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Ectomesenchymoma

Report of Two Cases

Cleto Cozzutto[1], Adele Comelli[2], and Roberto Bandelloni[3]
Departments of Pathology, Giannina Gaslini Institute
Children's and Women's Hospital[1]
and Ospedale Galliera[3] and the Department of Hematology-Oncology[2],
Giannina Gaslini Institute, Via 5 Maggio 39, I-16148 Genoa, Italy

Summary. Two cases of ectomesenchymoma are reported. This tumor type is defined as a form including ectodermal components represented by neuroblasts or ganglion cells and differentiated mesenchymal structures of various types. Some authors classify this tumor with the peripheral nerve neoplasms but we consider it to be a distinct neoplasm. Clinically and pathologically the tumors have no features of peripheral nerve tumors and may occur with nerves or away from them.

Key words: Soft tissue neoplasms – Peripheral nerve neoplasms – Mesenchymoma

In 1932 Masson described a peculiar peripheral nerve tumor characterized by intermingling of schwannian and rhabdomyosarcomatous features, for which the term "triton" tumor was devised. Later, it became increasingly apparent that different elements such as bone, osteoid, benign and malignant striated muscle, cartilage and gland-like structures might occur in peripheral nerve tumors (Gore 1952; McCormack et al. 1953; D'Agostino et al. 1963; Harkin and Reed 1969; Woodruff et al. 1973; Dehner 1974; Takahara et al. 1979). Most recently, Karciouglu et al. and Naka et al. reported cases which were not ascribed to a peripheral nerve origin, and contained ganglioneuroblastoma and malignant mesenchymoma components. They applied the term "malignant ectomesenchymoma" for these tumors suggesting their possible origin from remnants of migratory neural crest cells, an embryological concept of a tissue which is usually referred to as "ectomesenchyme". In a strict sense, all peripheral nerve tumors containing mesenchymal derivatives should be considered to have the same possible origin from the suggested ectomesenchyme. However, the presence of ganglion cells or neuroblasts associated to mesenchymal components impart to some tumors peculiar and unique features justifying a new definition and the term "ectomesenchy-

Offprint requests to: C. Cozzutto at the above address

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moma". We present two cases of this tumor type. The present study confirms the consistency of such concepts as "ectomesenchymoma" and "ectomesenchyme" and further suggests that this tumor type could be peculiar to children.

Material and Methods

Case 1 of the present report was extensively investigated. Twelve large samples of the tumor mass were processed for routine histology. Sections were stained with haematoxylin-eosin, Masson trichrome, phosphotungstic acid-hematoxylin, silver reticulum, PAS, Sudan III. Imprint smears were stained with May-Grünwald Giemsa, PAS, Sudan black, alpha-naphtil-esterase, acid and alkaline phosphatase. Ten specimens from different sites of the mass were processed for electron microscopy.

In regard to *case 2* only histological sections stained with H and E, PTAH and PAS were available for study.

The peroxidase-anti-peroxidase technique was used for the research of myoglobin, lysozyme, and carcinoembryonic antigen. The immunostaining packages were supplied by Immulok Inc. Carpinteria California.

Case 1

Clinical Findings

A 3-year-old asymptomatic male child was referred in 1979 to Giannina Gaslini Institute Children's and Women's Hospital after his parents noted a rapid enlargement of the right testis. Palpation revealed a hard intrascrotal extra-testicular mass connected to the epididymis. Blood chemistry, laboratory and radiological routine examinations including X-ray films of the lung and mediastinum showed no abnormality. At surgery, a 2.5 × 4 cm ovoid encapsulated mass related to the spermatic cord and epididymis was excised. Two weeks later, a laparotomy was performed for iliac and aortic lymph node dissection; the histology of which was reported negative. Following surgery, the child underwent a chemotherapeutic protocol which included Vincristin, Actinomycin D, Endoxan and Adriamycin. He is disease-free at 3 years.

Pathological Findings

The tumor mass revealed a grey-yellow mottled fasciculated cut surface. The Sudan stain showed small fat droplets in several cells; in imprint smears naphtil-alpha-estherase and acid phosphatase stains were positive in 40% of the total cell number. Histology revealed malignant tumor tissue with a fasciculated pattern and dense cellularity alternating with intensely oedematous areas. In some places, the streaming fascicles of plump spindle cells acquired a slight storiform pattern (Fig. 1); cellular atypia and pleomorphism were marked and mitoses were numerous. The majority of the cell elements were spindle shaped with ovoid hyperchromatic nuclei and bipolar cytoplasmatic elongations. Numerous cells had a more histiocyte-like appearance consisting in round pleomorphic nuclei and ample sharply outlined cell boundaries; in these cells the cytoplasm was eosinophilic and vacuolated (Fig. 2). While in some areas the general appearance of the tumor tissue suggested a fibrohistiocytoma-like differentiation, in others it acquired characteristics similar to a leiomyoma (Fig. 3). The most remarkable finding

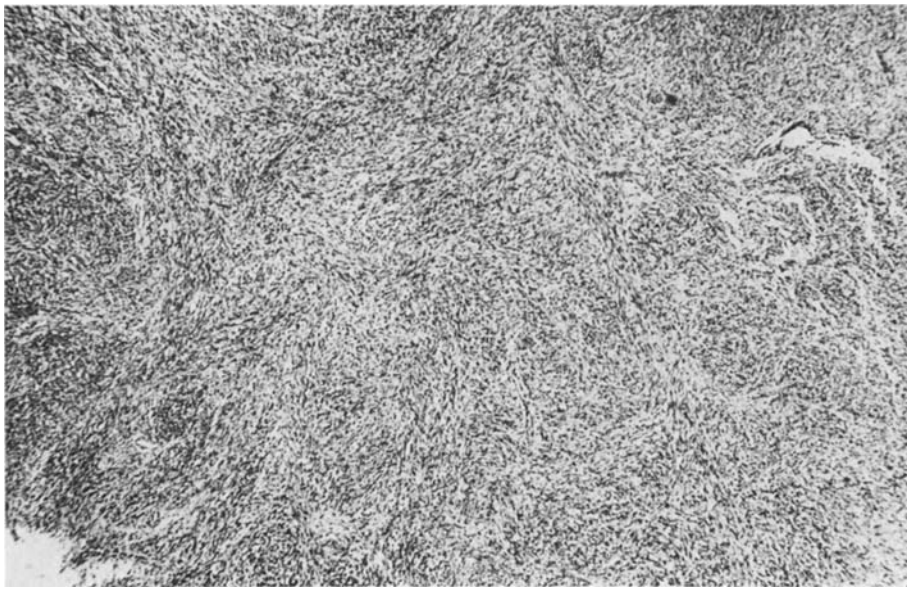

Fig. 1. Case 1. Low-power view of the tumor tissue showing fasciculated tumor tissue and slight suggestion of storiform pattern (H&E, ×40)

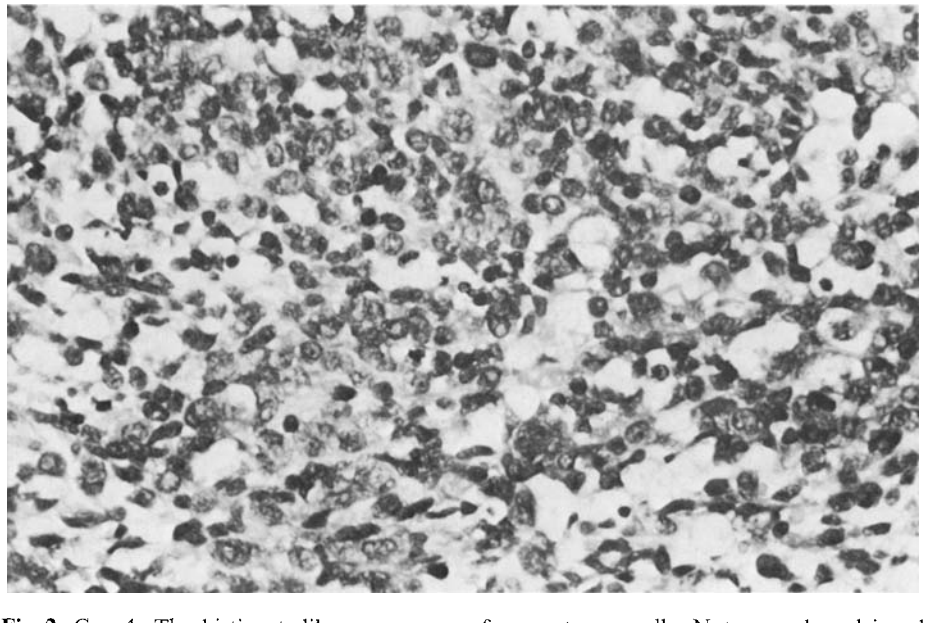

Fig. 2. Case 1. The histiocyte-like appearance of many tumor cells. Note round nuclei and abundant vacuolated cytoplasm (H&E, ×400)

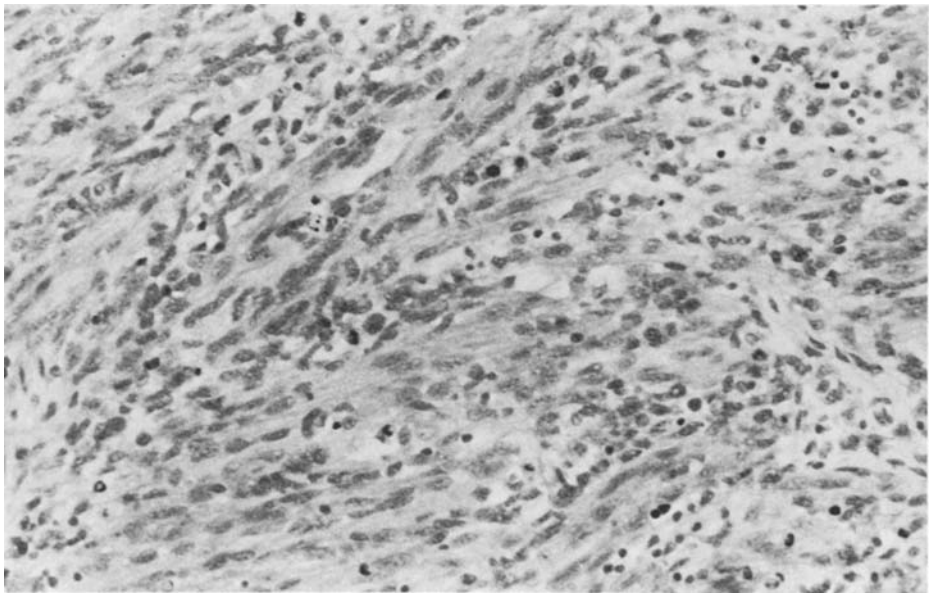

Fig. 3. Case 1. A focus of spindle-cell fascicles with a leiomyomatous pattern. Note thin longitudinal fibrils (H&E, × 150)

was represented by numerous mature ganglion cells which were clustered or randomly scattered inside the sarcomatous tissue (Fig. 4). In these cells, round nuclei, large nucleoli, Nissl substance and amphicytes were easily recognized (Fig. 5); frequently they contained huge pink hyaline or clear inclusions which displaced the nucleus. Some of these ganglion cells had a pleomorphic and bizarre or immature appearance (Fig. 6). The cells of the sarcomatous tissue acquired at times a distinct rhabdomyoblastic differentiation, exemplified by distinct eosinophilic cytoplasmatic strips, whereas in other areas they assumed a more histiocyte-like appearance with numerous vacuoles. In those foci where smooth muscle differentiation became apparent, thin cytoplasmatic longitudinal fibrils were seen.

Numerous pleomorphic cell elements had intermediate features between large rhabdomyoblast-like cells and ganglion cells (Fig. 7). The immunostaining procedures did not provide consistent additonal data.

Ultrastructural Study

The ultrastructural study of the tumor tissue revealed numerous fibroblast-like cells with pleomorphic indented nuclei and fairly abundant cytoplasm consisting of rough endoplasmic reticulum cisternae, mitochondria and ribosomes. Numerous spindle-cells were identified as myofibroblasts by foci of longitudinal myofibrils.

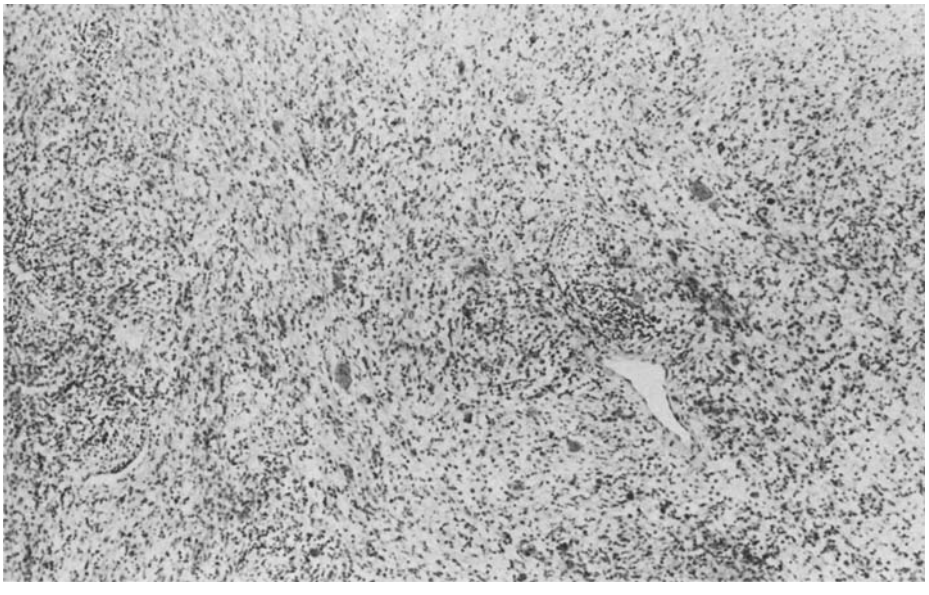

Fig. 4. Case 1. Oedematous cellular tissue with several scattered ganglion cells (H&E, ×100).

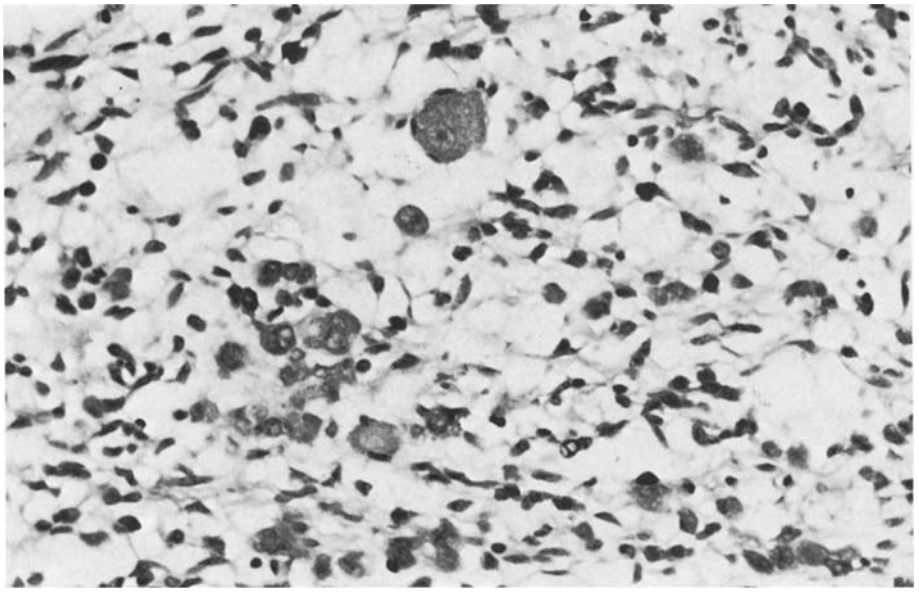

Fig. 5. Case 1. A fully mature ganglion cell (upper) and a less mature form (bottom). Note tigroid substance, satellite cells, and large nuclei and nucleoli (H&E, ×400)

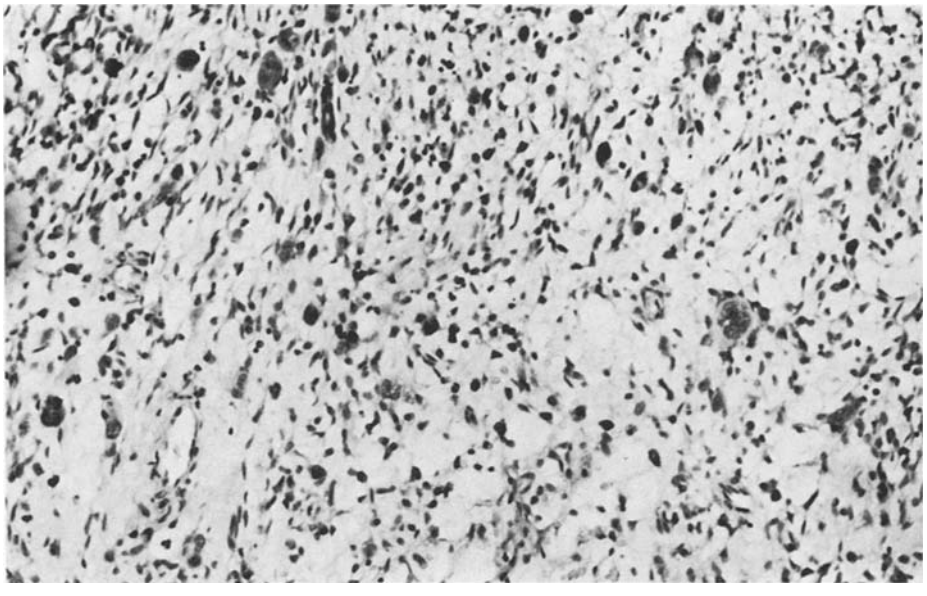

Fig. 6. Several abnormal and pleomorphic ganglion cells are seen (H&E, ×150)

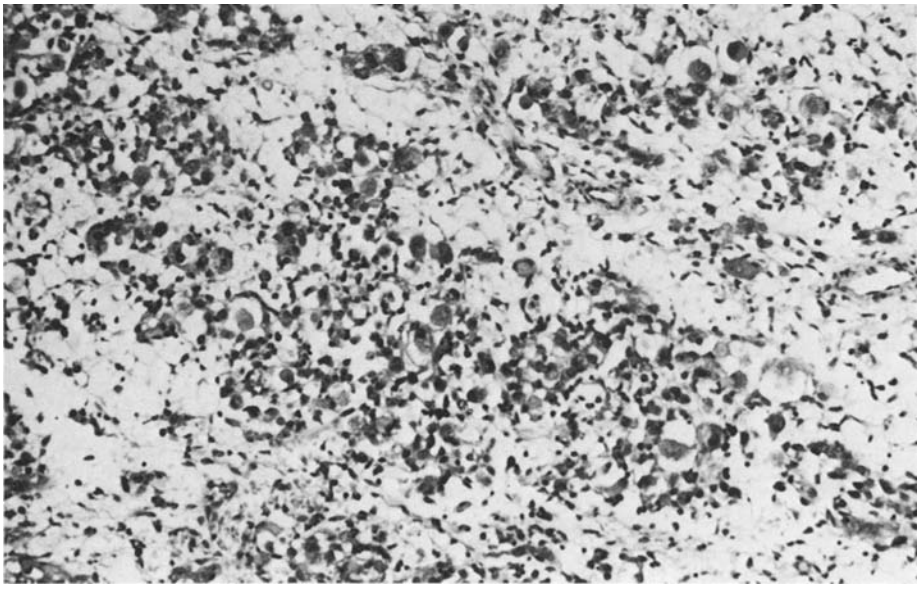

Fig. 7. Case 1. A cluster of cell forms with intermediate features between rhabdomyoblasts and immature ganglion cells (H&E, ×150)

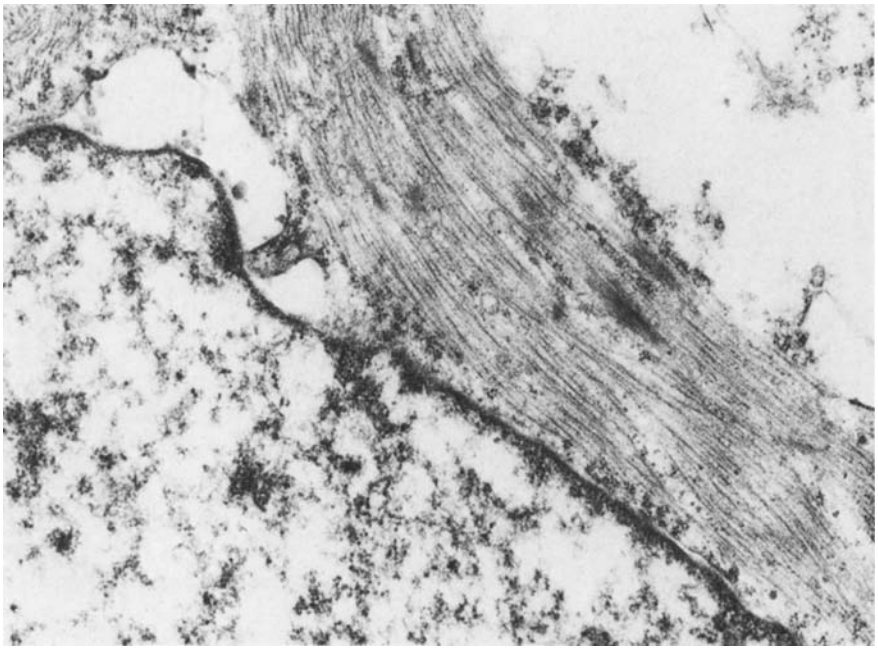

Fig. 8. Case 1. Microphotograph of a tumor cell showing longitudinal fibrils with focal densities suggesting smooth cell differentiation (× 15,000)

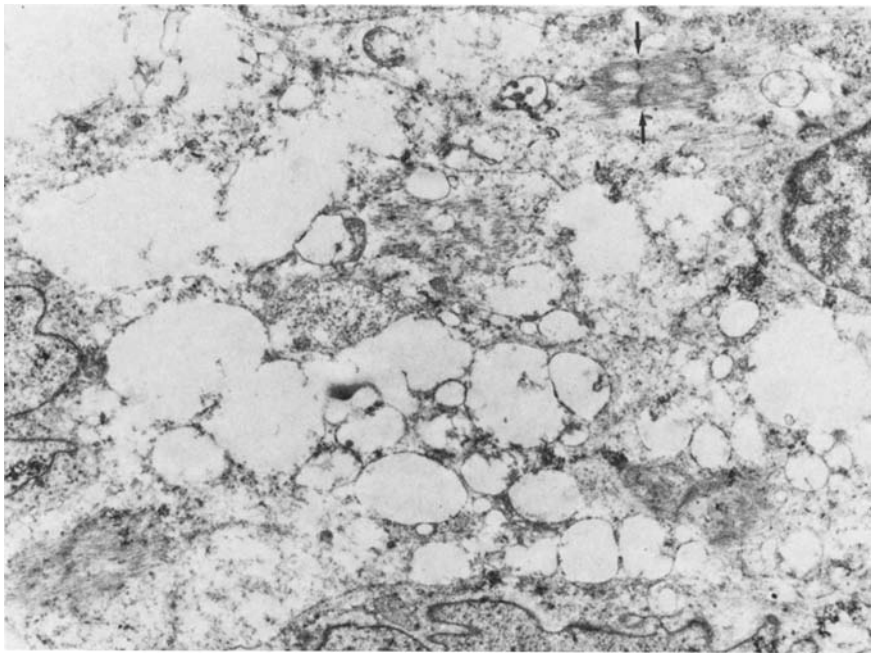

Fig. 9. Case 1. Another tumor cell showing numerous vacuoles and longitudinal myofibrils with Z band striations demonstrative of rhabdomyoblastic differentiation (upper right corner, *arrows,* × 4,500)

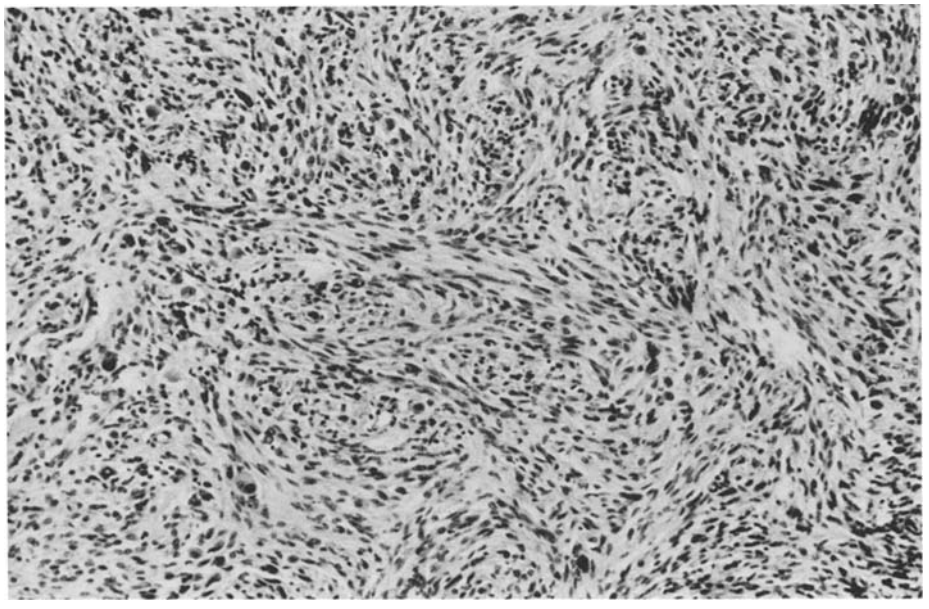

Fig. 10. Case 2. The markedly fasciculated tumor stroma with storiform pattern (H&E, ×150)

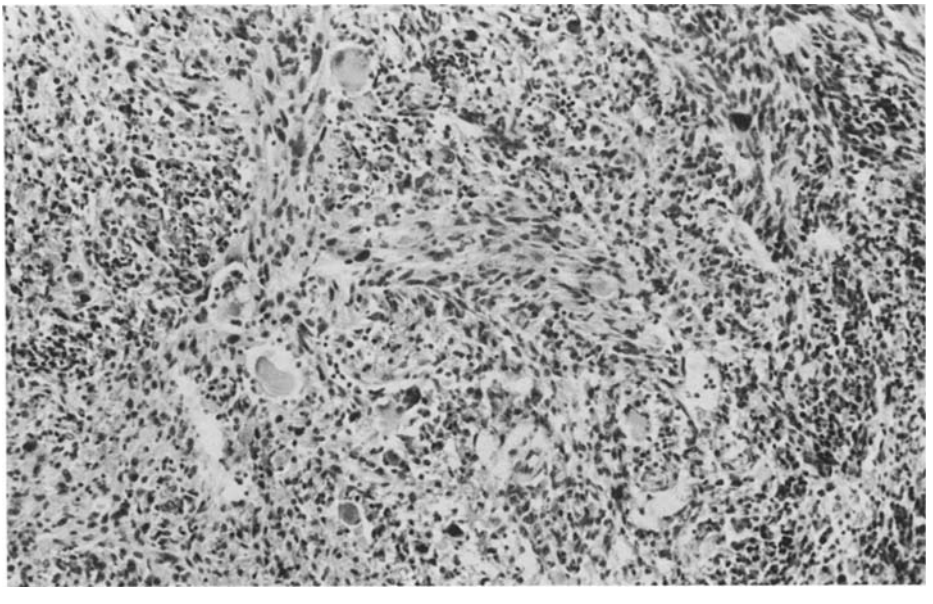

Fig. 11. Case 2. Numerous immature and mature ganglion cells are scattered inside the tumor stroma (H&E, ×150)

In several cells abundant longitudinal myofibrils with focal densities characteristic of smooth muscle differentiation were seen (Fig. 8), whereas in other cells myofibrils with band striations revealed a distinct rhabdomyoblastic differentiation (Fig. 9). In numerous cells the cytoplasm was ample and contained large clear vacuoles; in others, abundant thin cytoplasmatic filaments were haphazardly developed in a watery matrix. Cytoplasmic organelles including RER cisternae, mitochondria, ribosomes and scattered lysosomes were numerous in every cell type. Basal lamina tracts and junctional complexes were sporadically observed.

The overall impression gained after prolonged observation was that of a cellular progression from primitive and activated fibroblasts to myofibroblasts, to muscle cells, and finally to undetermined large and pleomorphic epithelioid cells rich in cytoplasmatic vesicles, organelles and filaments.

The latter corresponded to those cell elements histologically singled out as histiocytes, rhabdmyoblasts or immature ganglion cells.

The mature ganglion cells had usual ultrastructural features. Some scattered cells had ultrastructural characteristics of histiocytes.

Case 2

This case can only be evaluated on a histological basis. It showed the same architectural pattern of case 1, exemplified by a dense and fasciculated spindle-cell stroma (Fig. 10), numerous epitheliomorphic cells and ganglion cells, and indefinite elements with intermediate features between the two latter types (Fig. 11). In this case cellular atypia was moderate and mitosis absent. A slight storiform pattern was also noted in some foci (Fig. 10). The tumor was defined as an atypical ectomesenchymoma.

The diagnosis of cerebral gangliocytoma was ruled out because the PTAH stain did not reveal glial fibers. The presence of a dense spindle-cell stroma in cerebral gangliocytoma is very unusual.

A stroma of this type is undoubtly of mesenchymal derivation and its association to ganglion cells justifies the definition of ectomesenchymoma.

Discussion

The concept of *ectomesenchyme* is based on the assumption that some mesenchymal structures of the head and neck are derived from the neural crest (Naka et al. 1975; Karcioglu et al. 1977). For instance, the cartilage of the visceral arches and the dentine are derived from the ectoderm. This hypothetical origin can explain the coexistence in some rare tumors of both ectoderm and mesoderm derivatives. Hence the term "ectomesenchymoma" (Hörstadius 1969; Naka et al. 1975; Karcioglu et al. 1977).

Specifically, the ganglion cells result from the development of neuroblasts and glioblasts, thus they are of ectodermal origin (Williams and Warwick 1980). The glioblasts further develop into Schwann cells and satellite cells which tightly surround the ganglion cell body. Conversely, all the connective and sclerous tissue and the entire skeletal and visceral musculature with exclusion of the iris muscle are of mesodermal derivation (Williams

and Warwick 1980). Some authors include the ectomesenchymoma within the erratical variants of malignant schwannoma (Haidu 1979). We do not agree with this assumption for the following reasons.

The two cases of ectomesenchymoma reported by Karcioglu et al. and by Naka et al. were remarkable for the presence of neuroblasts and ganglion cells in addition to mesenchymal derivatives. The presence of mature ganglion cells is extremely unusual in malignant schwannoma. We were unable to identify any single report of this occurrence, whereas epitheliomorphic cell elements are not an unusual finding. If Schwann cell differentiation and other typical findings of peripheral nerve tumors are lacking as in the cases reported herein, it is difficult to recognize these tumors as variants of schwannoma. Therefore, for diagnostic purposes the term "ectomesenchymoma" is justifiable.

On the other hand, the not infrequent occurrence of mesodermal structures in malignant schwannoma would imply that this tumor should also be regarded as an "ectomesenchymoma". It is also interesting that the first of the presently described cases was located in an anatomical site which is extremely unusual for malignant schwannoma, whereas in that location ectopic adrenal tissue is a common finding in children. The adrenal gland is an organ of combined mesodermal and ectodermal derivation.

It is difficult to regard the second case as a malignant schwannoma because of its cerebral location.

In conclusion, the term "ectomesenchymoma" should be applied to those tumors which do not originate from a major nerve trunk, do not have typical histological features of malignant schwannoma, and are represented by a mixture of neuroblasts or ganglion cells and mesodermal components. The cases reported by Karcioglu et al. and by Naka et al. and our two cases were found in children. Therefore it can be reasonably suggested that this tumor type is peculiar to children. The differential diagnosis must include the so-called polyhistioma; a malignant mesenchymal tumor whose basic proliferative element is a small round undifferentiated cell which progresses to cartilagineous and osseous but not muscular metaplasia.

An important observation in the present study is the *apparent progressive transition from myoblastic cell elements to immature ganglion cells,* and their seeming common origin, a finding which is important in establishing a kinship relation between mesodermal and ectodermal cells, and in giving further confirmation to the concept of ectomesenchyme. The real neoplastic nature of the ganglion cell component is demonstrated by the appearance of numerous immature and pleomorphic forms. The presence of transition forms between mesenchymal and ectodermal cell lines in peripheral nerve malignant tumors has been noted by Woodruff et al. (1973).

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