approximately 25 × 15 mm. The mass was firm, non-painful on palpation and didn't appear to be fused to the abdominal wall (Fig. 1A). Ultrasonography revealed that the mass was homogeneous and hyperechogenic, with well defined borders. Blood was collected from the cranial vena cava while the patient was under gas anesthesia with 3% sevoflurane (Sevoflurane Baxter, 100%, Baxter Healthcare Limited, Utrecht, the Netherlands). Complete blood count (CBC) and biochemistry were within the physiological range. Radiological examination was performed to determine the possible presence of metastases, but no visible masses were detected. Based on the clinical findings, surgical removal of the mass was recommended. Before surgery, the hedgehog was premedicated with meloxicam

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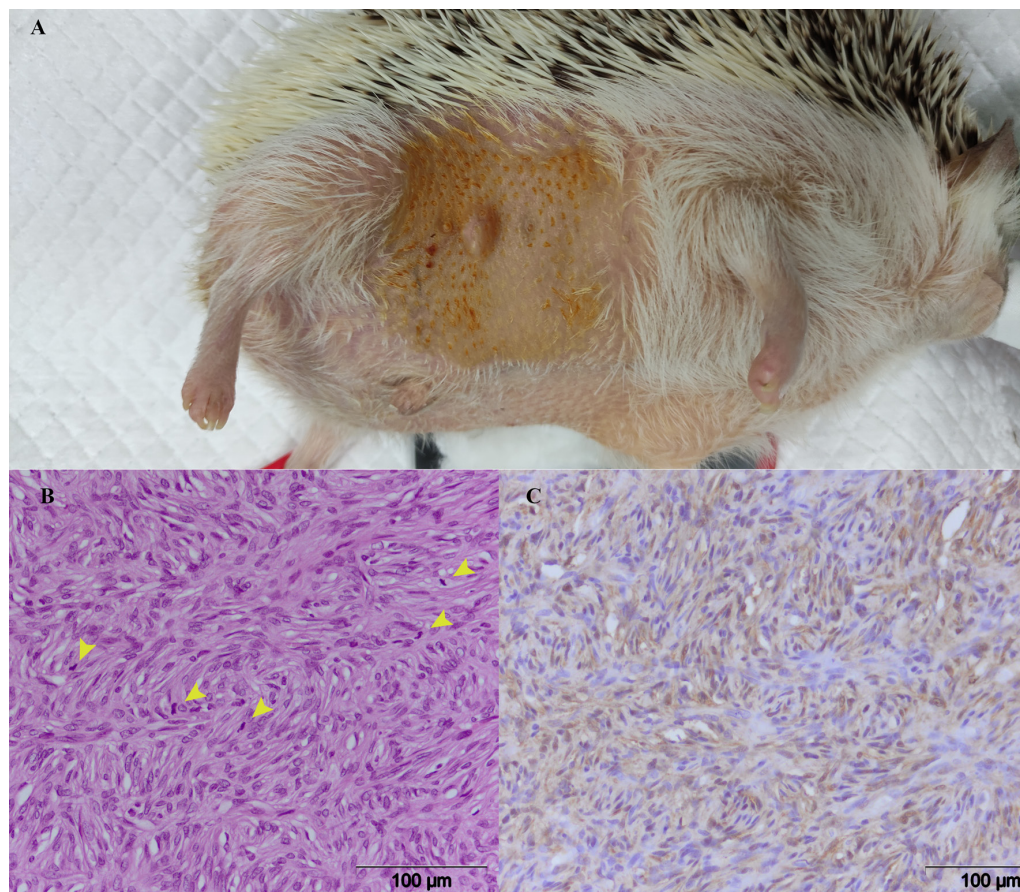


Fig. 1. Nerve sheath tumor in a pet African pigmy hedgehog. **A)** Preoperative appearance of a subcutaneous tumor mass. **B)** Representative photomicrograph showing ovoid to spindle tumor cells with nuclear pleomorphism and high mitotic activity (arrowheads). HE, $\times 400$. **C)** Tumor cells showing moderate to strong cytoplasmic and nuclear positive reaction for S 100 protein (anti-S 100, $\times 400$)

(Movalis, Boehringer Ingelheim, Ingelheim am Rhein, Germany) (0.5 mg/kg SC) and tramadol (Trodon, Hemofarm, Vršac, Serbia) (4 mg/kg SC). Anesthesia was induced with a combination of ketamine (Ketamidol, Richter Pharma AG, Wels, Austria) (5 mg/kg) and medetomidine (Domitor, Orion Pharma, Espoo, Finland) (0.1 mg/kg) and maintained with 3% sevoflurane. The mass was removed *in toto* with excision margins of at least 10 mm. After surgery, the patient received therapy with enrofloxacin (Enroxil 5%, Krka, Krka, Slovenia) (5 mg/kg SC q12 hr) and meloxicam (0.5 mg/kg SC q24 hr) for the next 10 days. In the weeks following surgery, the hedgehog recovered completely. The owners agreed that the mass should be sent for histopathological examination.

Microscopic examination revealed a subcutaneous, sharply demarcated, non-encapsulated, hypercellular mass composed of proliferated mesenchymal cells (Fig. 1B). The tumor cells were oval to spindle, with indistinct margins, a small amount of eosinophilic cytoplasm, and surrounded by a moderate amount of wavy fibrillar extracellular matrix. The nuclei were oval to elongated, pleomorphic, and euchromatic, usually without prominent nucleoli. Anisokaryosis was moderate. Tumor cells formed whorls and bundles, with occasional palisading. The mitotic count was 12 mitotic figures in 10 HPFs (2.37 mm²). The tumor cells infiltrated cutaneous muscle and surrounded muscle fibers were atrophic and dystrophic. The mass appeared completely excised with deep margins composed of adipose tissue. Necrotic changes were not observed. The immunohistochemical staining with anti-S 100 antibody (rabbit polyclonal, Z0311, Dako; Agilent Technologies, Inc., Santa Clara, CA, USA) revealed that majority of tumor cells showed moderate to strong cytoplasmic and nuclear reactivity (Fig. 1C). Based on these findings and the proposed grading system for cutaneous soft tissue sarcomas (STS) in dogs [3], the tumor was diagnosed as a high-grade nerve sheath tumor (grade 2).

Eight months later, the hedgehog was brought to the clinic due to poor general condition, loss of appetite, sudden weight loss, and hyporeactivity. Based on clinical examination and ultrasound findings, which indicated the presence of multicentric changes in visceral organs, lymphoma was suspected, and the owners decided to euthanize the animal.

Necropsy was performed shortly after euthanasia. Inspection and careful palpation revealed no new mass in the area of a previously removed tumor. The left prescapular and right axillary lymph nodes were markedly enlarged (2.5 \times 1.5 \times 1 cm and 1.5 \times 1 \times 1 cm, respectively), firm, with a bulging, homogeneous, light pink cut surface with no apparent cortex or medulla (Fig. 2A). Many other lymph nodes were prominent. The abdomen was distended and contained 3 mL of blood. A large, partially organized clot was found attached to the ruptured spleen. The spleen was enlarged, approximately 8 \times 2 \times 2 cm, friable and deformed by many nodular, confluent, grayish, soft masses that almost completely replaced the splenic parenchyma (Fig. 2B). Larger masses had necrohemorrhagic areas. A similar mass was present in the stomach, with the overlying mucosa covered with a thick, greenish pseudomembrane (Fig. 2C). The liver was slightly enlarged, light brown, with many dark red, irregular foci ranging from 1 mm to 1 cm in diameter, which were also seen on the cut section. The other pathologic findings were unremarkable.

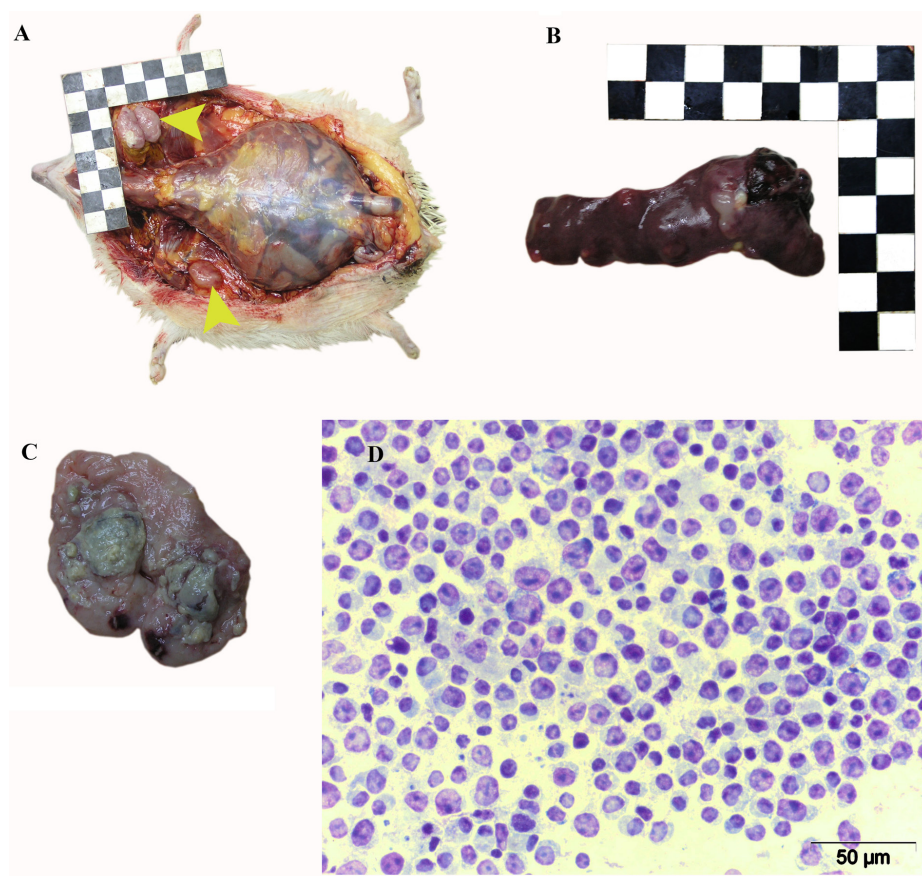


Fig. 2. Macroscopic and cytologic necropsy findings in a pet African pygmy hedgehog with multicentric T cell lymphoma. **A)** Enlarged left prescapular (cross section) and right axillary lymph nodes (arrowheads). **B)** Enlarged, deformed, nodular, ruptured spleen with partly organized clot. **C)** Stomach bulging mucosa covered with thick, greenish pseudomembranes and areas of hemorrhage. **D)** Imprint cytology microphotograph of a spleen showing pleomorphic round cell population, with many criteria of malignancy. Diff Quick, $\times 600$.

Imprint cytology of a lymph node and spleen, stained with Diff Quick (Bio-Diff kit, BioGnost, Zagreb, Croatia), revealed a population of neoplastic round cells, medium to large, with dark blue cytoplasm, and polymorphic nucleus with coarse-grained chromatin and 1–2 nucleoli (Fig. 2D). Anisokaryosis was moderate. Occasionally, a large number of eosinophils were present.

The enlarged lymph nodes, spleen, liver, and stomach samples were fixed in 10% buffered formalin, embedded in paraffin blocks, cut into 5 μm thick sections, and stained with hematoxylin and eosin. Histopathologic examination of the spleen showed indistinct, confluent nodules of intermediate to large lymphoid cells, with a small amount of pale cytoplasm and polymorphic vesicular nuclei with a distinct nucleolus. Anisokaryosis was moderate. The mitotic count was high (more than 10 per 1 high power field). Among the tumor cells were numerous tingible bodies and hemophagocytic macrophages (Fig. 3D). Among these neoplastic foci, the remaining splenic tissue contained a large number of megakaryocytes and megakaryoblasts, lymphocytes, eosinophils, and a few plasma cells. Massive necrohaemorrhagic areas were present. In the enlarged lymph nodes and stomach tissue sections, the normal parenchyma was completely effaced and replaced by neoplastic cells (Fig. 3A, 3B), sparing only a small part of the stomach's outer muscular layer (Fig. 3C). In place of the gastric mucosa was a wide linear fibrinonecrotic area. The liver parenchyma showed signs of diffuse marked macrovacuolar dystrophy, with multifocal periportal infiltration of neoplastic and inflammatory cells and a mild ductular reaction consisted of biliary hyperplasia.

Immunohistochemical staining was performed on the lymph node and gastric tissue sections using anti-CD3 antibody (mouse monoclonal, clone F7.2.7.38, Dako; Agilent Technologies, Inc.) and anti-CD 79 α antibody (mouse monoclonal, clone JCB117, Dako; Agilent Technologies, Inc.). Most tumor cells showed a strong membranous and cytoplasmic positive reaction for CD3, whereas CD79 α positive B-cells were occasionally found among neoplastic cells, especially in the lymph node section. Based on the macroscopic, cytologic, histopathologic and immunohistochemical findings, the tumor was diagnosed as multicentric high-grade T-cell lymphoma (Fig. 3E and 3F).

The occurrence of neoplastic proliferations is very common in African pygmy hedgehogs. The most prevalent neoplasm in these animals are tumors of the female reproductive organs, integumentary tissue and oral cavity. In the vast majority of cases, neoplasms in African pygmy hedgehogs were malignant [14]. Lymphomas are also commonly described in African pygmy hedgehogs [4, 18], with most being multicentric as in this case. Tumors of the nervous system were also reported in a number of case reports. According to one retrospective study on 762 individuals, tumors of the nervous tissue occurred in 1.6% of African pygmy hedgehogs [13]. Nerve sheath tumors are relatively common in dogs, uncommon in cats and rare in other species [3, 6, 9]. Nerve sheath tumors include schwannomas and neurofibromas/sarcomas which are rarely distinguished in veterinary medicine due to the lack of and overlapping specificity of available markers [6]. In the past, these tumors were described as benign and malignant, but now they are diagnosed only as NSTs with subsequent grading. The high-grade NSTs are more likely to be malignant and exhibit aggressive biological behavior [6]. Based on cellularity, nuclear pleomorphism, high mitotic count, infiltrative growth, and immunohistochemical reactivity for S-100 antigen,

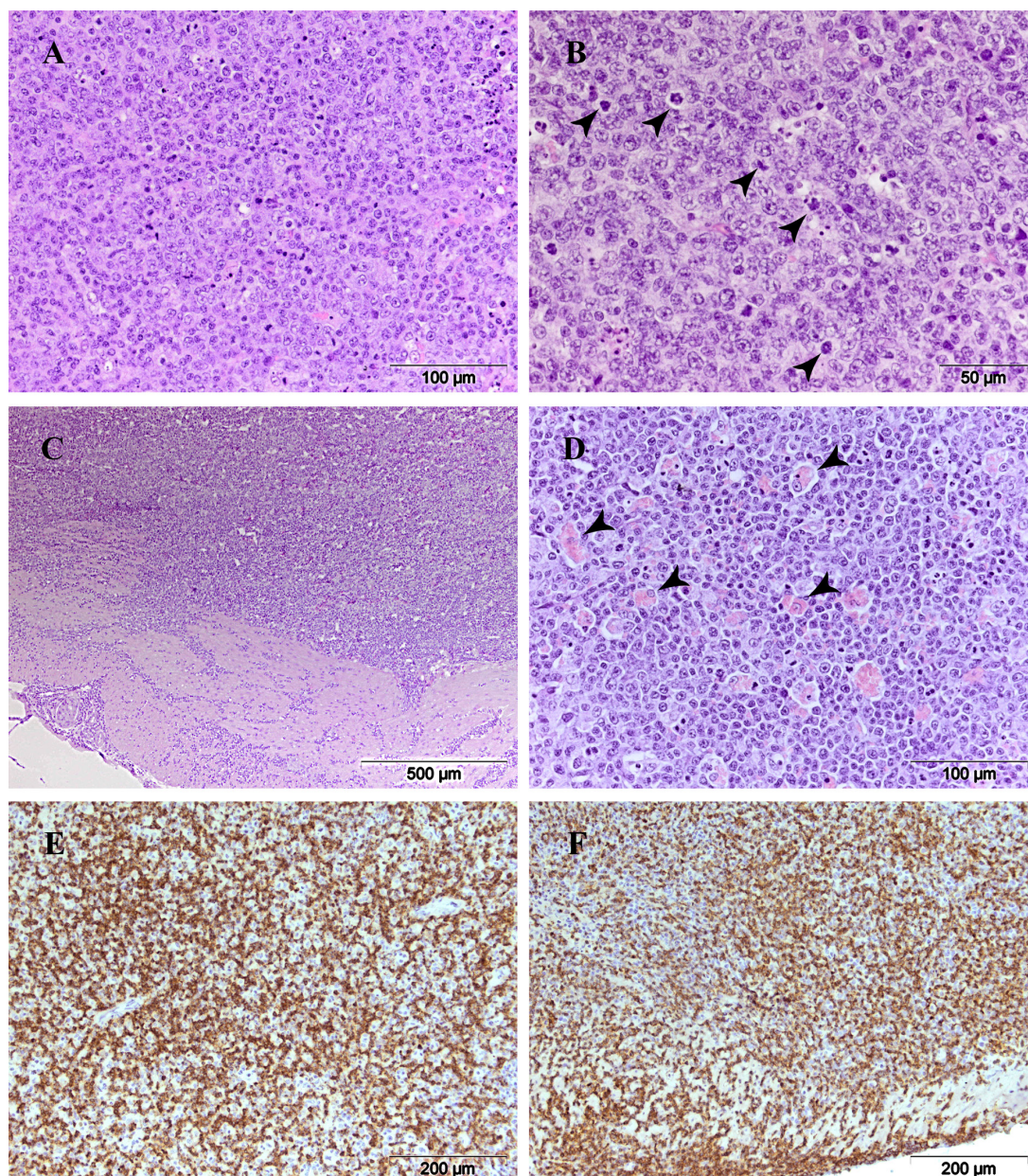


Fig. 3. Microphotographs of histopathologic and immunohistochemical findings of lymph node, stomach and spleen from an African pigmy hedgehog with a multicentric T cell lymphoma. **A)** Monomorphic population of intermediate to large lymphoid cells, with pale cytoplasm, polymorphic vesicular nuclei and high mitotic activity. Lymph node, HE, $\times 400$. **B)** Higher magnification with numerous mitotic figures (arrowheads). Lymph node, HE, $\times 600$. **C)** Tumor cells infiltrate and completely efface stomach tissue sparing only a small part of the stomach outer muscular layer. HE, $\times 100$. **D)** Presence of hemophagocytic macrophages among tumor cells (arrowheads). Spleen, HE, $\times 400$. **E, F)** Majority of tumor cells showing strong cytoplasmic and membranous positive reaction for CD3 antigen in a lymph node (E) and stomach (F) (anti-CD3, $\times 200$).

this tumor was diagnosed as high-grade NST (grade 2). In this case, after the successful removal of the neoplasm patient lived for eight months without showing signs of disease. Above mentioned suggests that tumors of the peripheral nerves are unlikely to recur in these individuals with timely detection and removal with wide surgical margins. This would be consistent with recommendations for the treatment of MPNST in humans, where complete surgical resection with wide negative margins is the current standard of care for localized high-grade MPNST and is a strong predictor of survival time [8].

Although the stomach has been mentioned as the site of the primary lymphoma [18], we believe that transmural neoplastic infiltration of the stomach was part of the multicentric lymphoma in this case. Only two lymph nodes were markedly enlarged due to the proliferation of tumor cells, while other prominent lymph nodes were reactive. Major characteristics of the spleen neoplastic proliferations were a large number of hemophagocytic macrophages as well as eosinophils. The hemophagocytosis could be part of a lymphoma-associated hemophagocytic syndrome (LAHS), a well-known entity in human medicine. LAHS is a type of secondary hemophagocytic syndrome (HPS, also known as hemophagocytic lymphohistiocytosis, HLH), which is usually associated with T-cell

or natural killer (NK)/T-cell lymphoma, and has a poor prognosis and very short survival time in humans [10]. In veterinary medicine, it has been described in dogs and a cat [20, 22, 23]. It is primarily a clinical condition, and the diagnosis, at least in dogs, is based on evidence of bicytopenia or pancytopenia in the blood and >2% of hemophagocytic macrophages in the bone marrow [20, 23]. Large numbers of megakaryoblasts and megakaryocytes in the spleen, which are usually present to some extent in this species, could indicate subacute to chronic thrombocytopenia. On the other hand, the large clot in the abdominal cavity suggests that the platelet count was sufficient. Unfortunately, we did not perform any blood test before euthanasia, so we cannot say with certainty whether this was a case of LAHS, as suggested by the histopathologic findings. Another interesting finding was a large number of eosinophils, which were almost exclusively seen in the cytological and histological preparations of the spleen. The hypereosinophilic paraneoplastic syndrome, common in mast cell tumors, has also been described in lymphomas in dogs and cats, usually in association with T-cell intestinal lymphoma [11, 21]. In this case, we believe that the presence of eosinophils was also part of the paraneoplastic syndrome.

This report describes a nerve sheath tumor, a rare type of neoplasm in an African pygmy hedgehog. In this case, the tumor was discovered and removed with wide margins before it metastasized, and the animal lived for almost another year without apparent health problems. The animal was euthanized after its condition deteriorated due to multicentric high-grade T-cell lymphoma. The presence of large numbers of hemophagocytic macrophages could be part of a LAHS that has not been previously described in this species.

CONFLICTS OF INTEREST. The authors have no conflicts of interest directly relevant to the content of this article.

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