CASE REPORT

Juvenile hemangioma: A case report with an emphasis on its clinical phases (evolution and involution), and immunohistochemically distinctive physiologic differences

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ABSTRACT

Hemangiomas occupy a grey zone between hamartomatous malformations and true neoplasms. They are frequently designated and regarded as neoplasms because of their usually localized nature and mass effect. Although clearly benign, they can become very large and unsightly, and can even be fatal if they affect vital structures. They almost never become malignant, although a few documented examples of this complication are on record. A high percentage occur in children, manifesting within the first month of life. One half of these cases are in the head and neck area. Hemangiomas have been classified according to their clinical appearance and the caliber of vessel involved, namely, capillary, cavernous and venous. Capillary hemangiomas are made up of small vessels of capillary caliber. One such capillary hemangioma, the juvenile hemangioma (JH), is usually present at birth or appears during the first month and enlarges rapidly during the first few months of life (infancy), only to stop growing when the child is approximately 6 years old. We present one such JH, seen in a 3 year old male child, which appeared when the child was 2 months old. Routine histopathological (H and E) and immunohistochemical analysis (CD 34, CD 31) was done on biopsy received.

Key words: Capillary hemangioma, infancy, juvenile hemangioma

INTRODUCTION

The juvenile hemangioma (JH) is a form of capillary hemangioma which occurs during infancy at a rate of about 1 in every 200 live births. During the early stage it may resemble a common birthmark in that it is a flat, red lesion that intensifies in color when the infant strains or cries. With time it acquires an elevated, protruding appearance that distinguishes it from birthmarks and has earned it the fanciful designation of "strawberry nevus". Deeply situated lesions impart little color to the overlying skin and consequently may be misdiagnosed preoperatively. These tumors may be located on any body surface but are most common in the region of head and neck, particularly parotid, where they seemingly follow the distribution of cutaneous nerves and arteries. The evolution of these lesions is characteristic. Although described as congenital they actually appear within few weeks after birth and rapidly enlarge over a period of several months, achieving the largest size in about 6-12 months, after which they regress over a period of a few years. Regression is usually accompanied by fading of the lesion from scarlet to dull red-gray and by concomitant wrinkling of the once-taut skin. It has been estimated that by age 7 years, 75-90% have involuted, leaving a small pigmented scar. In the lesions that have ulcerated the cosmetic defect may be more significant.[1]

Histologically, the tumor varies with its age. Early lesions are characterized by plump endothelial cells that line vascular spaces with small inconspicuous lumens. Mitotic figures may be present in moderate numbers. Mast cells and factor-VIII – positive interstitial cells are a consistent feature of these tumors. The former may be important in the production of angiogenic factors that regulate the growth of these tumors. At this early stage of development the vascular nature of the tumor may not be readily apparent unless a reticulin preparation is done that demonstrates connective tissue fibers encircling myriad tiny vessels. As the lesions mature and blood flow through the lesion commences, the endothelium becomes flattened and resembles that seen in adult forms of capillary hemangioma. Maturation usually begins at the periphery of the tumors but ultimately

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involves all zones. Regression of the JH is accompanied by a progressive, diffused interstitial fibrosis and is believed to be mediated by way of apoptosis. In unusual cases, infarction of the tumor may occur, due to thrombosis.[2]

CASE REPORT

A 3 year old male child was referred to the Department of Oral and Maxillofacial Surgery at NIMS Dental College, Jaipur, Rajasthan, due to a painless, dome-shaped lesion of the upper lip, extending upto the cheek on the right side, light red in color, measuring 2 × 4 cm, present since 20 days after birth, when it first appeared. Parents revealed that the lesion would change color to a deep red when the child cried. On intraoral examination there was no ulceration seen. The child did not suffer from any medical problems. The lesion, firm on palpation, was excised under local anesthesia, and the specimen was sent to the Department of Oral Pathology, NIMS Dental College, Jaipur, Rajasthan, for histopathological evaluation. The specimen was fixed in 10% formalin and subsequently embedded in paraffin. Five micrometer sections were made for staining with H and E and 3-µm sections were made for immunohistochemical analysis for the traditional markers CD 34 and CD 31. The immunohistochemical analysis was performed in the Department of Histopathology at Santokba Durlabhji Memorial Hospital, Jaipur, Rajasthan.

Gross features

The tissue received after excisional biopsy had a wrinkled surface [Figure 1] and revealed a cream colored, gelatinous cut surface [Figure 2]. The gross tissue appears small due to decrease in size after compression of the lesion to drain out the blood during and after performing excisional biopsy procedure.

Histopathological features

Sections stained with H and E were observed under ×4, ×10 and ×40 to reveal normal epithelium, under which was a band of normal connective tissue. The lesional area commenced immediately after [Figure 3]. The lesional area revealed lobules separated by thin strands of normal connective tissue. The lobules contained plump endothelial cells lining vascular spaces with inconspicuous lumens [Figure 4]. Lobules also contained central feeding vessels. Some areas were more solid and organized containing a proliferation of endothelial cells [Figure 5]. On the basis of clinical and histopathological features, a diagnosis of JH was made.

Immunohistochemistry

The sections were positive for CD 34 [Figure 6] and CD 31 [Figure 7], which confirmed the diagnosis of our lesion which was in its proliferating phase in most regions of the neoplasm and involuting in a few areas.

DISCUSSION

In our case the clinical and histopathological features suggest that the lesion was in the proliferating and involuting phase. The solid areas gave a clear indication that the lesion was a long-standing one.

The clinical phases of JH have distinctive underlying physiological differences, which have been correlated with equally distinctive immunophenotypic profiles by Takahashi *et al*.[3] During the early proliferative phase (0-12 months) the tumors can be shown immunohistochemically to express proliferating cell nuclear antigen (PCNA), vascular endothelial growth factor (VEGF), and type IV collagenase, the former two localized to both endothelium and pericytes, and the last to endothelium. All of these substances are associated with proliferation and growth of vessels. During the involuting phase (1-5 years) these are dramatically reduced, whereas the tissue inhibitors of metalloproteinases (TIMP), anti-angiogenic factors, are markedly elevated. The traditional vascular markers CD 31, von Willebrand factor (vWF), and smooth muscle actin (pericyte marker) are present during the proliferating and involuting phases, but are lost after the lesion is fully involuted.[3]

JH also expresses GLUT1, a glucose transport receptor, the expression of which is independent of proliferative activity, and is not found in other forms of hemangiomas although it is present rarely in angiosarcomas. This protein is also expressed by human placenta and has led to the novel hypothesis that the proliferative component of JH may be derived from embolized placental vascular cells.[4]

CONCLUSIONS

Neonatal and infantile hemangiomas grow rapidly initially, but the majority spontaneously involute by age 7 years. Surgical excision during the proliferative phase should be avoided due to risk of major blood loss and injury to facial nerve.[5] Diagnosis may be made by aspiration cytology and conservative nonoperative management includes steroids to reduce growth, compression therapy, or embolization. No treatment may be required, however, a small percentage of hemangiomas present themselves with indications for prompt therapy (including surgical excision), such as severe disfigurement, airway compromise, excessive bleeding, and ophthalmological complication.[6,7]

The patient was examined after 2 months. Healing was normal, but scarring was observed. The lesion seemed to have regressed on subsequent recalls.

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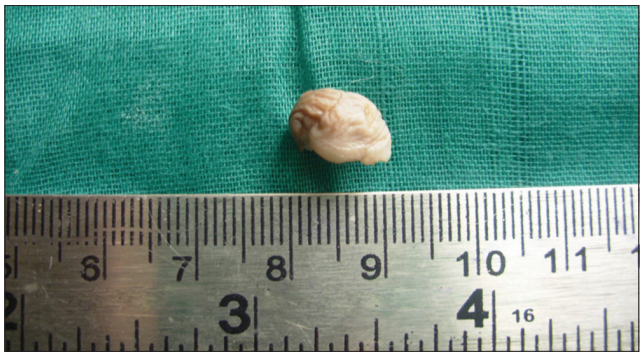

Figure 1: Wrinkled surface of excised lesion

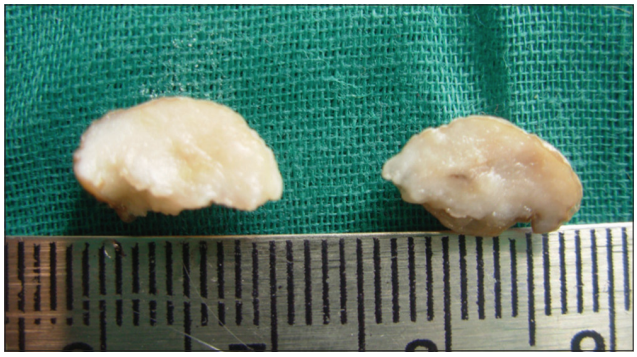

Figure 2: Cream-colored gelatinous cut surface

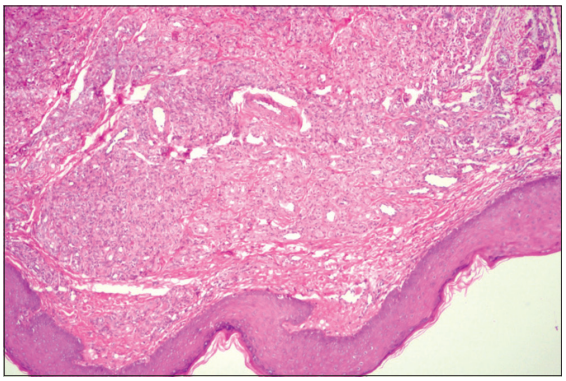

Figure 3: Lesional area showing lobules below normal epithelium and connective tissue (H and E, 4×)

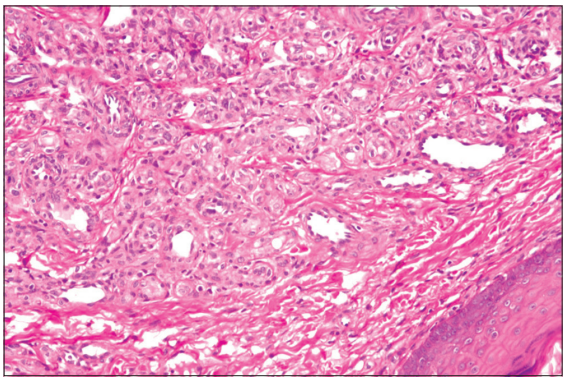

Figure 4: Plump endothelial cells lining vascular spaces with inconspicuous lumens (H and E, 10×)

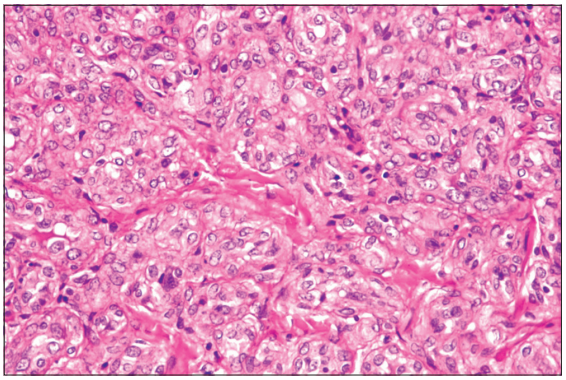

Figure 5: Solid areas containing proliferation of endothelial cells (H and E, 40×)

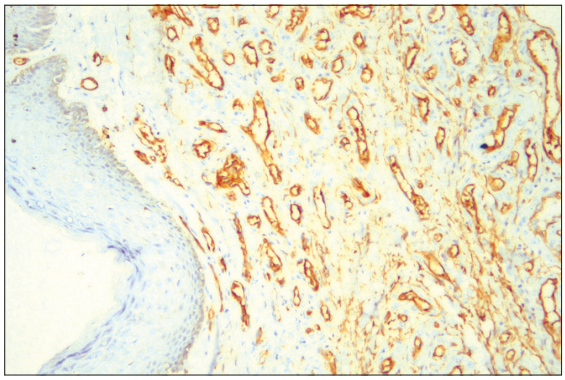

Figure 6: CD 34 expression in lesional areas (10×)

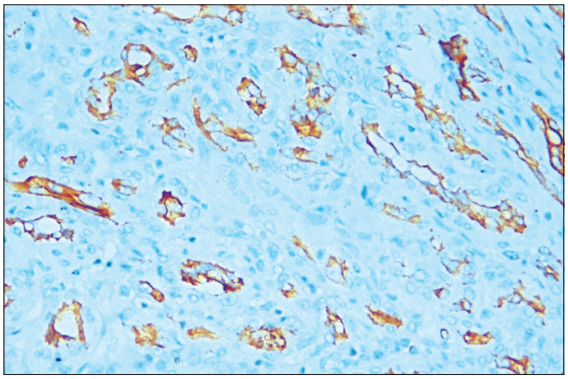

Figure 7: CD 31 expression in lesional areas (40×)

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